Executive Committee: DOS 2017-2019

DOS Office Bearers

Prof. Kamlesh
President

Dr. Sudarshan Kumar Kholkar
Vice President

Dr. Subhash C. Dadeda
Secretary

Dr. Arun Baweja
Treasurer

Dr. Manav Deep Singh
Joint Secretary

Dr. Bhavna Chawla
Editor

Dr. Jatinder Singh Bhailla
Library Officer

Executive Members

Dr. Radhika Tandon
Dr. Hardeep Singh
Dr. Alkesh Chaudhary
Dr. Nigandor Vashiht

Dr. Vinod Kumar
Dr. Sandhya Mahija
Dr. Pawan Goyal
Dr. M.C. Agarwal

Ex-Officio Members

Dr. Rishi Mohan
Ex-President

Dr. M. Vanathi
Ex-Treasurer

Sincere thanks to all DOS Office Staff

Office Secretary: Parveen Kumar • DOS Accountant: Sandeep Kumar • DOS Times Assistant: Sunil Kumar
DJO Assistant: Varun Kumar • Library Attendant: Niyaj Ahmad • Office Attendant: Harshpal
Dear Colleagues,

We once again bring out for you another sub-speciality issue of the DOS Times. Glaucoma is a widely prevalent and under diagnosed disease in our country. According to NPCB survey; glaucoma is responsible for 5.8% of the total blindness in the country. It’s a disease which needs increased awareness and early detection. With this issue we aim to spread not only knowledge about this disease, but also increase awareness that we should take upon ourselves this daunting task of early diagnosis and management of glaucoma.

This issue covers a lot of important topics. We have compiled an exhaustive discussion on steroid induced glaucoma. Also listed are extensive reviews on topics like ocular blood flow and bleb morphology which we do not read in finer details in our everyday post graduate text books. Newer perspectives on tools for checking medication compliance and anti VEGFs in Glaucoma are also highlighted. India being a developing country faces issues of compliance amongst patients and standardisation of protocols amongst surgeons; we also present certain articles in the Indian scenario.

The amalgum of case reports and photo essays make the DOS Times an interesting and informative read. We hope that this issue also serves as a collection of articles to be kept and quoted for years.

Sincerely yours,

Dr. (Prof.) Subhash C. Dadeya
Secretary - Delhi Ophthalmological Society
Room No 205, 2nd Floor, OPD Block,
Guru Nanak Eye Centre, Maharaja Ranjit Singh Marg,
New Delhi - 110002
Email: dadeyass@gmail.com, dadeya868@gmail.com
Mobile: 9968604336, 9810575899
WhatsApp: 8448871622
Dr. Mahipal Singh Sachdev, born on 17 July 1958, did his schooling from Delhi. Having an unwavering determination to choose the noble profession of medicine, he was selected for MBBS at AIIMS. This foundation put Dr Mahipal on the trajectory to medical excellence, MBBS being followed up by topping in MD in 1984, again from RP Centre for Ophthalmic Sciences, AIIMS. Thereafter he took on faculty positions in his alma mater, serving as Assistant Professor (1987-91) and then Associate Professor (1991-96). In the interim, he ensured acquaintance with the latest advancements in Ophthalmology completing his Fellowship in Cornea from Georgetown University, Washington DC, USA in 1990.

Dr. Mahipal’s vision of providing “Quality eye care in comfortable surroundings at the doorstep of the patient” was continuously nurtured and nourished, culminating in his leaving a secure life at AIIMS and venturing into unchartered territory. He set up a state-of-the-art eyecare centre, bringing into existence Centre for Sight, which from those humble beginnings has grown to be one of the leading chain of eye centres in the country today.

Dr Mahipal’s impeccable blend of a clinician and administrator, capacity for hard work, foresightedness and open arm policy has endeared him as a friend, philosopher and guide to over three generations of Ophthalmologists.

With over 94 publications in reputed journals - 34 of them in indexed journals, authorship of more than ten well appreciated books and manuals, Dr Mahipal is an authority on Cataract, Cornea and Refractive surgery internationally. He has presented scientific papers in more than 495 state, national and international conferences. He led his team into the Guinness Book of World Records for the maximum number of Diabetic Retinopathy screenings in a day.

Dr Mahipal's clinical excellence is only matched by his passion for being an active player in advancement of Ophthalmology. He has been an advisor to innumerable societies, associations and boards. It was his administrative skills in the following posts which were responsible for the transformation of DOS into a vibrant, progressive and academically relevant society:-

- Secretary - Delhi Ophthalmological Society (DOS) 1993 - 1995
- Vice President: DOS 2005
- President: DOS in 2006.

At the national level, he has held the posts of -
- Chairman, Scientific Committee - All India Ophthalmic Society (AIOS) 1996-98,
- Member Managing Committee (1996-1998)
- Currently - Chairman, Editorial Board, IJO
- Organizing Secretary, Annual Conference of AIOS - 1997
- Currently - Chairman, Scientific Committee, IIRSI

Whatever job Dr Mahipal Sachdev takes up, he puts in his heart and soul into it. Just recently, Dr Mahipal as chairman of the Trade Committee, AIOS used his persuasive skills to settle a dispute between a major ophthalmic equipment manufacturer and an AIOS member to the utmost satisfaction and benefit of the Ophthalmologist. His reputation and status in the Ophthalmic field makes it imperative for the industry representatives to hear and pay heed to what he says.

Of late, Dr Mahipal Sachdev has been burning the midnight oil, sifting through the response of AIOS members in reply to his mail soliciting ideas to take AIOS forward. His vision document – “VISION 2020: Action plan for AIOS” is a culmination of this effort and takes into account welfare of each and every AIOS member.

Though Dr. Mahipal Sachdev has been honoured with national and international recognition in the form of scores of awards and medals, the crowning glory to his illustrious career has been the PADMA SHRI award he received from the then President of India, Late Dr APJ Abdul Kalam in 2007.

The stupendous work done by Dr Mahipal S Sachdev for DOS during his tenure as Secretary DOS is well known to most of us. He was instrumental in taking DOS from being just another State Level Ophthalmic society and putting it at the pinnacle of professionalism. He put his heart and soul into raising the bar of academic interaction and increasing the membership to make DOS a shining example of what an academic society should be. I have no doubt in my mind that as Vice President and then President elect and finally President of AIOS, he will internationalize AIOS, just as he nationalized DOS, benefiting all its members in the process.

On behalf of DOS executive, we request all members of DOS to choose Dr Mahipal Sachdev, one of our own for the post of Vice President AIOS in the elections in February 2018.

Request By DOS Executive, Delhi Ophthalmological Society
69th Annual Conference of Delhi Ophthalmological Society

6th to 8th April, 2018
Ashok Hotel, Chanakyapuri, New Delhi

Newer Trends in Ophthalmology

www.doscon.org
Conference Highlights

- Specialty Sessions
- Live Surgery
- Free Papers, E-posters, E-videos & Interesting Cases in all sub-speciality
- Young Ophthalmologists Session
- Fellowship Dinner
- Wet labs
- Social Program for spouses & Kids
- Plenary Sessions
- Invited Instruction Courses
- Quiz 2018

Executive Committee

Dr. Kamlesh
President

Dr. Sudarshan Kumar Khokhar
Vice President

Dr. Subhash C Dadeya
Secretary

Dr. Arun Baweja
Treasurer

Dr. Manav Deep Singh
Joint Secretary

Dr. Bhavna Chawla
Editor

Dr. Jatinder Singh Bhalla
Library Officer

Executive Members

Dr. Radhika Tandon
Dr. Hardeep Singh
Dr. Alkesh Chaudhary
Dr. Naginder Vashisht

Dr. Vinod Kumar
Dr. Sandhya Makhija
Dr. Pawan Goyal
Dr. M C Aggarwal

DOS Representative to AIOS

Dr. Ashu Agarwal
Dr. Rohit Saxena

Ex-officio Member

Dr. Rishi Mohan
Dr. M Vanathi
Dr. Vipul Nayar
Since their discovery steroids both topical and systemic have been essential in the treatment of inflammatory and immune related pathologies. In ocular conditions topical steroids are the mainstay therapy in postoperative management of most ocular surgery both intraocular like cataract, glaucoma, corneal grafting or vitreoretinal surgeries and extraocular surgery like strabismus, lid surgery and refractive procedures. In addition steroids are used in treatment of allergic conditions like vernal catarrh, uveitis and other inflammatory disorders. The normal duration of steroid use ranges from intensive phase of 2-3 weeks followed by tapering dose over next 3-5 weeks, except in immune modulation like keratoplasty or uveitis where they continued in maintenance doses for longer time period over months.

Steroid responsiveness is a known entity since landmark studies of Armaly and Becker in 1965, therefore it is to be expected that secondary steroid induced glaucoma would mar the post-operative course of these responders and confound the visual recovery. In this issue we take the opinion of senior glaucoma specialists to share their inputs on some common scenarios of steroid induced glaucoma.
Scenario 1: Steroid responsiveness among patients undergoing phacoemulsification, strabismus surgery, oculoplastic procedures and vitreoretinal surgery

(AJ, DK): How common is steroid responsiveness among patients undergoing phacoemulsification, strabismus surgery, oculoplastic procedures and vitreoretinal surgery? What is the usual time frame of this response?

KD: Peer reviewed literature does not give precise incidence of steroid responsiveness or steroid induced glaucoma. However, steroid induced ocular hypertension, or elevated intraocular pressure in response to topical steroids is not uncommon following cataract, strabismus, oculoplastic or vitreo-retinal procedures. Steroid responsiveness or glaucoma have also been reported following periorcular corticosteroids, which are far more difficult to reverse, and hence are not routinely recommended. Steroid responsiveness is particularly common in the early to intermediate post-operative period following cataract surgery and vitreo-retinal procedures. Although the incidence and extent of IOP response depend on the type of corticosteroid, route of administration, and duration, it may be observed as early as two weeks or delayed up to several weeks following initiation of therapy in susceptible individuals. A higher preoperative IOP, myopia, family history of glaucoma, primary open angle glaucoma, higher cup to disc ratio may all be considered risk factors predisposing to elevation of intra ocular pressures following steroid administration in ocular surgeries. It is likely that steroid responder glaucoma is more common following penetrating keratoplasty since steroids are administered for a longer period than other ocular surgeries.

RS: Our studies after strabismus surgery report an incidence of 19% in patients with mild increase of > 20 m Hg and almost 28 % present with large increase, of >6 mmHg from baseline. Oculoplasty surgeries would be expected to behave similarly, with higher steroid response in about 20% of the Indian population.

HK: Steroid responsiveness of patients for glaucoma does not depend upon the type of surgery they are undergoing. It depends upon individual susceptibility to steroids, the type of steroid and route of administration. Armaly and Beckler independently reported that normal population could be divided into three groups based on their response to the topical administration of dexamethasone and betamethasone; 1) high responders developed arise of more than 15mmof Hg, 2) moderate responders-pressure rise of 6-15mm of Hg, 3) non-responders had pressure increase of less than 6 mm of Hg. It has been suggested that a genetic difference exist between steroid responders and non-responders. The possibility of high response is greater in patients with POAG, first degree relatives with POAG, old age, or age less than 6 years, connective tissue disease, high myopia, diabetes mellitus and angle recession.

KD: The incidence of steroid responsiveness is typically mild to moderate and occurs within 2 weeks. It is often difficult to reverse and may persist for several months. The precise incidence of steroid responsiveness is not well established, as it depends on several factors including the type of corticosteroid, dosage, duration of use, and individual susceptibility. The risk of steroid-induced glaucoma is higher in patients with a history of glaucoma or those with pre-existing ocular hypertension.

KS: The precise incidence of steroid responsiveness among patients undergoing phacoemulsification, strabismus surgery, oculoplastic procedures and vitreoretinal surgery is not well established. However, it is known that the incidence of steroid responsiveness is higher in patients with a history of glaucoma. The risk of steroid-induced glaucoma is also higher in patients with pre-existing ocular hypertension. The risk of steroid-induced glaucoma is also influenced by the type of corticosteroid, dosage, duration of use, and individual susceptibility. The risk of steroid-induced glaucoma is also influenced by the type of corticosteroid, dosage, duration of use, and individual susceptibility.
determined by the type of steroid, duration of steroid use, pre-existing damage to Trabecular meshwork and the genetic make up of the individual in terms of high/low steroid responder. Five to six percent of the normal population are high responders to steroid therapy. The time frame can vary from 2 weeks to 6 weeks, however in eyes which already have pre-existing trabecular damage (angle recession/glucoma), the response may be seen within a week of starting steroids.

**References**


**(AJ, DK): What is the reason behind the difference in incidence of steroid induced glucoma after different surgeries despite using the same medication?**

**RS:** Intraocular surgeries are invariably affected by the size of incisions made, use of viscoelastics and silicone oil, thereby accounting for the difference.

**KD:** The route of administration, potency of administered corticosteroids as well as duration of therapy may greatly differ among various ocular surgeries, which may explain the differences in incidence of steroid induced glucoma. In certain conditions like post keratoplasty, the causes predisposing to corneal damage and need for keratoplasty contribute to glucoma. Cases of penetrating trauma, infective keratitis with perforated corneal ulcer or adherent leucoma which require keratoplasty as therapeutic measures are likely to be confounded by pre existing glucoma due to various mechanisms. These factors also make differentiation from steroid induced causes of glucoma difficult.

**HK:** Difference in incidence of steroid induced glucoma does not depend upon the type of surgery.

**KS:** The mode of administration of corticosteroid and its half-life, duration of instillation, and strength/potency of the steroid used determine the postoperative IOP spikes. Risk factors such as ‘at risk disc’, family history of glucoma, myopia may be additional risk factors for steroid responsiveness. The additional causes of increased IOP e.g. silicone oil or intravitreal steroid injection in vitreoretinal surgery, tightness of muscle suturing in strabismus surgery or sub-optimal suturing in keratoplasty which determine difference in steroid response.

**TD:** The incidence of Steroid induced glucoma or Steroid induced ocular hypertension varies after different surgeries depending upon the duration for which steroid is being prescribed and on co-existing risk factors. Phacoemulsification is mostly carried out in elderly, where trabecular meshwork (TM) function is already compromised. Added steroid use, unmasks the TM dysfunction presenting as steroid induced glucoma. Vitreoretinal surgery and phacoemulsification can have rise in IOP due to other factors as well like vitreous substitutes and inflammation. In such cases the cause of raised IOP is multifactorial. More the number of risk factors, higher are the chances of raised IOP. Pediatric surgeries are associated with a higher response to steroid therapy and risk of progression to glucomatous optic nerve damage as the trabecular outflow pathways may not be fully mature/developed. Pre-existing glucoma, High myopia, Diabetes, Family history of glucoma, connective tissue disorders, closed globe injuries with angle recession are other factors which increase risk of steroid response.

**(AJ, DK): Is detailed glucoma evaluation feasible before prescribing steroids in our Indian scenario? If not, how better can we streamline steroid therapy among our patients?**

**RS:** Detailed evaluation before prescribing steroids is not feasible nor necessary in most cases, as long as IOP measurements are taken periodically while on therapy. However, patients needing prolonged use of steroids, as in steroid implants/depot for uveits, therapy for VKC etc, should be evaluated for pre-existing glucoma as well as a family history of glucoma. These cases should be followed up carefully over course of therapy, as they may show a rise in IOP later.

**KD:** Risk factors of positive steroid response have been identified and include higher IOP, presence of glucoma, family history of glucoma, and myopia. A detailed evaluation and documentation including slit lamp biomicroscopy, appplanation tonometry, gonioscopy and a dilated posterior segment examination to evaluate optic nerve head and Retinal nerve fiber layer can identify possible risk factors for steroid response. In suspect eyes, a referral to glaucoma practice to obtain baseline visual field by autoperimetry, fundus photography and quantitative evaluation of RNFL is also mandatory. Once therapy with corticosteroid is initiated, periodical monitoring of IOP, optic discs and visual fields is advocated as long as the individual is advised corticosteroid therapy. In those who are steroid responders, the drug is swiftly tapered and discontinued, if the primary ocular condition warranting steroid therapy is reversed. In case continued steroid administration is indicated, the least possible dose of steroid and frequency of administration is advocated. Any elevation of ocular pressure is managed by aqueous suppressants and periodical monitoring of the individuals to prevent progressive glucomatous damage. In chronic conditions requiring prolonged therapy of steroids, maintenance or intermittent pulse therapy may...
also be recommended, with the requisite ocular hypertensive therapy. Where possible, responders may also be recommended to try non steroidal anti inflammatory drugs or other non steroidal immune suppressive therapy. In rare instances, glaucoma may be progressive despite discontinuation of corticosteroid therapy and filtering surgery may be indicated. Since failure of trabeculectomy is very common in such individuals due to conjunctival or ocular inflammation or other co-morbid ocular pathology, a higher dose of intra operative mitomycin, and close monitoring of the bleb with appropriate modulation may be indicated.

**HK:** Yes, it is a very good idea to perform glaucoma evaluation before prescribing steroids. Every patient who has to be started on steroids for any disease, should be send to ophthalmologist to check steroid responsiveness and glaucoma evaluation. Close and regular monitoring of the IOP of patients needs to be done (especially those with a personal or family history of POAG or steroid induced glaucoma). Baseline visual field and disc photography should be done.

**KS:** A detailed evaluation is not feasible or required in all patients receiving topical steroid therapy for short durations. However, patients receiving long acting, depot preparation like intravitreal or posterior subtenon injection of steroids should be carefully screened. This is especially true of risk factors for steroid response exist eg history of open angle glaucoma, high myopia, connective tissue disorders and diabetes. The screening should include 2-3 IOP measures and dilated disc evaluation. Often perimetry is not possible or not reliable in patients requiring such depot injections since they would be suffering from macular pathologies, retinopathies or recalcitrant uveitis. If glaucoma risk cannot be ruled out, the patient must be informed of its flare up prior to injecting (informed consent).

To streamline therapy, IOP monitoring should be inbuilt into every scheduled follow up of such cases.

**TD:** A detailed glaucoma evaluation may not be feasible before prescribing steroids in Indian scenario, however follow up visits must be scheduled at 2 weeks, 6 weeks, 3 months and then at regular intervals with documentation of IOP and optic disc at each visit to ensure that an increase in IOP is not missed. A steroid response is defined as IOP > 6 mmHg from baseline. High risk groups should be identified and risk of a high steroid response noted with a more frequent follow up regimen. Baseline IOP, pachymetry, and optic nerve head status (with drawing) and photograph if possible should be noted.

**KD:** Refractive surgery is commonly performed for myopia, which is a major risk factor for steroid induced ocular hypertension and glaucoma. Topical steroids are routinely used for these patients and often given for extended periods in cases of stromal haze post photorefractive keratectomy (PRK). During LASIK, the IOP is transiently elevated to 60-90 mmHg which can compromise optic nerve blood flow in susceptible eyes. For suspected glaucoma, definite glaucomatous disc damage and ocular hypertension PRK is preferred over LASIK.

Another aspect is accurate measurements of IOP post refractive surgery. The resultant corneal thinning and changes in corneal curvature underestimate IOP measurements by GAT. More reliable measurements are by pneumotonometer, Tonopen or Dynamic contour tonometry. The ophthalmologist must rely on other parameters of glaucoma evaluation like stereoscopic optic nerve assessment, nerve fiber analysis and perimetry. Careful objective evaluation of ONH and RNFL is critical in eyes post refractive surgery and case reports of end stage glaucoma are not uncommon from masking of steroid response due to inaccurate IOP measurements after PRK and LASIK.

Presence of interstitial fluid following refractive surgery, also causes IOP to be underestimated.

Treatment for steroid induced glaucoma following refractive surgery is similar to steroid responsive glaucoma in normal eyes i.e. sequential ocular medications, and filtering surgery when target IOP is not achieved.

**HK:** Incidence of increased IOP after surface ablation has been reported in 11-25% cases. False low IOP subsequent to corneal ablation makes it easy to miss the diagnosis. As a general rule, measure IOP on every visit. If the IOP is in high teens, a diagnosis of steroid induced glaucoma should always be kept in mind. Since myopia itself is a significant risk factor, presence of other risk factors mentioned earlier need close monitoring.

One may get false low IOP when measured with GAT, so IOP measured by a tonopen or pneumotonometer in peripheral cornea may give a better estimate. If available, use of the newer devices like DCT or ORA or CST may be used.

Postoperatively, the clinical picture of raised IOP varies from mild corneal haze with milky vision to stromal swelling, fluid accumulation under the flap to frank interface edema which may mimic a diagnosis of DLK. This is critical as the treatment of the two conditions is opposite. While DLK needs intensive steroids, pressure induced stromal keratitis will need steroid withdrawal. Choice of antiglaucoma medication depends on IOP level. In general, beta blockers and CAI should be initiated. Postoperatively, these high risk patients should be kept under close follow up. Consider visual fields 6 months to a year later especially if the patient has presented with a high IOP after refractive surgery. Patients with high myopia or large disc or

**RS:** The duration of steroid use has come down after refractive surgery, however patients at risk such as family history of glaucoma should have serial IOP measurements from 2 week onwards.

**[AJ, DK]: How do you evaluate and manage suspected steroid responders post refractive surgery?**

**[HK]:** If there is an increase in IOP it may be due to steroid induced glaucoma or a high IOP secondary to corneal edema. In either case, the patient must be referred to an ophthalmologist for proper evaluation and management.

**[KS]:** A detailed evaluation is required to rule out other causes of elevated IOP such as anterior chamber inflammation or other co-morbid conditions.

**[TD]:** A detailed glaucoma evaluation may not be feasible before prescribing steroids in Indian scenario, however follow up visits must be scheduled at 2 weeks, 6 weeks, 3 months and then at regular intervals with documentation of IOP and optic disc at each visit to ensure that an increase in IOP is not missed. A steroid response is defined as IOP > 6 mmHg from baseline. High risk groups should be identified and risk of a high steroid response noted with a more frequent follow up regimen. Baseline IOP, pachymetry, and optic nerve head status (with drawing) and photograph if possible should be noted.

**[KD]:** Refractive surgery is commonly performed for myopia, which is a major risk factor for steroid induced ocular hypertension and glaucoma. Topical steroids are routinely used for these patients and often given for extended periods in cases of stromal haze post photorefractive keratectomy (PRK). During LASIK, the IOP is transiently elevated to 60-90 mmHg which can compromise optic nerve blood flow in susceptible eyes. For suspected glaucoma, definite glaucomatous disc damage and ocular hypertension PRK is preferred over LASIK.

Another aspect is accurate measurements of IOP post refractive surgery. The resultant corneal thinning and changes in corneal curvature underestimate IOP measurements by GAT. More reliable measurements are by pneumotonometer, Tonopen or Dynamic contour tonometry. The ophthalmologist must rely on other parameters of glaucoma evaluation like stereoscopic optic nerve assessment, nerve fiber analysis and perimetry. Careful objective evaluation of ONH and RNFL is critical in eyes post refractive surgery and case reports of end stage glaucoma are not uncommon from masking of steroid response due to inaccurate IOP measurements after PRK and LASIK.

Presence of interstitial fluid following refractive surgery, also causes IOP to be underestimated.

Treatment for steroid induced glaucoma following refractive surgery is similar to steroid responsive glaucoma in normal eyes i.e. sequential ocular medications, and filtering surgery when target IOP is not achieved.

**HK:** Incidence of increased IOP after surface ablation has been reported in 11-25% cases. False low IOP subsequent to corneal ablation makes it easy to miss the diagnosis. As a general rule, measure IOP on every visit. If the IOP is in high teens, a diagnosis of steroid induced glaucoma should always be kept in mind. Since myopia itself is a significant risk factor, presence of other risk factors mentioned earlier need close monitoring.

One may get false low IOP when measured with GAT, so IOP measured by a tonopen or pneumotonometer in peripheral cornea may give a better estimate. If available, use of the newer devices like DCT or ORA or CST may be used.

Postoperatively, the clinical picture of raised IOP varies from mild corneal haze with milky vision to stromal swelling, fluid accumulation under the flap to frank interface edema which may mimic a diagnosis of DLK. This is critical as the treatment of the two conditions is opposite. While DLK needs intensive steroids, pressure induced stromal keratitis will need steroid withdrawal. Choice of antiglaucoma medication depends on IOP level. In general, beta blockers and CAI should be initiated. Postoperatively, these high risk patients should be kept under close follow up. Consider visual fields 6 months to a year later especially if the patient has presented with a high IOP after refractive surgery. Patients with high myopia or large disc or

**[RS]:** The duration of steroid use has come down after refractive surgery, however patients at risk such as family history of glaucoma should have serial IOP measurements from 2 week onwards.
Post-operative: Monitor IOP by non-contact tonometry.

Pre-operative work up in CRT should include IOP readings. In OCR, patients who are myopes, they have an added risk factor for developing glaucoma. Steroid-induced glaucoma cases GAT with correction factor for new corneal thickness. Tonopen / DCT / ORA are preferred and cases GAT with correction factor for new corneal thickness and documented. In addition to a simple disc diagram and where possible a disc photograph is routinely done. In patients with family history of glaucoma, connective tissue diseases or chronic prior use of steroids should either not be taken up for surgery or counselled for requirement of stringent follow up to pick up IOP swings.

Treatment:
Discontinuation of steroids wherever possible, if not, substitute with low potency steroid like Loteprednisolone or Flurometholone. Use of aqueous suppressants, followed by carbonic anhydrase inhibitors or alpha agonist is the usual regimen. In case trabeculectomy is required for non-responsive glaucoma, post-operative modulation should be done by low potency steroid like loteprednisolone. A good alternative is topical 2% cyclosporine drops as steroid sparing ant inflammatory drug, used 4-6 times a day tapered over 4-6 weeks.

In all patients undergoing refractive surgery the basic work up with recording of IOP, CCT and disc status as mentioned above is mandatory prior to refractive surgery. In case of slightest suspicion of glaucoma it is advisable to get baseline diurnal variation of IOP, disc photo, visual fields and RNFL OCT done. These investigations may be normal at the outset, but they may be useful later to document progression, when IOP readings appear normal. As a majority of these patients are myopes, they have an added risk factor for developing glaucoma. Steroid-induced glaucoma is known to be masked following refractive surgery as IOP recordings are falsely low due to central corneal thinning, ocular rigidity changes, corneal edema or fluid accumulation beneath the LASIK flap. Using tonopen tonometer in the corneal periphery outside the operated zone is an option to estimate the IOP. If a patient post refractive surgery develops worsening of visual acuity on steroid therapy (being given for DLK) and there is evidence of interface fluid on slit-lamp biomicroscopy without inflammatory cells, corneal edema beyond the flap margin and steepening of central corneal topography- a steroid response should be suspected. The central IOP reading by GAT may be quite low, while the peripheral reading by Tonopen may be high. Immediate cessation of steroids and start of ocular hypotensive medications (other than prostaglandins) is the preferred line of management.

References

Scenario 2- Steroid response after posterior subtenon triamcinolone (PST).

(AJ, DK): How common is steroid induced glaucoma after injectable (PST/ Intravitreal) steroid for recalcitrant macular edema, in your experience?

RS: We have not done a formal study on PST, but the approximate incidence would be about 5% with a single injection, rising further with repeated injections.

KD: Data from various publications and our own clinical experience suggests that PST/ intravitreal steroid administration may result in elevated IOP and glaucoma in 28-52% of eyes. Glaucoma is more pronounced in eyes with higher baseline IOP, and pre-existing ocular hypertension or glaucoma. Persons with glaucoma with baseline IOP of 15 mmHg have 60% risk of IOP elevation to 24 mmHg, as compared to only 22% in individuals without glaucoma, following IVTA. The intensity of IOP rise is also related to the dose of intravitreal triamcinolone.

HK: A single injection of intravitreal Triamcinolone acetonide (IVTA) has been reported to cause IOP elevation in about 50 % of cases starting at 1 to 2 months post injection, with repeat injections causing IOP elevation of more than 30 mmHg in 65 % cases. IN posterior subtenon injection of triamcinolone, IOP rise has been reported in 21 - 44% of cases after 5-9 weeks, with chronic rise being demonstrated in 9% cases. Yamamoto et al. found that IOP elevation (>5mmHg) lasted longer after a PST injection compared to IVTA and mean IOP increased significantly in first month after IVTA but at all follow ups after PST. Another study found no significant difference in frequency of IOP more than 21 mmHg between IVTA and subtenon, however, incidence of
IOP rise within 1 week after IVTA was significantly more than with PST. Smithen has reported that among the non glaucoma patients with base line IOP more than 15 mmHg, 60% showed IOP rise with IVTA, compared to 20% who had base line IOP less than 15 mmHg.

KS: Studies suggest that ocular hypertension can be as high as 23% post PST and 12-50% post intravitreal implant with the propensity being less for more water soluble implants like dexamethasone implant vs triamcinolone. The risk increases with repeat injections, higher baseline IOP, positive family h/o glaucoma, formulation/ water solubility, pseudophakia, vitrectomized eyes and anterior positon of implant (near pars plana). Onset of IOP rise is within 2-4 weeks of injection and can persist for 6 months to a year, depending on the half-life of the drug.

TD: Approximately 15-25% of patients receiving PST show steroid induced rise in IOP. Nearly 35-50% of eyes receiving intravitreal steroids exhibit a rise in IOP within 1-2 months after injection. Since many of these patients are diabetic, it puts them at a higher risk of steroid responsiveness. A dosage of 1-2 mg of IVTA is safer as 4 mg has a high risk of steroid response for diabetic macular edema. It is advisable not to give IVTA for eyes with CRVO due to a high risk for development of glaucoma. In patients receiving IVTA, IOP should be checked 1 week after IVTA, then at 2-week intervals for the first month, and then once a month for 6 months.

References

(AJ, DK): How to manage steroid responsive glaucoma subsequent to depot steroid? Does excision of depot resolve glaucoma?

RS: Excision on diagnosis, followed by medical therapy to control IOP to "Target" is essential. Treatment can be tapered over time, generally over months.

KD: Glaucoma following depot steroids such as PST and IVTA are initially managed by medical treatment as in primary open angle glaucoma. When glaucoma is refractory to medical management, surgical management of glaucoma is indicated. Trabeculectomy with mitomycin is the standard treatment of choice in such individuals. Most eyes requiring surgical management in 6-9 month period or later, following depot steroid administration, benefit from removal of depot during surgery (excision of sub tenon plaque in PST/ vitrectomy in eyes with IVTA). The determination of need for depot excision depends on half life of the type of steroid administered. 4mg of IVTA, for instance, may persist in the vitreous for 3 months, while 20 mg dose of IVTA persists in the vitreous for about 1.5 years releasing the steroid into the vitreous.

HK: Overall 75% of eyes receiving the fluorocinolone acetone implant required IOP lowering therapy. Recognition of the condition is the most important step in its management including base line IOP measurement with disc evaluation to rule out pre-existing glaucoma. Subsequently IOP monitoring should be done every 2 weeks. The IOP increase is usually short lived and reversible by discontinuation of therapy within 2-4 weeks. Often anti-glaucoma therapy is required till crystals resolve, which usually takes six months. If IOP is still raised on maximal anti-glaucoma medications (topical and systemic), depot removal should be done within a year, keeping in mind potential surgical complication of vitrectomy. Glaucoma filtering surgery is often required with one study reporting need in fellow eye also.

KS: The half life of depot steroid should be taken into account while managing cases of ocular hypertension and/or glaucoma in such patients. Early IOP spikes can be managed by topical aqueous suppressants. Recalcitrant cases may benefit with excision of PST plaque/vitreectomy post intravitreal injections if done within the half life of the steroid. Cases not controlled with above means or maximum medical therapy may require trabeculectomy.

Sharing a typical case vignette: An adult male presented with uncontrolled IOP post subtenon triamcinolone injection (PST). Patient had developed macular edema OD (macular thickness 600 µ) 6 months post uneventful phacoemulsification with BCVA 6/60. This was the second injection of PST after partial response to first one. At 2 weeks post second injection; vision improved to 6/18, with quiet eye and IOP in forties, with no disc damage, requiring systemic acetazolamide along with topical β blocker and á agonist anti-glaucoma drugs. Since the patient could not be weaned off systemic acetazolamide, PST plaque excision was undertaken at 2 month after 2nd injection. Resultant postoperative course remained stormy and patient required Trabeculectomy with amniotic membrane transplant (AMT).

TD: Once steroid induced glaucoma is diagnosed with optic nerve damage, removal of the steroid depot should be done as soon as possible. Topical ocular hypotensive therapy (excluding prostaglandin analogs) should be initiated. If maximal medical therapy fails, trabeculectomy should be performed. A few studies have shown IOP lowering efficacy of SLT in such situations and this can be done of the surgery is to be delayed for medical reasons or patient is not willing for surgery.

(AJ, DK): How would trabeculectomy differ in such situations? What post-operative regimen should be followed in such steroid responsive cases?
RS: In this case as there is no disc damage, the trabeculectomy could be done without MMC, and routine steroids can be used. It is expected that the effect of steroids would reduce with time.

KD: A standard trabeculectomy with a high dose mitomycin is indicated since filtering surgery in such eyes is prone for failure due to enhanced conjunctival scarring. Post operatively, frequent post operative evaluation to monitor and modulate bleb healing is essential to increase the chances of long term bleb survival. Earlier intervention like suture release and bleb needling may be indicated with a higher frequency for enhanced success of surgical intervention.

HK: The most commonly employed surgery in patients with virgin conjunctiva is trabeculectomy. If conjunctiva is not healthy or other problems preclude its use, one can resort to a glaucoma valve surgery. Cyclodestructive procedures may be preferred when either of the two surgeries is feasible due to ocular status. Trabeculectomy with higher concentration of MMC is the preferred choice. In postoperative period low dose steroids can be used with early taper and NSAIDS if required, although it depends on the type of bleb, vascularity etc as the steroids help to make a better bleb and since alternative channel route should forestall steroid response.

KS: The most common steroid glaucoma’s requiring surgery in my experience has been post vernal catarrh or vitreo-retinal cases. In these conditions the conjunctiva is unhealthy and associated with dry eye, subsequent to prior drug use or ocular morbidity requiring steroid. Thus response to conjunctival handling is excessive and requires more frequent anti-inflammatory drugs. Trabeculectomy often fails and must be supplemented with antimitotic agents to decrease the postoperative fibrosis. This becomes a Catch 22 situation where use of steroids in postop period itself can case IOP rise. Albeit blunted due to bypass mechanism, we prefer to use topical 2% cyclosporin. In addition intensive lubrication to promote healthier bleb is must for such patients.

TD: The technique of trabeculectomy will remain essentially similar to other cases of open angle glaucoma. It is prudent to treat any active uveitis / conjunctival inflammation in VKC prior to trabeculectomy. Remember that if your trabeculectomy is not fully functional or starts to fail, and the patient is using post operative steroids, you can get a very high IOP due to steroid response.

(AJ, DK): Is it cost effective to do a glaucoma screening prior to PST?

RS: This could be considered if multiple PSTs are envisaged.

KD: Since there is a high incidence of glaucoma following PST, and treatment of steroid induced glaucoma is very challenging due to irreversible effects of drug delivery in depot steroid injections, it is must to thoroughly evaluate for risk of glaucoma. The cost and benefit of a thorough evaluation of eyes prior to steroid administration far outweigh the risk of glaucoma in eyes receiving PST.

HK: Definitely it is cost effective to check for steroid responsiveness before PST. The complications of steroid induced glaucoma may be far reaching, so it is best to do a pre-check for steroid responsiveness and existence of glaucoma in such patients.

KS: In most situations screening is not necessary unless risk factors of history of glaucoma, myopia, systemic connective tissue disorder or diabetes mellitus exist. In patients requiring frequent depot steroids, the high incidence of ocular hypertension warrants prior screening. As mentioned before if steroid injection is essential, informed consent from patient should be taken and documented.

TD: In eyes with high risk of steroid response and suspicion of glaucoma based on a cup disc ratio of > 0.7 or asymmetry > 0.2, an RNFL OCT can be performed in addition to the macular OCT being used to treat the retinal disease. A comprehensive routine clinical examination including baseline 1OP, optic nerve head evaluation and enquiring about family history of glaucoma may be sufficient for most cases.

Scenario 3- Steroid induced glaucoma with long term use of over the counter medication for allergy in a child with VKC.

An 11 year old male child with long term history of itchy watery eyes, using over the counter topical medications for 3 years, presented with diminution of vision OU. Patient had seasonal asthma requiring fluticasone / salmeterol inhalation. On examination, BCVA was 6/18 OU, IOP of 28 and 26 mm Hg recorded on GAT (OD, OS respectively), and optic disc cupping of 0.7: 1 OU for average disc size (DDLS 3). Gonioscopy revealed open angles in all quadrants OU, and early visual field damage seen on two consecutive but unreliable fields (HVF 24-2). He had a quiescent vernal catarrh with unhealthy conjunctiva and minimal posterior subcapsular cataract. Patient was started on topical antiglaucoma medications along with lubricants in step ladder fashion but IOP failed to get controlled.

(AJ, DK): What would be first line management in this child? What topical therapy would be preferred?

RS: Medical management with topical brimonidine and oral acetazolamide would control an IOP of 26/28 mmHg to about 14-16 mmHg. He should be asked to stop fluticasone and topical steroids immediately.

KD: Topical dorzolamide or brinzolamide are the only possible drugs that could be potentially used in this child. But monotherapy with topical CAI results in insufficient pressure reduction and it is not possible to obtain intended target pressure. Topical beta blockers are contraindicated due to bronchial asthma. Even selective beta blockers like betaxolol are relatively contraindicated in these children since they can
In this situation non selective beta blockers are contra-

TD: Tricky situation, refer to RPCentre !!!.
In this situation non selective beta blockers are contra-

HK: We need to evaluate this patient more thoroughly.
This is a young child and no decision can be taken without full facts.
First, we need to do CCT (pachymetry). If the cornea is substantially thick as it is in many children, it will need to be taken into account to assess the corrected IOP. Repeat visual field after dilatation is a must to conclude if the fields are truly defective since this one finding may tilt our decision from medications to surgery, as the patient has cataract and visual field changes may be due to cataract. We must get two consistent fields to reach any decision.

Stop topical steroids and start tacrolimus eye ointment with frequent lubrication, it has shown wonderful results in pediatric allergic conjunctivitis. If CCT is normal, then start with ½ tab Diamox two times a day and topical anti-glaucoma therapy with strict time control. If fields are minimally effected, we can wean off the child from acetazolamide. This will leave us with an option of continuing medication or going in for surgery if fields worsen over time or drug affordability or adherence issues crop up.

While using anti glaucoma medications, it is to be remembered that β Blockers like timolol cannot be used.

KS: It would be worthwhile to check corrected IOP (incorporating CCT values) since fields are unreliable and disc damage is minimal.
Firstly all topical steroids need to withdrawn and replaced by topical tacrolimus (first line) followed by cyclosporine (2nd line) or soft steroids like fluorometholone with its poor ocular penetration. A comprehensive study on children with vernal catarrh suffering from steroid response reported 44% control of glaucoma by steroid withdrawal alone and 81% cases could be managed with or without anti-glaucoma medications. To achieve target pressure in mid-teens for this child, judicious use of CA inhibitors/ alpha agonists under close monitoring if required.

RS: The ‘target’ IOP would be lowered to 10-12 mmHg, and he may require additional glycerol.

KD: Our preferred method of treatment would still be trabeculectomy with mitomycin and foldable IOL implantation taking sufficient precautions to preoperatively lower IOP by intravenous mannitol and take steps to prevent intraoperative and postoperative ocular hypotony. Gradual entry into the anterior chamber to avoid sudden decompression of the globe, pre placed scleral flap sutures prior to trabeculectomy and tight scleral flap closure may pre-empt prolonged hypotony, minimizing the risk of choroidal hemorrhage. Keeping the anterior chamber pressurized throughout the operative procedure by an anterior chamber maintainer or by a viscoelastic also prevents hypotony. Sequential suture lysis has to be planned meticulously in the post operative period to ensure there is no sudden hypotony or overfiltration. If lens changes are minimal, one could also plan a staged procedure- trabeculectomy to stabilize pressure followed by phacoemulsification and lens implantation within weeks to months of filtering surgery.

HK: If the same patient had advanced visual field defects, definitely treatment would be different. Stop all topical steroids and start with tacrolimus and all maximum topical anti glaucoma medications and systemic acetazolamide are given only to control for pending surgery and recovery of conjunctiva. Even then if pressures are not controlled go for surgery.

KS: If we do not have any visual fields in young patients and normative data for OCT RNFL is also not available. So I would re confirm disc damage before accepting the visual fields as true representatives of advanced glaucoma. Disc damage must corroborate the visual field damage. If advanced damage is confirmed, surgical option is the only modality. The surgery should be attempted only once VKC is controlled.
Expert Corner

First choice would be trabeculectomy with multiple antifibrotic modulation like mitomycin C in addition to amniotic membrane and/or Ologen implant with surrogate releasable in the form of polyglactin (9-0 Vicryl) sutures. Often these children require bleb resuscitation with needling within a year, as scarring response is significant.

The cataract would need to be assessed and if the near vision is also affected, clear corneal temporal phacoemulsification would need to be done at a second sitting.

**TD:** If advanced visual field damage with high IOP not getting controlled on topical medical therapy – go ahead with trabeculectomy and Mitomycin C for 1-2 minutes. At this stage there is irreversible damage to trabecular meshwork and unlikely to respond to cessation of steroids.

If cataract surgery is to done after trabeculectomy, defer it by at least 6-12 months as there is a high risk of bleb failure. Also remember that long term outcomes with combined phaco-trabeculectomy are poor in the pediatric age group.

**(AJ, DK): This patient requires cataract surgery eventually as the cataract is obscuring central vision, disabling school performance. What precautions should be taken during cataract surgery and what would be the postoperative regimen with respect to steroid use?**

**RS:** Cataract surgery does very well, but IOP should be lowered with Diamox peri-operatively, and the IOP monitored carefully. Steroids may be used to prevent postoperative inflammation as required.

**KD:** Precautions while performing cataract surgery are similar to the steps described above and are principally aimed to prevent prolonged hypotony. Clear corneal phacoemulsification with intra operative pressurized anterior chambers are preferable as compared to scleral incision manual phacoemulsification techniques for lens extraction. Intraocular pressures need to be monitored post operatively to prevent acute pressure spikes. Preoperatively, acetazolamide and topical brimonidine preceding and immediately following the surgical procedure may prevent acute postoperative pressure spike in these eyes. Post operatively continuing oral acetazolamide and topical aqueous suppressants also prevents IOP elevation. Steroids may be continued post operatively but IOP needs to be monitored. If pressure response to steroids is marked, they can be substituted by non-steroidal anti-inflammatory drugs to prevent inflammatory response. Acute post operative pressure spikes and need for glaucoma medications may also be significantly reduced by combining trabeculectomy with cataract extraction.

**HK:** Since the cataract surgery will be done under GA, intubation and extubation should be smooth. Any extra pressure elevation at these times could be harmful for the compromised nerve. Avoid the anesthetic drugs which raise IOP e.g. succinylcholine, ketamine. Avoid spontaneous respiration as CO2 retention will raise IOP during the surgery. During phacoemulsification, ports should be slightly larger so that excess pressure never builds up, decrease bottle height so that IOP should not increase during surgery. At the end of surgery AC wash should be thorough, no cortical material should be left, as later on it causes inflammation and increased IOP. Complete removal of viscoelastics is a must for the same reasons. Experienced surgeon should do the surgery. In the post operative period, give low dose steroids, taper early and start with NSAIDS if required.

**KS:** After achieving good preoperative IOP control, the patient should be undertaken for a lens aspiration with hydrophobic foldable intraocular lens implantation. Slow decompression while making side ports, clear corneal incisions to spare conjunctival conductions for future surgeries, judicious use of visco-cohesives during capsulorhexis, with complete wash out of viscoelastic at end of surgery and use of intracameral pilocarpine to prevent post op IOP spike. Postoperative course is as mentioned for trabeculectomy before, with the addition of cycloplegics like homatropine drops used HS to prevent synchia. Despite meticulous polishing these children often have anterior capsule rim opacification, thus a rhexis larger than optic size of IOL should be aimed for, which requires high cohesive visco-elastic drug like Healon GV.

**TD:** Use low potency steroids and substitute early with non-steroidal anti-inflammatory drugs in post operative period period to prevent IOP spikes. In case Cataract surgery is being undertaken after trabeculectomy, inject 5FU (5mg) adjacent to bleb after cataract surgery.

**(AJ, DK): If and when trabeculectomy is required, what would be the postoperative regimen and prognosis?**

**RS:** The postoperative regimen is as usual, and trabeculectomies work very well in most cases, except in very congested eyes having VKC. Over a few years, the IOP tends to get lower, reaching 6 mmHg in some cases.

**KD:** Topical steroids are still indicated to reduce conjunctival inflammation and fibrosis. The IOP should be frequently monitored and any steroid response warrants reduction in the frequency of use of steroids. Post operative IOP rise and steroid response is not unknown in steroid responders and may be appropriately treated by ocular hypotensive medications.

**HK:** If trabeculectomy is to be performed in this child, time must be taken with the parents to explain in detail regarding the procedure. They must be informed of the reasons for performing the surgery and a written consent must be signed after reading the consent form which must be in the language of the patient or that understandable to him. They must be explained that the surgery has many complications including the possible loss of vision if the fields are showing advanced damage. The child may require
repeat anesthesia for repeat interventions which may be unforeseen. They must also understand that doing surgery would not guarantee a lifelong exemption from drugs and that repeat surgery may be required at any time and the child will have to follow up lifelong at intervals. However, they must also be conveyed that under the circumstances there are no other options to prevent blindness and the results are usually good but it is our duty to inform them of these possibilities. In the postoperative period, start with low dose steroids and taper early and start NSAIDS, although postoperative medications would depend on the type and vascularity of the bleb.

KS: In addition to informed and detailed consent from parents or guardians, the need for life long follow up and lack of vision gain should be clearly explained and documented. Trabeculectomy is often required in such children in as much as 25% cases. Postoperative regimen includes use of soft steroids like FML with its poor ocular penetration, Loteprednisolone, Cyclosporine and tacrolimus with lubricants. These children have unhealthy conjunctiva and are “rubbers”, which cause bleb dehiscence and/or bleb failure. The bleb morphology should be monitored in addition to IOP and on evidence of fibrosis and reduction of bleb dimensions, early resuscitation with bleb massage, release of releasable sutures and needling with Mitomycin C or 5 Fluorouracil is done under general anesthesia.

TD: The post operative management does not differ for a case of SIG vis a vis any other indication as the patient does not show a response to administration of steroids due to creation of an alternative conduit for aqueous outflow. On the contrary, the steroids should be prescribed liberally postoperatively especially in cases with VKC to prevent early bleb scarring. Intraoperative use of a higher dose of mitomycin-C (upto 0.2mg/dl) and post-operative application of mitomycin-C over the bleb if needed, can help to reduce scarring.

Reference

(AJ, DK): For asthma control, what advice should be the advice to the paediatrician managing such cases?

RS: Omitting all steroids or reducing the frequency of use as much as possible.

KD: Non steroid drugs to treat bronchial asthma may be advocated. The least effective steroid dosage may be recommended and if necessary pulse steroid therapy to treat exacerbations of episodes of bronchospasm with a maintenance dose of corticosteroids may also be considered.

HK: I think that the management of asthma is best left to the pediatrician.

KS: Patient should be advised lifestyle modification and steroid sparing drugs like montelukast (Montair).

Steroid use must be kept to a minimum and that too only topical, in the form of inhalers. Patient must be educated about informing the treating physician of his steroid responsiveness else an acute exacerbation may prompt him to prescribe a high dose of steroids. Sometimes a change of residence or city may help reduce both the VKC and asthma. A recent review- The ICOUGH Study, failed to document any significant IOP response after use of inhaled steroids used in glaucoma cases and an Indian review also failed to attribute glaucoma to inhaled steroids. A database review of adults with asthma in United Kingdom gave a 4% prevalence of developing cataract which was dose related.

TD: First and foremost it is important to create awareness among all medical practitioners (Physicians, pediatricians, Pulmonologist, dermatologist) about the potential of steroids (inhaled, oral and locally applied) to cause increased IOP. They should advice their patients to seek a regular ophthalmic consultation when using steroids. If a diagnosed case of glaucoma needs steroid therapy for any health ailment, the dose and duration of steroid should be kept to the minimum required and the ophthalmologist should be kept informed so that necessary changes can be made in the treatment. Leukotriene receptor antagonists and inhaled bronchodilators could be used as first line modality of treatment in patients who are especially steroid responders. Deep breathing exercises (Pranayam) can also help to reduce morbidity caused by chronic respiratory diseases.

In chronic disorders like rheumatoid arthritis, DMARDS (Disease Modifying Anti-rheumatic Drugs) and immunosuppressive therapy can be substituted for chronic steroid therapy to prevent the development of long term side effects.

Reference

(AJ, DK): What difficulties are encountered during trabeculectomy or postoperatively in steroid induced glaucoma? What is the rate of cataract post trabeculectomy in your patients? Do such cases have higher bleb failures?

RS: Most trabeculectomies for steroid induced glaucoma do very well. Very congested VKC eyes tend to have more fibrosis, if the VKC is uncontrolled. The use of
Tacrolimus has helped considerably. Cataracts tend to be present preoperatively, I have not seen any after a trabeculectomy. The blebs are very good in fact, except in congested VKC eyes.

**KD:** Progression of cataracts and failure of trabeculectomy due to increased incidence of subconjunctival fibrosis are the two most common challenges in young individuals with steroid responsive glaucoma. Bleb fibrosis is very common in these individuals necessitating high dose of intra operative mitomycin and early suture release to facilitate early trans-scleral filtration. Most individuals require adjunctive drugs to adequately control IOP. Rarely, the glaucoma is refractory to conventional treatment, necessitating glaucoma drainage implants.

**HK:** We have not encountered any specific difficulties during trabeculectomy in such cases. The rate of cataract extraction after initial trabeculectomy is usually around 24%. The average time from trabeculectomy to cataract extraction was 26 months (range 5-58 months). Progression of lenticular opacities occurred throughout the follow-up period. There was no increased rate of cataract formation in subjects with uveitic and steroid-induced glaucoma when compared with all other types of glaucoma. In patients with both eyes in the study, the first eye was a predictor of cataract progression in the fellow eye.

**KS:** Surgery in these young children has the problem of unhealthy conjunctiva and thick Tenon. Preoperatively surgery should be done in quiescent eyes. Intra-operative manoeuvres are - judicious tenonectomy away from incision site, titration of fluid egress at end of releasable suturing with intra-operative adjustments, meticulous closure of conjunctival incision and bleb titration at end of surgery via a side port help ensure a watertight closure with healthy bleb formation. Safe technique of MMC application (0.02% for 2-3 minutes), use of conjunctival frill incision (devised by us and called Singh’s smile incision), additional use of Amniotic membrane help in minimizing fibrosis in these children.

Yes, bleb failure is higher in these children and controlling the vernal catarrh in the post-operative period helps to prevent this as do copious lubricants. Cataract incidence is higher and in our experience around 10% cases require lens aspiration within 5 years (an estimate). It invariably is a progression of pre-existing cataract.

In cases other than VKC, most patients of steroid induced glaucoma have a healthy conjunctiva and the surgery is essentially similar to any other open angle glaucoma. About 20-30% of steroid induced glaucoma have associated posterior subcapsular cataract at the time of presentation. Another 1/3rd cases develop cataract after trabeculectomy. Such cases do not have higher bleb failure and often optimal outcomes can be obtained as the conjunctiva has been pre-treated with steroids. VKC eyes require appropriate therapy for reducing conjunctival inflammation in the peri-operative period and may require a short course of steroids just before trabeculectomy and long term anti-allergic and lubricant therapy in the post operative period.
G

uarded filtration surgery or trabeculectomy, introduced by Sugar and Cairns in 1968 remains the gold standard surgical procedure for majority of patients with glaucoma. Aqueous outflow through the inner sclerostomy and peripheral iridectomy percolates around the superficial scleral flap and creates an elevation of overlying conjunctival to form a filtering bleb. Aqueous from this bleb is then absorbed by conjunctival vessels, lymphatics and partly excreted through tears. Optimal wound healing envisages suboptimal sub scleral healing around the sclerostomy and subconjunctival healing around superficial scleral flap with complete healing of outer walls of bleb including conjunctival incision, a dichotomy baffling glaucoma surgeons over decades.

Use of antimetabolites like 5-Fluorouracil (5-FU) and Mitomycin C (MMC) permits modulation of wound healing by modifying fibrotic response to surgical insult. Most mature filtering blebs contain loculations delimited by internal fibrous walls primarily at the sclerostomy site surrounded by peripheral smaller loculations. An ideal filter is low lying; diffuse, with reduced vascularity and cystic changes which maintain intraocular pressure (IOP) in low teens along with a formed anterior chamber.

Unlike cataract surgery where the surgical maneuvers have the maximum say in deciding the final outcome, for trabeculectomy it is the constant evaluation and vigilance during early bleb maturation which decides functional outcome. In this journey, knowledge of bleb morphology is essential to differentiate physiological maturation from pathological alterations, as they predict functional outcome of success or failure. This article attempts to provide this knowledge, thereby enabling the ophthalmologist with requisite armamentarium to pick up clues predicting failure and intervene.

**Abstract:** An ideal filter is low lying; diffuse, with reduced vascularity and cystic changes which maintain intraocular pressure in low teens along with a formed anterior chamber. Classifications of blebs attempt to standardize various bleb forms and improve ability to monitor bleb filtration function utilizing an objective and consistent assessment and also correlate predicted outcomes with bleb morphology. Clinical classification has evolved from earliest Kronfeld to Moorfield to IBAGS while bleb imaging modalities have also evolved from UBM to confocal microscopy to AS-OCT which is a non-contact modality providing three-dimensional, high resolution bleb images that in turn have been used to predict bleb functionality. Bleb features that have been quantitatively and qualitatively documented by AS-OCT include bleb height, bleb wall thickness, internal bleb structure, presence and number of micro and macro cysts, and internal bleb reflectivity. Although outcomes have varied, most studies have concluded that well-functioning blebs are diffuse, moderate high with low internal reflectivity, micro cysts, macro cysts and have thick walls. More recent studies examining additional properties of blebs such as phase retardation, bleb ooze, and bleb tear fluid sign report that these features of the bleb are also associated with lower IOP. Although most commonly deployed for bleb imaging one of the major limitations of AS-OCT is that it does not provide microscopic information, which is essential for detecting early signs of failure, such as the stromal collagen deposition and the reduction of AH filled epithelial microcysts.

**SLIT LAMP BASED BLEB CLASSIFICATION SYSTEMS**

Classifications of blebs attempt to standardize various bleb forms and improve ability to monitor bleb filtration function utilizing an objective and consistent assessment. They also attempt to correlate predicted outcomes with bleb morphology. A uniform system of classification also facilitates early recognition of failing blebs patterns and promote timely, aggressive intervention.

Classification has evolved from earliest Kronfeld to Moorfield to latest IBAGS. All the classifications detailed below are derived from the ophthalmologist perception on clinical features evaluated on slit lamp examination, and are therefore subjective.

1. **Kronfeld classification of blebs**
   a. **Type I:** Thin-walled, polycystic bleb with transconjunctival flow of fluid, well-functioning bleb.
   b. **Type II:** Flatter, thicker, more diffuse, per ilimbal extent, relatively avascular bleb with good function.
   c. **Type III:** Flattened bleb with scarred conjunctiva firmly adhering to the underlying sclera with little or no function.

2. **Van Buskirk modification** added encapsulated bleb/ Tenon cyst to the above stated Kronfeld system.

3. **Vesti classification 1993** classified blebs according to function as:
   a. **Diffuse blebs:** Functional success rate of 92%
   b. **Flap-sized blebs:** Functional success rate of 64%
   c. **No bleb group:** Functional success rate of 43%

   These authors also evolved a linear association between a diffuse bleb with good intraocular pressure control and reported that bleb wall played a key role in bleb function.

4. **Indiana bleb appearance grading scale (IBAGS) 2003**

   This standardized classification of blebs is based on clinical characteristics. IBAGS attempts to unify and expand...
upon previous classifications systems based on filtering bleb morphology and establish a simple standardized method of bleb grading (Figure 1).

The standard IBAGS slit lamp images felt to be representative of a comprehensive range of bleb morphology were selected from patient slide library of the Glaucoma Service at Indiana University School of Medicine Department of Ophthalmology. These standards consist of 4 images for grading bleb height (H), 4 images for grading bleb extent (E), 5 images for grading bleb vascularity (V), and 3 images using topical fluorescein application viewed through cobalt-blue filter illumination for assessing leakage with Seidel test (S). Each of the standard images within a specific parameter (height, extent, vascularity, and Seidel test) generally represents an equal scaling interval (H0–3, E0–3, V0–4, S0–3), serving as boundaries/cutoffs for classification. Thus, IBAGS grades the blebs using standard photographs.

a) Bleb Height: assessed by a narrow vertical slit beam that measures the vertical dimension of the filtering bleb representing elevation of the conjunctival flap above the scleral surface and was divided into 4 scaling intervals serving as compared to standard images.

H0 - flat bleb without visible elevation
H1 - low bleb elevation
H2 - moderate bleb elevation
H3 - high bleb

b) Bleb Extent: represents the horizontal dimension of the filtering bleb, or bleb area, and was also divided into 4 scaling intervals based on clock hours

E0 - no visible bleb extent to less than 1 clock hour
E1 - extent equal to or greater than 1 clock hour but less than 2 clock hours
E2 - extent equal to or greater than 2 clock hours but less than 4 clock hours
E3 - extent equal to or greater than 4 clock hours

If appearance falls on a standard interval, then higher standard is used. For example, if a bleb is exactly 2 clock hours, it would be graded as E2.

Bleb extent is directly associated with bleb functionality and lower IOP, with flat and diffuse blebs being more effective filters. A negative correlation between posterior extensions of internal cavity with IOP has also been reported. There have been few contrary reports including our own study where no significant correlation was noted between bleb extent and IOP.

c) Bleb Vascularity: represents an assessment of surface and deep vessel visibility upon slit lamp examination of conjunctiva over site of the filtration bleb and was divided into 5 scaling intervals. To grade vascularity, only blood vessels visible on filtration bleb are used, and not peri-bleb conjunctival injection.

V0 - avascular/white (no micro-cysts visible on slit lamp examination)
V1 - avascular/cystic (microcysts of the conjunctiva visible on slit lamp examination)
V2 - mild vascularity
V3 - moderate vascularity
V4 - extensive vascularity (vascular engorgement).

Although both V0 and V1 represent avascular blebs, the absence or presence of microcysts can be distinguished. In addition, the V1 bleb is relatively transparent, whereas the V0 is white and relatively opaque.

d) Seidel’s test

A positive Seidel test represents leakage of aqueous humor through the bleb surface. Application of fluorescein with a fluorescein strip to the filtration bleb and examination through the cobalt-blue slit lamp filter is required. The Seidel test assessment is divided into 3 scaling intervals.

S0 - no leak
S1 - pinpoint transconjunctival leakage visible on the bleb surface (at multiple points), without streaming of fluid within 5 seconds of application
S2 - streaming aqueous egress visible within 5 seconds of application of fluorescein (diffuse or localized).

5. Moorefield’s Bleb Grading System (MBGS, 2004)*

This was built on telemedicine system and subsequently expanded to include an assessment of vascularity away from center of bleb and a way to represent mixed-morphology blebs. In this classification, central area (1-5), maximal area (1-5), bleb height (1-4) and subconjunctival blood (0-1) are assessed. In addition, three areas of bleb were graded separately for vascularity, including bleb center conjunctiva, peripheral conjunctiva and non-bleb conjunctiva. Vascularity in each area is assigned a score from 1 to 5.

The clinical utility of IBAGS and MBGS has been strengthened with excellent consistency and inter-observer agreement in assessment of height, extent, and vascularity10. Since it is not easy to completely correct for variability in grading among observers within a system that relies on clinical judgment
with inherent subjectivity, sources of measurement error are minimized by photograph derived standards.

**BLEB FEATURES PREDICTING SUCCESS OR PORTENDING FAILURE**

Painstaking work by researchers over years has identified key features of blebs predicting failure of function to be - presence of microcysts, quantity and shape of conjunctival vessels, bleb height and encapsulation, bleb wall11. 

a. Predicting success

- Diffuse blebs, paucity of vessels, quiet surface, elevated blebs and microcystic changes in conjunctiva12.
- Increased microcysts, reduction of conjunctival vasculature and cork screwing, lower prevalence of encapsulation, low bleb height (Figure 2).

b. Portending failure

Bleb injection, large ropelike vessels, thickening of bleb wall, localization of blebs and high-domed blebs

A study by Sacu et al reported the first two postoperative weeks of bleb maturation to be critical in predicting the outcome with appearance of conjunctival subepithelial microcysts heralding lower mean IOP and vessel corkscrewing predicting poorer outcomes13.

In addition to functionality, bleb morphology also provides clues to imminent complications. Blebs with large avascular areas and thin walls have been more commonly associated with bleb leakage14,15.

**BLEB IMAGING MODALITIES**

The advent of imaging tools has enhanced the clinician’s ability to seek beneath visible shapes and refined knowledge of bleb parameters. Bleb wall, extent of microcysts and macrocysts are few such aspects which are not easily amenable to slit lamp photography, requiring bleb imaging modalities.

Bleb wall thickness and shape has direct implications for IOP control and complications like bleb leak and endophthalmitis. Assessment of bleb wall thickness is challenging both clinically and photographically with poor inter-observer reproducibility and studies reporting inability of MBG grades to distinguish between low, diffuse blebs and completely flat blebs on stereo or mono photographs16. Presence of microcysts in bleb wall indicate aqueous flow and are a measure of bleb functionality.

A. Ultrasound biomicroscopy (UBM)

This instrument delineates internal structures of bleb and assesses intra-bleb reflectivity, aqueous route under scleral flap, cavernous fluid-filled space, and bleb height17.

**Yamamoto classification**

Yamamoto et al correlated degree of IOP control to intra-bleb reflectivity and aqueous route under scleral flap and identified reflectivity as the most important criteria, upon which they based their bleb classification as (Figure 3)

- **Type L** (low-reflective): favorable outcome
- **Type H** (high-reflective): less favorable outcome
- **Type E** (encapsulated): poor outcome
- **Type F** (flattened): associated with failed or poorly functioning bleb

The association between internal bleb structures and bleb function was good and the authors stated UBM characteristics predicting a functioning bleb with 91% sensitivity and 70% specificity.

Limitations of UBM imaging is the requirement for contact, use of jelly and supine positioning. The contact aspect is not feasible in the initial postoperative period and undesirable due to concerns of infection and trauma to the immature bleb. In addition, UBM imaging causes significant discomfort to patients due to use of eyecup and sound of oscillating probe18.

B. In Vivo Confocal Microscopy (IVCM)

This modality used by Labbe et al identified intraepithelial microcysts, density of subepithelial connective tissue, presence of blood vessels, and encapsulation as the important bleb parameters. The researchers linked quantity of intraepithelial microcysts and density of subepithelial connective tissue to bleb functionality. Increased number of microcysts and wide spacing of subepithelial connective tissue was linked to good functioning and dense connective tissue layering to nonfunctioning blebs. Tissue level images provided by IVCN depicted microcystic changes more clearly than even AS-OCT imaging.

C. Impression Cytology

Impression cytology is used in conjunction with IVCM to identify cellular characteristics that corresponded to IVCM appearance and bleb function19. Goblet cells with weak or no MUC5AC immunostaining were identified as key cells predicting functionality. These goblet cells were numerous on surface of functional blebs and corresponded to microcysts observed with IVCM. In non-functional blebs the numbers of these cells was very low numbers and highly stained goblet cells were seen outside bleb limits. The authors suggested that numerous goblet cells corresponded to microcysts, were probably channels for aqueous passage and represented transconjunctival outflow.

D. Anterior Segment Optical Coherence Tomography (AS-OCT)

Anterior Segment Optical Coherence Tomography is a noncontact method providing cross-sectional, three-dimensional, high-resolution images of anterior segment of the eye, with an axial resolution ranging from 3 to 20μm. Since AS-OCT provides qualitative
and quantitative assessment of the iridocorneal angle, it is used to evaluate anatomical variations of these structures after glaucoma surgery and to assess bleb features and functionality. Two OCT platforms are currently available: time domain (TD-OCT) and spectral domain (SD-OCT).

- **Time domain OCT**

  Visante OCT (Carl Zeiss Meditec, Inc., Dublin, CA), with scanning speed of 4,000 axial scans per image, image acquisition rate of 8 frames/sec, axial resolution of 18-25μm and a lateral resolution of 60μm.

- **Spectral domain OCT**

  RTVue (Optovue, Inc., CA), Cirrus (Carl Zeiss Meditec), Spectralis (Heidelberg Engineering, Inc.) and Casia SS-1000 OCT (Tomey, Nagoya, Japan). Spectral domain platforms score over time domain by yielding high-resolution images (similar to histological preparations) with a scanning speed of 26000 to 40000 A-scans per second leading to reduction in measurement time and examination duration. Dedicated software permits a three-dimensional assessment of conjunctival bleb but optical cross-sections obtained have less resolution images (similar to histological preparations) with a scanning speed of 26000 to 40000 A-scans per second leading to reduction in measurement time and examination duration. Dedicated software permits a three-dimensional assessment of conjunctival bleb but optical cross-sections obtained have less resolution than intensity of OCT signal with the term 'thickening' is used in for linear dimension of height rather than intensity of OCT signal with the

- **Type B** Features a thin wall and multiple large fluid-filled spaces
- **Type C** Features multiple, irregular fluid-filled spaces

Again, presence of fluid-filled spaces correlated well with good IOP control.

The bleb features highlighted by various studies using OCT are summarized below:

**i) Bleb height**

High or moderate height blebs have been associated with low IOP with contrasting results by few studies showing positive correlation between bleb height and IOP. Authors of latter findings hypothesized pushing effect of IOP in elevating the bleb. Few authors however have not found any significant correlation between bleb height and IOP. A study conducted at our institution showed no significant correlation between bleb height and IOP (Figure 4).

**ii) Presence of Macrocysts and microcysts**

Fluid-filled microcystic spaces seen on OCT represent degree of transconjunctival aqueous flow and correlate with functioning of blebs. Presence of macrocysts (fluid filled cavities under bleb wall) have also been described as part of the functional bleb spectrum. While these micro and macrocysts are present between scleral surface and bleb wall, microcysts have also been noted in functional bleb walls and called as superficial microcystic spaces. A study by Khamar et al showed that bleb walls with multif orm wall reflectivity, multiple internal layers with presence of microcysts to be more effective filters. A significant positive correlation between IOP control and microcystic spaces was noted in a study conducted at our institution (Figure 5).

**iii) Internal structure of bleb**

Ample number of studies concluded that AS-OCT resolution was significant in evaluating bleb internal structure. The sclerostomy could be well appreciated in functioning blebs for patency and size in few reports. Scleral flap and aqueous route under it were delineated by Visante OCT with its visibility being related positively to bleb function. In most failed blebs structural cause of failure such as internal ostial occlusion, apposition of conjunctiva-episclera to sclera or apposition of scleral flap to its bed were documented (Figure 6).

**iv) Internal reflectivity of bleb**

Functioning blebs show low OCT signal and slack internal texture, while nonfunctioning ones deliver high OCT signal and dense internal texture. Low internal reflectivity of the bleb as well as it’s wall has been regarded as a good sign in terms of bleb function. High internal reflectivity indicates bleb scarring and OCT serves to assess the postoperative healing process with possibility of early intervention in cases of impending scarring. Pfenninger et al reported a significant direct correlation between reflectivity of the fluid-filled cavity and IOP. Positve correlation between bleb height and vascularity of IBAGS and bleb reflectivity by AS-OCT has been documented by Fahrie et al. Our experience echoes this finding (Figure 7).

**v) Bleb wall thickening**

The term ‘thickening’ is used in for linear dimension of height rather than intensity of OCT signal with the

---

*Figure 4: OCT guided measurement of bleb height and wall thickness*

*Figure 5: Bleb with microcysts- clinical (a), OCT (b). Bleb with macrocysts- clinical (c), OCT (d)*
Singh K et al. Morphology of Trabeculectomy bleb: A review

The latter indicating density of tissue in bleb wall. Thickening of bleb wall is found to correlate with functionality. However, one study demonstrated a positive correlation between wall thickness and higher IOP. This difference of opinion could be due to different definition of wall thickness.

In summary, well-functioning blebs are diffuse, moderate high with low internal reflectivity, microcysts, macrocysts and have thick walls.

More recent studies examining additional properties of blebs such as phase retardation, bleb ooze, and bleb tear fluid sign report that these features of the bleb are also associated with lower IOP.

E. Anterior segment polarization-sensitive OCT (PS-OCT)

Anterior segment polarization-sensitive OCT (PS-OCT) has been recently used as a noninvasive method of evaluating phase retardation in blebs. Phase retardation is the phase difference induced by tissue birefringence. Based on SS-OCT technology PS-OCT can evaluate birefringence by imaging phase retardation of biological fibrous tissues and offers an excellent method of evaluating intrableb fibrosis not feasible with conventional AS-OCT. Thus it is useful in determining potential antifibrotic treatment for blebs.

Filtering bleb morphology following GDDs

Jung et al. observed a significantly lower maximum bleb-wall thickness in successful Ahmed glaucoma valve (AGV) implantation eyes compared to unsuccessful AGV implants, most likely due to presence of silicone drainage device impeding direct absorption of aqueous by the conjunctiva. In addition, the authors noted functionality to be inversely linked with bleb wall thickness, in that thinner walls had lower IOP, a finding opposite to that seen in trabeculectomy. Also, other authors couldn’t identify microcysts and collections of multiloculated fluid cavities within the bleb wall above the plate of the valves, which are commonly seen in trabeculectomy. Therefore, the bleb morphology above the drainage valve plate was similar to that of encapsulated blebs after unsuccessful filtration surgery with a fluid-filled space surrounded by a connective tissue with a high reflectivity, suggesting that aqueous reabsorption is only in part linked to the bleb drainage ability.

Limitations of AS-OCT

One of the major limitations of AS-OCT in assessing filtering blebs is that it does not provide microscopic information, which is essential for detecting early signs of failure, such as the stromal collagen deposition and the reduction of AH filled epithelial microcysts. Moreover, features indicative of bleb inflammation (dendritic cell activation and lymphocyte infiltration) or infection (infiltration of mononuclear inflammatory cells) cannot be detected.
reflectivity (R) and his Bleb OCT images showing thinner bleb wall, fewer microcysts with moderate internal reflectivity (R)

Figure 8: Clinical photo of an operated tube shunt (AGV) in a young male with aphakic glaucoma (L) and his Bleb OCT images showing thinner bleb wall, fewer microcysts with moderate internal reflectivity (R)

REFERENCES

Ocular Blood Flow in Context to Glaucoma: Major Review

Dr. Mainak Bhattacharyya1 MS, DNB, Dr. Kirti Singh1 MD, DNB, FRCSE, Dr. Nikhil Gotmare1 MBBS, Nishu Raj2 DMRD, DNB

1. Glaucoma Services, Guru Nanak Eye Centre, New Delhi, India
2. Department of Radiodiagnosis, G.B. Pant Hospital, New Delhi, India

Abstract: While the role of intraocular pressure (IOP) in the causation of glaucoma is well established, and current treatment of glaucoma aims to reduce IOP to a target pressure low enough to prevent or significantly slow progression, the role of optic nerve and retinal blood flow with subsequent ischemia in glaucoma is still subject of much debate. Ocular blood flow is highly regulated in order to adapt to changing metabolic needs during changing visual function, to compensate for varying perfusion pressures and to keep temperature at back of eye constant. Evidence exists that glaucoma patients clearly have abnormal autoregulation. This has led to a change in treatment algorithms from having medications lowering IOP to those improving ocular perfusion dynamics, influence vascular dysregulation or protect neural cells directly especially in those with disturbed autoregulation.

The recent role of CSF has placed another player in the delicate balance of perfusion at optic nerve head, the site of much activity and end damage.

The pathogenesis of glaucomatous optic atrophy has remained a matter of controversy since the mid-19th century. In 1858, Muller proposed that elevated IOP led to direct compression and death of the neurons (mechanical theory), while von Jaeger suggested that a vascular abnormality was the underlying cause of the optic atrophy (vascular theory). In 1892, Schnabel proposed another concept in the pathogenesis of glaucomatous optic atrophy suggesting that atrophy of neural elements created empty spaces, which pulled the nerve head posteriorly (Schnabel’s cavernous atrophy). Initially, the mechanical theory received the greatest support until LaGrange and Beauvieux popularized the vascular theory in 1925.

While the role of intraocular pressure (IOP) in the causation of glaucoma is well established, and current treatment of glaucoma aims to reduce IOP to a target pressure low enough to prevent or significantly slow progression, the role of optic nerve and retinal blood flow with subsequent ischemia in glaucoma is still subject of much debate. In the 1990s, Hayreh, Drance, and others raised the important issues of systemic hypotension and nocturnal blood pressure dips in the progression of glaucoma and the desirability of accurate clinical measurements of ocular blood flow. Interest in such issues has gained momentum in light of recent epidemiologic data concerning low blood pressure and low calculated “ocular perfusion pressure” as risk factors for both the development and progression of glaucoma.

RISK FACTORS IN GLAUCOMA

Intraocular pressure control still rules as being the most important risk factor in glaucoma genesis and progression, and focus on it is partly due to its measurability and treatability. Other risk factors associated with glaucoma implicated by multitude of authors over the years have been systemic and ocular. In the systemic factors increasing age, race, gender (with predilection for males in OAG and females in AG), basal metabolic rate BMI and systemic co morbidities like diabetes. The ocular risk factors include disc dimensions with increased cup-to-disc (CD) ratio and disc crowding, visual field indices, central corneal thickness and concurrence of certain oculo-systemic morbidities like pseudoexfoliation syndrome.

The risk factors implicated by proponents of blood flow etiology have been ischemia, vascular dysregulation and low ocular perfusion pressure (OPP).

RELEVANCE OF OCULAR BLOOD FLOW IN GLAUCOMA

Evidence from landmark epidemiological trials of glaucoma has been equivocal in their inferences of blood flow implication in glaucoma. The Baltimore Eye Survey found that patients with DPP lower than 30 mmHg had six times higher risk of disease development versus DPP higher than 50 mmHg. The Barbados Eye Study corroborated this and averred that individuals with lowest DPP (20%) were 3.3-times more likely to develop glaucoma. The Egna-Neumarkt Study also reported a 4.5% increase in glaucoma prevalence in patients...
of DPs less than 50 mm Hg compared to patients with DPP greater than or equal to 66 mmHg.21 Despite the fact that these studies targeted populations of variable ethnicity and age, the common theme of reduced DPP as an important risk factor for the development of glaucoma emerged from them.

On the other hand, the Beijing Eye Study was the only epidemiological study that found no association between OPP and OAG prevalence, neither in univariate nor in multivariate analyses.29 The Rotterdam Study found that low DPP (<50 mmHg) showed an inverse association with NTG only in subjects treated for systemic hypertension, and the association between OPP and OAG was significant only when the analysis was not adjusted for IOP i.e. OPP appears to be associated with incident OAG, because IOP is a part of OPP.17

RELEVANT ANATOMY

Blood supply of ONH

Arterial supply of four divisions of optic nerve head correlate roughly with a four-part vascular supply::

i) The surface nerve fibre layer is mainly supplied by arteriolar branches of the central retinal artery (CRA) which anastomose with vessels of prelaminar region and become continuous with peripapillary retinal and long radial peripapillary capillaries. One or more of ciliary-derived vessels from the prelaminar region may occasionally enlarge to form a cilio-retinal artery (15-25% cases).

ii) The prelaminar and laminar regions are supplied primarily by short posterior ciliary arteries (SPCA) which form a perineural, circular arterial anastomosis at the scleral level, called circle of Zinn-Haller.

iii) The retrolaminar region is supplied by both ciliary and retinal circulation, with the former coming from recurrent pial vessels.

Retinal and choroidal circulation

Retinal layers are supplied by the central retinal artery, a branch of ophthalmic artery. Retinal circulation has certain unique characteristics which have implications in blood flow dynamics and treatment options. These are:

a. Retinal circulation lacks autonomic innervation
b. Retinal circulation is characterized by a low level of flow and high level of oxygen extraction.

The lamina cribrosa is the critical border between intraocular and orbital spaces, which determines the pressure and vascular gradient across optic nerve head. Translaminar pressure difference (TPD) is the term given to difference between IOP and optic nerve cerebrospinal fluid pressure (CSF). This aspect was highlighted by landmark study of Jonas et al who postulated that variations in this pressure difference (TPD) apply damaging force to optic disk.2 The authors concluded that low CSF pressure could be associated with normal (intraocular) pressure glaucoma and low systemic blood pressure, particularly at night, could physiologically be associated with low CSF pressure, leading to an abnormally high trans-LC pressure difference. Also, patients with normal pressure glaucoma as compared with patients with high-pressure glaucoma have a significantly narrower orbital CSF space and hence lower CSF pressure.

RELEVANT PHYSIOLOGY

ESPECIALLY-AUTOREGULATION

Ocular blood flow is highly regulated in order to adapt to changing metabolic needs during changing visual function, to compensate for varying perfusion pressures and to keep temperature at back of eye constant. Autoregulation of blood flow adjustment can be classified into two types static and dynamic according to responding rate. Static autoregulation involves several diverse factors, including myogenic, neurogenic, and metabolic factors; dynamic autoregulation is an instantaneous process facing up sudden variation in perfusion pressure. Dynamic autoregulation of outer ocular vascular system has been extensively studied and revealed a rich sympathetic innervation in the outer ocular vessels. Whether the same can be extrapolated for ONH blood flow is uncertain but if so, it would be of immense relevance in glaucoma, where IOP fluctuations could impair blood flow and/or its regulation more than arterial pressure fluctuations.

GLAUCOMA AND BLOOD FLOW

PATHOLOGY

Evidence exits that glaucoma patients have abnormal autoregulation. A lack of autoregulation, a vasospastic reaction to stimuli such as psychological stress or cold, has been considered as a possible contributing factor to OAG, particularly without associated IOP changes. There is evidence indicating that disturbed autoregulation in glaucoma, results in the retinal vascular parameters response to OPP changes to be more passive, elevating to the higher level when the OPP rises or reducing to the lower level if the OPP drops.

The circulatory beds impaired in open angle glaucoma patients have been identified as retrobulbar, optic nerve head (ONH) and choroidal. Vascular deficits involving any of these circulations may in fact be one of the early manifestations of glaucoma. In addition vascular dysregulation, which in itself can cause vasospasm, also plays a pivotal role in glaucoma pathophysiology, and it has been proposed that OBF disturbances are partly related to systemic vascular dysregulation. At cellular level vascular disturbances result in endothelial dysfunction, which in turn manifests by an imbalance of vasoactive substances such as nitric oxide and ET-1 (endothelin-1), which has been observed in glaucoma patients.
Ocular perfusion pressure (OPP) is defined as arterial blood pressure (BP) minus IOP. Ocular perfusion pressure (OPP) is generally calculated as two-thirds of mean arterial pressure minus IOP. Occasionally, OPP is further divided into systolic perfusion pressure (SPP = SBP minus IOP) and diastolic perfusion pressure (DPP = DBP minus IOP). Low DPP has been reported as an independent risk factor for development of glaucoma and is often used in clinical practice instead of the more complicated MOPP.

Mean OPP = 2/3 × (Diastolic BP + 1/3 × (Systolic BP - Diastolic BP)) - IOP

Systolic OPP = Systolic BP - IOP

Diastolic OPP = Diastolic BP - IOP

**TECHNIQUES TO MEASURE OCULAR BLOOD FLOW**

The methods of measuring ocular blood flow may be classified into noninvasive and invasive techniques. Noninvasive techniques include color Doppler imaging (CDI), laser Doppler velocimetry (LDV), laser speckle technique, laser Doppler flowmetry (LDF), retinal function imaging, retinal vessel analyzer (RVA), retinal oximetry, blue field entoptic technique, Doppler Fourier domain optical coherence tomography (Doppler FD OCT) and optical coherence tomography angiography (OCT A) while invasive techniques include scanning laser ophthalmoscopic angiography with fluorescein and/or indocyanine green (ICG) dye.

The following section describes cardinal principles and techniques of various imaging devices.

**Color Doppler imaging**

Color Doppler imaging (CDI) is an ultrasound technique using a combination of B-scan gray scale imaging of an anatomical detail, colorized representation of blood flow using Doppler shifted frequencies, and velocity data obtained from Doppler shift of moving red blood cells (Figure 1). The technique utilizes a phased array transducer in a pulsed Doppler mode with an ultrasound frequency of 6.5 MHz and has been used to study retrolubar vessels such as the ophthalmic artery, short posterior ciliary arteries and blood vessels inside the eye including central retinal artery/ vein, vortex veins, vessels supplying ocular tumors, vessels in detached retina, and vitreoretinal neovascular membranes.

These individual vessels are visualized using Doppler frequency shifts from specific sample volume. This sample volume is placed over a vessel of interest, and frequency shifts received are assembled into a spectral wave form. This spectral wave form represents the cumulative frequency shifts present is displayed as a time-velocity wave form.

The velocities present in the sample volume follow the cardiac cycle, allowing measurements to be taken at the peak of systole; peak systolic velocity (PSV) and at lowest point of diastole; end diastolic velocity (EDV). Both these measurements are dependent on angle subtended between probe and vessel, the Doppler angle. Since PSV and EDV are both dependent on Doppler angle used in the Doppler formula, they are to an extent operator dependent. Relation of systolic and diastolic velocities are depicted by a ratio, the resistive index, (Poircelot’s index). This ratio is angle independent and is regarded as a good method to quantify vascular resistance of vessel studied.

Apart from glaucomatous pathology, CDI has been used in study of various retinal diseases including diabetic retinopathy, vascular occlusions, ocular ischemia and retinopathy of prematurity. An effective method for assessing large arteries, CDI is subject to several limitations. If the gains are too high or Doppler display threshold is too low, noise overwhelms the image. As mentioned before it is angle and hence operator dependent. It needs to be remembered that Doppler imaging describes blood flow velocity at specific points in the vascular tree, it does not measure blood flow per se, which would require vessel diameter dimensions for calculation.

**Laser Doppler Velocimetry (LDV)**

Bi-directional LDV allows for assessment of absolute blood flow velocities in retinal arteries and veins. A red diode laser of 675 nm wavelength is used to measure up to a maximum velocity of 120 mm/second. The technique is based on Poiseuille principle and Doppler effect; which says that when a vessel is illuminated with a high coherent laser beam, there is a change in frequency due to the reflected light. This change in frequency is directly proportional to velocity of blood flow. Thus, for each vessel, maximum velocity, which corresponds to frequency shift at vessel center, is calculated. The technique measures center line blood velocity (mm/s), vessel diameter (m), cross-sectional area and thus total blood flow (l/min)²⁹. The main drawback of this method is that it is confounded by eye motion and centerline displacement along with tear film break up, upper lid obstruction, inadequate dilation, image blur due to media opacities; and it cannot be used to measure optic nerve head circulation.

**Laser Speckle Technique**

The technique uses a fundus camera with a diode laser, image sensor; infrared charge-couple device camera (CCD), and a high resolution digital CCD camera. When a coherent laser light is dispersed from a diffusing surface i.e., retinal, choroidal vessels and circulation of ONH, it results in a rapidly varying pattern; this rate of variation can be utilized to determine retinal blood cell velocity, which can be...
quantified to ascertain retinal blood flow. The variation pattern depends on flow of blood cells in tissue, higher the blood flow, greater is rate of variation.

This technique generates two dimensional images of blood flow with high spatial and temporal resolution. The major limitations are: it measures only relative blood flow velocities and does not assess vessel diameter. The flux values cannot be compared directly in different eyes, and the values cannot be compared in the same eye at different times since the scattering properties of the tissue may not be the same in the setting of pathology.

**Laser Doppler flowmetry**

The laser Doppler flowmeter is a laser Doppler device with a modified fundus camera and a computer that quantifies retinal and choroidal flow. It has been described in two modes: (a) Continuous mode wherein Doppler signal is continuously recorded online after focusing the laser on a discrete area; a relative measurement of mean velocity and (blood flow) BF volume can be obtained. (b) Scanning mode where fundus camera combined with scanning laser tomography provides a two-dimensional image of ONH and retina depicting erythrocyte flux in capillaries of optic disk, as well an intensity image of perfused vessels.

**Retinal Functional Imager**

The device identifies motion of red blood cells in retinal vessels by comparing several images of retina taken under green light within a very short time interval. The prototype RFI system (RFI 3005, Optical Imaging Ltd., Rehovot, Israel) is based on a standard fundus camera extended by a customized stroboscopic flash lamp system and a digital camera. The device also provides a means to image capillary perfusion map with foveal avascular zone, along with an option to measure vessel oxygenation and even metabolic mapping of retinal tissue. It is limited by the fact that it provides only flow velocity data and not flow volume information due to inaccuracy of vessel width measurement.

**Blue field entoptic technique**

This method utilizes the blue field entoptic phenomenon, which manifests due to difference in absorption properties of red blood cells and leukocytes. It measures number, velocity, and pulsatility of leukocytes in perilveolar vessels of retina. An inherently subjective method, it requires patient cooperation for accurate measurement.

**Retinal Oximetry**

This technique measures relative oxygen saturation in retinal blood vessels. Oximetry requires the capture of images at two distinct wavelengths at about 600 nm (sensitive to oxyhemoglobin) and about 570 nm (not sensitive to oxyhemoglobin). Comparison of difference in brightness of reflectance from vessels at these two different wavelengths provides an indirect assessment of level of oxygenation.

**Scanning laser ophthalmoscopic angiography**

Scanning laser ophthalmoscopy (SLO) produces dynamic high resolution retinal images at lower retinal irradiance than conventional fundus photography. It can be used for both fluorescein angiography (FA) and ICG angiography. It increases the temporal resolution for visualizing the hyper and hypo-florescent segments in perifoveal and superficial ONH capillary circulation. In ONH three types of defects have been described: (a) local filling defects (b) slow filling and (c) increased leakage. In patients with glaucoma, SLO angiography has shown reduced total retinal blood flow and dye leakage from ONH capillaries suggesting peripapillary ischemia.

**Doppler Fourier-domain Optical Coherence Tomography**

Doppler OCT provides information about three-dimensional anatomy of retina and also Doppler shift of reflected light from vascular structures, which is used to evaluate blood flow. The most commonly utilized instrument for Doppler OCT acquisition is the RTVue FD-OCT. For blood flow measurement, only peripapillary veins are considered since arteries cause multiple phase wrapping issues due to their faster velocities. For Doppler OCT, in addition to magnitude of Doppler shift itself, Doppler angle is also necessary for computing flow velocity. Phase detection caused by retinal blood flow has been incorporated into the prototype system by creating two circular scans comprising two concentric rings 3.4 and 3.75 mm in diameter centered on the ONH. It is a noncontact, noninvasive technique which measures total volumetric RBF. Limitations of this technique is by eye motion and tear film disturbance.

**Optical Coherence Tomography Angiography (OCT-A)**

This is a noncontact imaging technique that allows visualization of retinal and choroidal vasculature sans dye injection. The motion of red blood cells is detected as intrinsic contrast, with sensitivity to both transverse and axial flow in time. This tool is capable of evaluating optic disc perfusion and confirms attenuation of dense parapapillary microvasculature in both superficial layers and deeper lamina cribrosa in glaucomatous eyes. Flow index which is calculated by averaging decorrelation signals in OCT angiograms has high sensitivity and specificity in differentiating glaucomatous eyes from normal. Different OCT-A protocols available are - split spectrum amplitude-decorrelation angiography (SSADA), speckle variance and phase variance.

Limitations as for all imaging devices are lined to motion artifact (due to eye movements), attenuation artifact (due to loss of signal with depth), segmentation artifact (due to difficulties in selecting consistent boundaries), and projection artifact (due to decorrelation tails from more superficial vessels).

**SYSTEMIC FACTORS CONTRIBUTING TO OPP**

**Systemic hypertension and its treatment**

A meta-analysis concluded systemic hypertension to be a risk factor in development of POAG. This effect of blood pressure is modified by age, with a stronger association among older subjects. A study by Gangwani et al found 8% of adults with systemic hypertension to have concomitant glaucoma with normotensive glaucoma subtype being most common. The reason for this correlation with increased IOP could be either aqueous overproduction or impaired outflow.

The Baltimore Eye Survey reported an interesting finding of protective effect of systemic hypertension on POAG subjects younger than 60 years, and adverse effect on those older than 70 years. This was
hypothesized to result from no vessel damage in younger people resulting in improved perfusion in response to higher blood pressure, whereas older people with atherosclerotic narrowed vessels would respond to high BP by reduction of OPP and subsequent glaucomatous damage.

The effect of systemic antihypertensive medications on the incidence of POAG has been widely debated. (Table 1) Antihypertensive medication may cause non-physiologic hypotension, rendering systemic pulse pressure and OPP fluctuation wider in subjects with autonomic dysfunction, and causing ischemia-reperfusion damage to the optic disc in glaucoma pathogenesis.

The Thessaloniki Eye Study revealed that diastolic BP less than 90 mmHg (subsequent to antihypertensive treatment) to be associated with increased cupping and decreased rim area of optic disc as measured by Heidelberg Retinal Tomography in non-glaucomatous eyes\textsuperscript{85,87}. This finding was not seen in untreated group with diastolic BP of < 90mmHg, nor in group with diastolic BP > 90mmHg on antihypertensive treatment.

Rotterdam Eye Study confirmed lower diastolic perfusion pressure in patients on antihypertensive medication resulting in higher prevalence of hypertensive OAG; odds ratio for glaucoma being 4.68 for subjects taking antihypertensive medication with diastolic PP >50mmHg versus those having OPP > 65mmHg\textsuperscript{89}.

The type of antihypertensive drug linked to reduced OPP was studied by Harris et al and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, diuretics as mono or combination therapy were reported to be more significantly associated with larger cup size and higher C/D ratio compared to treatment naïve patients. Subjects on beta-blocker and/or calcium channel blocker on the other hand, were protected and did not exhibit similar cup damage\textsuperscript{89}.

**Arterial Stiffness**

Increased arterial stiffness has been recognized as an independent risk factor for cardiovascular diseases\textsuperscript{88} but its role in glaucoma pathogenesis is still debatable. Factors associated with arterial stiffness include central BP, arterial waveform analysis derived from pulse tonometry, and dynamic retinal vessel reactivity analysis to flicker light\textsuperscript{91,93}.

According to the Rotterdam Eye Study, participants with an increased pulse wave velocity, especially those with low carotid distensibility coefficient (both indicative of high arterial stiffness), had higher prevalence of POAG, but not for NTG. Another report however documented no difference in brachial-ankle pulse wave velocity among POAG or NTG patients and controls, when arterial stiffness was interpreted by parameter of brachial-ankle pulse wave velocity\textsuperscript{94}.

The inconsistency could be due to unstandardized research modalities to assess arterial stiffness and different proportions of open-glaucoma subgroups (POAG, NTG, and PAC).

**Nocturnal Dip**

Normal healthy people have physiological nocturnal BP reduction of about 5-10% at nighttime compared to daytime. The remaining individuals are classified as either non-dippers or over-dippers\textsuperscript{95,96}. Physiologic BP reduction at nighttime is caused by a reduction in sympathetic activity with a reduced amount of circulating catecholamine hormones, which can in turn lead to a decrease in heart rate, cardiac input and peripheral resistance. This response may be augmented or blunted in certain subsets of population with vasospastic disorders, orthostatic hypotension, atherosclerosis, or obstructive sleep apnea syndrome. Systemically, non-dippers have a high incidence of cardiovascular and vascular diseases, whereas extreme dippers show greater progression of asymptomatic cerebrovascular disease than physiologic dippers.

Few studies have documented increased tendency of VF progression in both non-dipper and extreme dipper group versus physiologic dipper group\textsuperscript{97} whereas others have found that exaggerated nocturnal BP fall to be the risk factor for progressive VF loss in glaucoma cases\textsuperscript{98,99}. The mechanism of how exaggerated nocturnal BP reduction affects development and progression of glaucoma is not clearly known. Yazici et al found excessive and repetitive nocturnal BP reductions to occur more frequently in some NTG cases compared to those with POAG or ocular hypertension\textsuperscript{100}. The hypothesis put forward by Choi et al states that nocturnal BP reduction affect circadian variability of ocular blood flow expressed in term of MOPP\textsuperscript{101}.

**Primary Vascular Dysregulation**

Insufficient or improper adaption of blood flow, despite anatomically healthy vessels and absence of a causative disease, is termed primary vascular dysregulation (PVD). Glaucoma patients are more vasospastic than controls\textsuperscript{102}. Vasospastic syndrome could interfere

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baltimore Eye Survey</td>
<td>5308</td>
<td>DPP &lt; 30 mmHg had a 6X increased risk of developing POAG compared to</td>
</tr>
<tr>
<td></td>
<td></td>
<td>individuals with DOPP &gt; 56 mmHg</td>
</tr>
<tr>
<td>Barbados Eye Study</td>
<td>3222</td>
<td>Lower OPP was associated with increased risk of OAG</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SPP ≤ 98 mmHg; RR = 2.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DPP ≤ 53 mmHg; RR = 2.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MPP ≤ 40 mmHg; RR = 2.6</td>
</tr>
<tr>
<td>Egna-Neumarkt Study</td>
<td>4087</td>
<td>Higher DPP was associated with decrease prevalence of POAG</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DPP &lt; 68 mmHg; OR = 1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>76 mmHg &lt; DPP &lt; 68 mmHg; OR = 0.33</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DPP &gt; 76 mmHg; OR = 0.29</td>
</tr>
<tr>
<td>Blue Mountains Eye Study</td>
<td>3654</td>
<td>Higher SPP (for each 10 mmHg) had a 10% increase in OAG prevalence</td>
</tr>
<tr>
<td>Beijing Eye Study</td>
<td>3222</td>
<td>No association between OPP and OAG risk</td>
</tr>
<tr>
<td>Rotterdam Study</td>
<td>5317</td>
<td>In subjects taking BP-lowering treatment, DPP &lt; 50 mmHg – OR = 0.25</td>
</tr>
</tbody>
</table>
with OBF in two ways; these patients tend to have lower blood pressure and may have periods of low perfusion pressure. Secondly, glaucoma patients often have disturbed autoregulation which might be a manifestation of the primary vasospastic syndrome. Reduced OBF might therefore in some cases be the result of an insufficient adaptation to low perfusion pressure. A study found the correlation coefficient between fundus pulsation amplitude and MAP to be higher in patients with glaucoma than in healthy control subjects implying lack of proper autonomic regulatory response in glaucoma. Harris et al also demonstrated presence of a reversible vasospasm specifically within the ocular vasculature of patients with NTG compared with normal control, using color Doppler imaging and hypercapnia.

Role of CSF pressure
Optic nerve has a surrounding sheath of dura mater, within which CSF circulates, accounting for its probable role in physiopathology of glaucoma. Glaucomatous damage to optic nerve could result from “retrorgade” atrophy (i.e. changes in CSF components due to compartmentalization syndrome), in contrast to “anterograde” injuries to retinal ganglion cells caused by elevated IOP.

Histopathologic study of enucleated eyes with acute glaucoma by Jonas et al. found lamina cribrosa to be thinner, distance between intraocular space and CSF shorter, and part of lamina cribrosa exposed to CSF to be wider than in control eyes. Berdal et al postulated that retrolaminar pressure correlates well with lumbar CSF pressure (measured by lumbar puncture) and found the latter to be 33% lower in glaucoma patients versus controls. Furthermore, NTG patients were found to have a lower CSF pressure and significantly higher translaminar pressure than POAG patients and/or controls. The correlation was established by Ren et al who reported glaucomatous damage extent to be more strongly correlated with translaminar pressure difference than with IOP or CSF pressure alone. Refined imaging by MRI reported smaller subarachnoid space around optic nerve in NTG patients than POAG cases or controls (suggesting that orbital CSF pressure is abnormally low in NTG). Reverse finding of larger optic nerve sheath diameter in NTG patients than control group was reported by computed tomography.

TREATMENT OPTIONS FOR IMPROVING OCULAR BLOOD FLOW

Anti-glaucoma Medications
When using antiglaucoma medications, one assumes that by reducing IOP, the OPP is immediately increased. However, several studies have demonstrated that the effects of antiglaucoma medications on OPP may be variable. Dallinger et al reported that carbonic anhydrase inhibitor (CAI) group of drugs benefit ocular perfusion. Acetazolamide has been reported to cause short-term improvement in visual field, and dorzolamide (topical CAI), increases optic nerve oxygen tension. Costagliola et al have reported in a crossover trial with 30 consecutive NTG subjects that latanoprost significantly increased mean 24-h OPP, whereas timolol did not, possibly due to accompanying reductions in BP, subsequent to its beta blocker activity.

Quaranta et al compared the short-term effects of timolol 0.5% twice daily brimonidine 0.2% twice daily, dorzolamide 2% three times daily and latanoprost 0.005% once daily on IOP, BP and DOPP after 6-weeks treatment. There was no significant difference in mean 24-hr DOPP between timolol and baseline while brimonidine induced a significant decrease in mean 24-hr DOPP. Dorzolamide and latanoprost both induced a significant increase in the mean 24-hr DOPP when compared to baseline.

Experimental Drugs
Adenosine receptor agonists are thought to increase aqueous outflow facility by remodeling ECM and shrinking TM cell volume. OPA-6566 is an adenosine A2a receptor agonist in phase I/II studies that in addition to promoting aqueous outflow facility mediates vasodilation. Development of OPA-6566 may be limited due to conjunctival hyperemia and tachyphylaxis.

Rho Kinase (ROCK) inhibitors reduce IOP by modifying TM endothelial cells and extracellular matrix (ECM) of TM, ciliary muscle, and Schlemm’s canal and increasing trabecular outflow facility through relaxation of these structures. ROCK inhibitors may have additional benefits in glaucoma management with reports of improved ocular blood flow and promotion of retinal ganglion cell survival. In fact, this vasodilatation leads to the common side effect, hyperemia, seen with all ROCK inhibitors. A new drug, AM40076 has been shown to have little associated hyperemia, making it a promising treatment option.

Dietary supplements
Ginkgo biloba leaf extract (GBE) is a dietary supplement used in a wide variety of vascular diseases whose core components include flavonoid glycosides, terpene lactones (ginkgolides), and other organic acids. In various studies, GBE has been shown to improve ocular blood flow and to slow the progression of normal-tension glaucoma.

Bilberry (Vaccinium myrtillus) fruit extract is another dietary supplement whose active constituents, anthocyanins and anthocyanidins, exhibit potent antioxidant activity. A recent two-year randomized, placebo-controlled study of glaucoma patients showed that daily oral administration of anthocyanins significantly slowed visual field deterioration and increased optic nerve head and retinal blood flow without increasing IOP.

Cod liver oil, a dietary supplement, contains vitamin A and omega-3 polyunsaturated fatty acids (PUFAs). Omega-3 fatty acids decrease IOP, increase ocular blood flow, and improve optic neuroprotective function and a combination of vitamin A and omega-3 fatty acids, has been proposed for the treatment of glaucoma.

Lifestyle and Environmental factors
Lifestyle and environmental factors that are associated with elevated IOP levels and altered blood flow include total body inversion/headstand posture yoga positions, tight neckties, playing high-resistance wind instruments, and caffeine consumption. In addition, psychological stress transiently and significantly increased IOP on a short-term basis, although its magnitude was less than that of a standardized Valsalva maneuver. Use of tight swimming goggles has been linked to elevate IOP.
by to 4.5 mmHg along with reduction of blood flow to optic nerve head by few authors [30,31,32] but negated by others [33,34].

Lifestyle choices that may lead to decreases in IOP include aerobic exercise [27] and alcohol consumption [28]. In non-smoking and healthy volunteers, aerobic exercise increased heart rate, systolic blood pressure and OPP, decreased IOP and diastolic blood pressure, but caused no change in ocular pulse amplitude [29]. Some studies have suggested smoking might be a risk factor for the development of glaucoma, yet a recent meta-analysis found no causal association [34].

CONCLUSION

Research over last two decades has conclusively proved reduction in blood flow in some glaucoma patients, especially NTG cases and those who progress despite normalized IOP. The recent role of CSF has placed another emphasis on NTG cases and those who progress despite normalized IOP.

REFERENCES

71. N. Collignon, W. Dewe, S. Guillaume, and J. Collignon-Brach, “Ambulatory blood pressure monitoring in glaucoma patients The nocturnal systolic dip and its relationship with disease progression,”


**Adherence to Glaucoma Medications: Strategies and use of Enabling Tools**

Parul Ichhpujani

*Government Medical College and Hospital, Sector 32, Chandigarh, India*

**Abstract:** Suboptimal medication adherence is one of the important factors that significantly affect the outcome of glaucoma treatment. This article aims to suggest a multipronged approach that may address the poor adherence rate. The salient strategy should be discussion between the treating doctor and patient regarding adherence, persistence, and practical aspects of drop administration. Strategies must not only aim to improve a patient’s involvement in their own care but should also be flexible, adapting to specific requirements and expectations of an individual.

**Key words:** Adherence, Compliance, Persistence, Glaucoma

**Defining Adherence**

The World Health Organization (WHO) defines adherence as, “... the extent to which a person’s behavior – taking medication, following a diet, and or executing lifestyle changes – corresponds with the agreed recommendations from a provider.”

This definition highlights the importance of good communication and an active involvement of the patient with the healthcare personnel.

Adherence is often used as a more patient-centered way to express how a patient is using the medications as prescribed, whereas “compliance” has been used as a physician-centered approach.

Compliance has more to do with the accuracy with which a patient follows the treatment plan as opposed to adherence which refers to the extent to which he/she continues the treatment.

**Adherence is quantifiable.** For example, a patient who is prescribed timolol twice daily in both eyes for 28 days (112 drops/28 days) and uses it once daily in both eyes for the first week (14 drops/7 days), then uses it twice daily in both eyes for two weeks (56 drops/14 days), and then stops using it for the last week (0 drops/7 days) would be 62.5% adherent (70 drops/28 days divided by 112 drops/28 days).

Medication persistency is defined as the total time on therapy. Persistence represents a measure of the time until the patient first discontinues a medication.

**Measures of persistency allow for some degree of patient noncompliance;** for instance, a patient who takes a daily-prescribed medication every other day is persistent with therapy, although his level of compliance is 50%.

**Patient adherence and persistency represent a pervasive problem in the care of patients with a chronic disease like glaucoma.**

**WHAT HAPPENS IN CASE OF NONADHERENCE?**

The typical course of glaucoma, the “silent thief of sight” —an initially asymptomatic, chronic process—sets the stage for suboptimal patient adherence. Patients with glaucoma are not reminded by the symptoms of the disease regarding the importance of taking prescribed medications. This is further compounded by medications that are associated with side effects, some of which can potentially reduce a patient’s quality of life.

Poor adherence and persistence leak leads to worsening of the disease. Sleath B and co-workers conducted a cross-sectional study and found that participants with adherence rates less than 80% have worse visual field defects than those with greater adherence rates.

**CAUSES OF NON-ADHERENCE**

The body of literature on adherence interventions in chronic diseases such as systemic hypertension and glaucoma shows there are myriad causes of nonadherence. The interventions to improve compliance need to be multifaceted and tailored to the individual patient.

In the Glaucoma Adherence and Persistency Study (GAPS), adherence was inversely associated with the cost of medication, travel and time away from home and job, the receipt of free samples from the clinician, race, the absence of appointment reminders, a lack of physician acknowledgment of medications’ adverse effects, no self-education about glaucoma, and a patient’s lack of understanding of the risks of missing doses of medication.

**HOW TO MEASURE ADHERENCE?**

Many a times ophthalmologists are not able to detect nonadherence, with one large study finding that approximately one-fifth of patients had non-adherence undetectable by their physician.

Some patients are not even aware of the name and proper dosage of the medication they are instilling. Clinicians must ask patients to name their drops or bottle cap colors and explain how they are using them. One of the way to ask about persistence is, “How often do you miss your drops?” rather than “Do you miss your drops?” The doctor may ask, “How many times in a week (or month) do you miss your drops?” or “Do you have more difficulty remembering in the morning or evening?” Slight changes in wording of the questions related to
adherence, may elicit a different answer and reveal the "truth". The clinician must ask open-ended questions in ask-tell-ask sequences.

An often overlooked issue is the supply of eye drops that insurance companies or government dispensaries allow patients to obtain. Many such agencies have a policy that an empiric number of drop bottles must last 90 days (3 months). However, daily eye drop usage is not a precise measurement, unlike daily prescribed pills. Although we know how many drops may be in a bottle or what the volume of an eye drop bottle is, the angle at which the patient administers a drop, and the force that he/she uses to squeeze the bottle and the temperature of the air when the bottle is squeezed, all influence the number of drops there are per bottle.

Patients resume administering a medication shortly prior to their appointment and continue briefly thereafter, a phenomenon known as "white-coat adherence" or the "dental floss phenomenon".

Without a biologic metabolite to measure, no "gold standard" for quantifying glaucoma medication adherence exists.

Glaucoma medication adherence can be measured in several ways, including self-report, pharmacy refill reports, electronic monitoring, and direct observation. Self-reporting is the most common way, but it is affected by selection bias and recall bias.

 Medication compliance has been measured using a variety of methods.
   a. Medication possession ratio: This is calculated as the number of days' supply the patient received divided by the number that should have been received if the medication had been taken as prescribed.
   b. Medication monitor: This is regarded as the gold standard in compliance measurement, as it provides the most objective data on patients' dosing histories.

Gaps in therapy can be quantified in terms of number and lengths of gaps over a given period. Although both medication possession ratio and gap analysis are useful tools, it is possible that a patient might appear adherent by one measure and nonadherent by the other. For example, a patient who struggles to properly instill an eye-drop and ends up using more drops by squeezing hard or instilling more number of drops than prescribed may request multiple bottles in the early months of commencing the treatment, leading to a high medication possession ratio. If the same patient later becomes frustrated with failed attempts to use the medication properly, he/she may not get a refill for the medication again for some time, leading to a gap in therapy.

Pharmacy records are only accurate in a closed pharmacy system and do not account for sample medications. In the GAPS, approximately 20% of patients reported routinely receiving samples.

**IS EDUCATING THE PATIENT ENOUGH?**

Patients that understand and believe in the necessity for eye drops are more adherent and studies that have targeted patient beliefs have been effective in improving adherence. Conversely, whilst poor glaucoma education has been cited as an explanation for non-adherence to treatment, interventions that purely focus on providing education have failed to achieve significant improvement in adherence.

A Cochrane database of randomized controlled trials on adherence in chronic medical disease such as diabetes, hypertension, showed that 19 of 39 interventions led to a statistically significant increase in patients' adherence to taking medication. The effective interventions usually involved multiple modalities and the increase in adherence were usually modest.

**MULTIPRONGED APPROACH FOR INCREASING ADHERENCE**

**Behavioural intervention**

Behavioural interventions aim to modify patients' behavior toward treatment.

Interventions are characterized by cognitive–behavioral techniques and therapies focused on dysfunctional emotions, behaviors and cognitions with the aim to promote healthy lifestyles, and positive changes toward symptoms and treatment.

Behavioural interventions seem to work best for non-adherent patients who regularly forget to take their medication.

1) Use of Electronic monitoring devices:

The Norwich Adherence Glaucoma Study (NAGS), was a randomised controlled trial with a 13-month recruitment and 8-month follow-up period, conducted in the Glaucoma Clinic of a UK National Health Service (NHS) teaching hospital.

Patients with Ocular hypertension/glaucoma who were starting treatment with travoprost were enrolled and randomised into two groups and adherence was measured over 8 months, using an electronic monitoring device (Travalert® dosing aid, TDA; Figure 1). The control group received standard clinical care, and the intervention group received glaucoma education and motivational support package using behaviour change counselling. Contrary to evidence from literature, whilst the NAGS intervention group were more satisfied with information received about travoprost, there was no measurable effect on adherence.

Devices such as the TDA may be an objective measure of adherence, but they assume that the eye drop will always be successfully administered; when all that can really be inferred is that the patient attempted instilling the drop at a specified time. Additionally, routine use of electronic adherence monitoring in clinical practice is not yet practical because of the prohibitive costs.

**Caution:** Hawthorne effect: In a study setup, participants are aware of adherence monitoring and this is likely to produce Hawthorne effect causing participants to be more adherent to their medication regimen.

**Switching to generic medication**

Patients may be embarrassed to tell the doctor that they cannot afford a medication but may reveal this important information if asked. Some patients adopt the "pill-splitting" technique of using one drop every other day of a once-daily medication to lengthen medication use. Switching to a lower-cost generic alternative or exploring pharmaceutical company coupons or rebates may help.
**Educational intervention**

Education is a cognitive didactic approach that includes teaching and providing information and knowledge. Different ways to educate patients include individual and/or group education by face to face communication with doctor/ counsellor, audio-visual aids; written letter, email, telephonic or SMS/Whats App group reminders, or occasionally via home visits. The GAPS showed that phone calls significantly improved patients’ keeping of appointments.

It is a good idea to watch patients instill drops, such as artificial tears, in the clinic. This allows the clinician to provide helpful suggestions such as to make the head horizontal, hold the bottle perpendicularly, close the eyelids or use punctal occlusion, and wait at least 5 minutes between drops.

Patients can improve their adherence to glaucoma treatment if properly educated. In a randomized controlled trial, Okeke et al used an educational video, a compliance meeting with a study coordinator, and phone calls and electronic reminders to increase patients’ use of medical therapy.

On each visit the clinician must ask about side effects (eg, redness, burning, stinging, blurred vision, or systemic side effects such as depression, shortness of breath, etc.). If a patient is experiencing a side effect, then a change in medication may improve his or her adherence. If the problem and medication are clearly unrelated, then correcting this information may prevent non-compliance. For example, a patient who complains of somnolence but is not using Brimonidine may blame any new medical problem on his or her eye drops. The clinician must clarify what is and is not related to an adverse effect of a patient’s specific medication, which can help him or her to be compliant with therapy.

**Self-management intervention**

The self-management encompasses multiple concepts, such as self-care, self-monitoring, adherence and health behavior change. The use of technological devices in self-management interventions is increasing. Technology-based self-management includes telephone support/counseling, telemedicine/home telecare/telemonitoring, web-based interventions/interactive computerized health communication and cell phones/text messaging.

One must not forget that access to these technologies are generally associated with younger age, higher education, and higher income group patients. Smartphones offer several drug reminder applications (Figure 2).

Given that glaucoma patients are generally older and may have barriers to adoption of technology and sustainability is an important issue on self-management interventions, they can associate medication with their daily routine. Examples include:

- Setting a cell phone alarm
- Keeping an extra bottle at work
- Putting the bottle on the bedside table or by the toothbrush
- Associating dosing with daily activities such as taking a systemic medication or at dinnertime
- Keeping the bottle where the patient puts down his/her watch to associate taking at the same time
- Ask patients to keep a calendar and check off when drops are instilled or keep a Medication reminder chart (Figure 3)

**HOME MONITORING**

These days smartphones are being used for IOP monitoring and vision testing. Several companies are testing implantable IOP sensors that communicate with a smartphone, which can automatically send encrypted data to the cloud for analysis and IOP fluctuations can indirectly be helpful to increase adherence.

To conclude, to avoid overuse, underuse and misuse of medications, a multipronged approach needs to be followed. Hospital staff, family members, media resources, and frequent adherence assessments, may help improve adherence to glaucoma treatment.

**REFERENCES**

3. Sleath B, Blalock S, Covert D, Stone


10. Lacey J, Cate H, Broadway DC: Barriers to adherence with glaucoma medications: a qualitative research study. Eye (Lond). 2009;23: 924-932.


MANAGEMENT OF GLAUCOMA: A TEAM WORK!

Glaucoma is the third largest blindness causing disease and in India, the estimated number of cases of glaucoma is 12 million, around one fifth of the global burden of glaucoma. The vast country has around 15,000 ophthalmologists and another 15,000 optometrist active in clinical practice. We do not have many specialized eye centers which can cater to the advanced investigations required for apt management of glaucoma patients.

Today, it is estimated that around 50% of the optometrists are working in eye hospitals and have some clinical role. They are the primary eye care providers and do history taking, vision assessment refraction and primary comprehensive glaucoma workup including gonioscopy, tonometry and visual fields; Ophthalmologist in their busy schedule can leverage their time and expertise in medical and surgical management of advanced disease or complex glaucoma cases.

Thus, the effective management of Glaucoma can be archived by pertinent teamwork doctrine. Optometry role is varied and new and may need extensive education and training to impart such service. Communication of this message to both optometrist and ophthalmologist is important.

Co management in evaluation - MERGING IT ALL TOGETHER

Qualified Optometrists are well trained in all basic evaluation and associated advanced investigation like OCT, HRT, GDX. They can also assist the surgeon in laser therapy.

Glaucoma involves continuous follow up care and compliance with therapy specially when involved in the medical therapy. Studies found that patient's compliance to medication is poor because they do not understand the benefit or risk of the treatment. Reinforcement of treatment and creating seriousness of Glaucoma is imperative which can be done by the optometrists.

Optometrist as a primary health care provider can educate and counsel patients on importance of follow up care and enhance compliance by reviewing it on follow ups. The Ophthalmologist in their busy schedule can utilize this time in medical and surgical management of glaucoma patients.

Monitoring of Intraocular pressure and Optic nerve head assessment, visual field and vision assessment is basic which must be done on each follow up. Effective teamwork of ophthalmologists and optometrists can ease this task of comprehensive eye check up during each follow up visit.

Early detection: CATCHING THE RISK

Key to successful management of glaucoma is early detection. In a study done in urban Chennai the awareness of Glaucoma was lowest in the population, overall 8.7% had some knowledge about it.

The optometrist, being the first line of contact with the patient could detect the glaucoma and refer patient to the ophthalmologist for further intervention.

The well trained optometrist can pick up symptoms of frequent changes in near glasses and unexplained headaches by a complete and concise history taking. Adding tonometry, evaluation of Disc and Angle as a routine protocol of vision assessment and refraction helps in detecting many such underlying cases.

Thus, primary comprehensive eye and vision examinations may be the most cost-effective way to detect glaucoma in a high-risk population.

Abstract: Glaucoma is the third largest blinding disease In India, management of glaucoma requires a team work consists of physician and optometrist. With the involvement of qualified optometrist the management of this complex disease becomes facile. Optometrists are the primary eye care providers and do history taking, vision assessment refraction and primary comprehensive glaucoma workup including gonioscopy, tonometry and visual fields; Ophthalmologist in their busy schedule can leverage their time and expertise in medical and surgical management of advanced disease or complex glaucoma cases.

Thus, the effective management of Glaucoma can be archived by pertinent teamwork doctrine. Optometry role is varied and new and may need extensive education and training to impart such service. Communication of this message to both optometrist and ophthalmologist is important.

Dr. Sumit Grover DO, DNB, FICO, Dr. N.P. Singh MD, Prof. Monica Chaudhary M.Optom, FIACLE, Ms. Shreya Ghosh M.Optom

1. Dr. Baba Saheb Ambedkar Medical College and Hospital, New-Delhi, India
3. Department of Optometry and Vision Sciences, Amity University, Gurgaon, Haryana, India

4. Key to successful management of glaucoma is early detection. In a study done in urban Chennai the awareness of Glaucoma was lowest in the population, overall 8.7% had some knowledge about it.

The optometrist, being the first line of contact with the patient could detect the glaucoma and refer patient to the ophthalmologist for further intervention.

The well trained optometrist can pick up symptoms of frequent changes in near glasses and unexplained headaches by a complete and concise history taking. Adding tonometry, evaluation of Disc and Angle as a routine protocol of vision assessment and refraction helps in detecting many such underlying cases.

Thus, primary comprehensive eye and vision examinations may be the most cost-effective way to detect glaucoma in a high-risk population.
Low vision and Rehabilitation: ASSISTIVE TECHNOLOGY

Patients who have had severe or partial visual impairment can be rehabilitated by use of specialized optical, non optical and assistive devices. In India many institutions are growing day by day where the optometrists provide low vision and rehabilitation services. Low vision services work well in controlling the functional and psychological impacts of visual impairment in blinding diseases like glaucoma.

Non mydriatic fundus camera: USE OF GADGETS and TELEOPHTHALMOLOGY

With advancement in imaging techniques a non mydriatic retinal camera has proved to be sensitive in early detection of Glaucoma. Utilization of this as a routine for screening by optometrist can be the future trend which can help in early detection and prompt referral.

Referrals: EXPANDING HORIZONS

The optometrists may refer patients with skeptical appearance of the optic nerves and questionable visual fields. In this arrangement, the optometrist performs a battery of tests but the patient has access to needed expertise. Based on the stage of advancement treatment modalities are undertaken and thereby referral for the surgeries is accepted. The expanding role of optometry in glaucoma management is not a threat to either side of the referral equation.

CONCLUSION

To conclude, the effective management of Glaucoma can be achieved by pertinent teamwork doctrine. Optometry role is varied they may need extensive education and training to impart such service. Despite minimal resources and increasing number of patients eye care can be improved with healthy working relationship between Optometrist and Glaucoma physicians by utilizing their expertise and training to maximum potential. Communication of this message to both optometrist and ophthalmologist is vital.

REFERENCES

For Kind Attention of DOS Members
Non Receipt of DOS Times issue

DOS members not receiving DOS Times may please write to dosrecords@gmail.com with their details.

Call for contribution to DOS Times

* All DOS Members may send good quality manuscripts to me for consideration for publication in DOS Times – 2017-2019.
* Acceptance will be subject to editorial review
* Please refer to Author Guidelines for manuscript preparation
* Please note change in email address for all future correspondence to me.

Dr. Subhash Dadeya
MD
Secretary – DOS
dosrecords@gmail.com, dadeyassi@gmail.com
011-65705229, +91-9868604336
WhatsApp: 8448871622

Correspondence to:
Dr. Sumit Grover
Dr. Baha Sahib Ambedkar Medical College and Hospital,
New-Delhi, India
Relevance of Eagle Study: An Indian Perspective

Sonal Dangda MS, DNB, FICO, Joseph Panarelli MD

1. Centre for Sight, Safdurjang Enclave, Delhi, India
2. New York Eye and Ear Infirmary of Mount Sinai, USA

Abstract: Treatment in glaucoma aims to prevent future visual loss keeping in mind natural course of the disease. While current trend moves towards lens extraction, as the new treatment modality for glaucoma of anatomical origin namely angle closure, multiple opinions emerge. Keeping in mind the position of lens in anatomy of the anterior chamber angle, lens extraction does seem a reasonable option for widening the narrow angle. The EAGLE (Effectiveness of early Lens Extraction for the treatment of primary Angle closure Glaucoma) study looked further into whether this can be extrapolated to clear lens extraction in angle closure eyes and reported positively. This article aims to highlight its relevance on both the global and Indian scenario.

Primary angle closure glaucoma (PACG) is a multifactorial disease with ocular anatomy contributing in a major way to the frequency of this disease in Asia; where 87% of patients with PACG reside1. Not merely axial length, but iris configuration, lens volume and angle pathology all contribute to its genesis. The role of lens in angle closure is even more talked about today and lens removal is one such modality which has been in the forefront of many recent debates.

As is widely known, the etiopathogenesis of angle closure glaucoma is the presence of relative resistance to aqueous flow from posterior chamber to anterior chamber and this generates a pressure gradient which ultimately determines the iris contour and the resulting irido-trabecular contact2. The 'pinch region' or iris-lens channel between posterior iris surface and anterior lens surface is in turn determined by iris configuration, lens size and lens position3. Keeping in mind the above and role of lens in anatomy of anterior chamber angle configuration, lens extraction seems a reasonable option for widening the narrow angle. This has been amply documented with imaging studies confirming increased angle opening distance at 500um (AOD500) post-phacoemulsification, which correlates with improved anterior chamber dynamics4,5. In fact, lens removal surgery has always been known to be associated with reduction of intraocular pressure (IOP)6. Even in normotensive and primary open angle glaucoma (POAG) eyes, a beneficial effect on IOP has been noted after uneventful lens extraction7. For PACG eyes, the IOP response is much more with a mean reduction of 6mmHg documented by a recent report by American Academy of Ophthalmology (AAO)8. In fact, performing lens extraction as primary treatment modality to control PACG has been advocated in the past. The soaring popularity of the more elegant and less tissue destructive phacoemulsification procedure above the manual extracapsular cataract surgery (ECCE) over the last two decades has led to a phenomenal increase in reports confirming increased utility of lens extraction as a viable method for treatment of PACG. Others while corroborating role of lens in etiopathogenesis of glaucoma, advise caution in terms of patients who would ultimately gain, taking into consideration the severity of synechial angle closure and the amount of glaucomatous disc damage9.

However, the decision and dilemma to perform clear lens extraction for glaucoma is still unresolved. There are studies advocating extraction of incipient cataracts and clear lenses in patients with subacute or chronic angle closure glaucoma10,11. Tham et al noted that for medically uncontrolled PACG eyes without cataract, trabeculectomy is more effective in reducing dependence on glaucoma drugs but is associated with more complications.

In this regard, the recent multi-centric trial EAGLE i.e., Effectiveness of early Lens Extraction for the treatment of primary Angle closure Glaucoma, has generated quite a frenzy around the world and has garnered equally vocal proponents both supporting and questioning the practice. Before discussing its implications and relevance, to the Indian subcontinent in particular, a brief overview of the study is given below.

This multi-centric randomised control trial was conducted between Jan 2009-Dec 2011, at 30 hospitals over 5 countries, including Australia (1), Mainland China (1), Hong Kong (2), Malaysia (2), Singapore (2), and the United Kingdom (22). The patients included were 50 years and older, phakic and had newly diagnosed primary angle closure (PAC) with IOP more than 30mmHg or PACG.

PAC was considered as irido-trabecular contact, either appositional or synechial, of atleast 180° and considered PACG when associated with glaucomatous optic neuropathy and/or reproducible visual field defects with IOP higher than 21mmHg at least on one occasion. However, patients with advanced glaucoma (MD > -15dB or C:D > 0.9) were excluded. Also excluded were patients with symptomatic cataract, those with a history of acute angle closure attack or previous laser procedure or surgery.

The patients were randomly assigned to either Clear Lens Extraction (CLE) or standard care. In the CLE group, phacoemulsification with monofocal lens implantation was done while standard care involved Laser Peripheral Iridotomy (LPI) followed by topical medications and laser iridoplasty, depending upon the discretion of the treating physician, if angle closure persisted. While the need for glaucoma surgery was classified as treatment failure.

The aim was to study whether clear lens extraction would be associated with better quality of life indices, lower IOP and lesser need for glaucoma surgery than the present standard care after 36 months follow up period.

The study population comprised 419 patients of which 208 were in CLE group and 211 in standard care/LPI group.
Of these, females comprised 59% of the CLE group and 57% of LPI group; Chinese (Asian) ethnicity was 30% in both and the average age was 67 years. PAC comprised 38% (80/208) in CLE group and 36% (75/211) in LPI group, while PACG was 61% (127/208) and 65% (136/211) respectively.

The refractive error ranged from 0 to +3D; axial length was between 22.0-23.2mm while anterior chamber depth was 2.3-2.7mm and corneal thickness ranged from 522-582um.

Around 60% of patients in both groups were on one or more topical anti-glaucoma medications and the IOP was in the range of 24-33mmHg.

In the CLE group, baseline IOP of 29.5±8.2mmHg reduced to 15.7±4.3mmHg at 6 months, which was stable at 16.6±3.5mmHg at final follow-up of 36 months. In the LPI group, baseline IOP of 30.3±8.1mmHg reduced to 19.2±5.2mmHg at 6 months and remained at 17.9±4.1mmHg at the 36 month follow-up. Thus, the IOP scores, although marginally (1.18mmHg) but significantly (p=0.004) lower, favoured the CLE group.

The average number of medications required reduced from 1.0±1.0 to 0.4±0.8 in CLE group while it increased from 1.0±1.0 to 1.3±1.0 in LPI group. At the end of 36 months, 60% patients in CLE group and 20% in LPI group did not require any medications while 20% and 53% respectively needed 1 or 2 medications which went up to 10% needing 3-4 medication in LPI group. Visual field severity at 36 months was similar in the two treatment groups; worsened in 24 participants in the CLE group and 30 patients in LPI group.

Among patients who underwent CLE, 9% had viscosynechiolysis intraoperatively while in standard care group, 5% needed additional laser iridoplasty.

Out of 211 in LPI group, 24 patients needed additional surgery. Of these, 16 underwent lens extraction while 6 required trabeculectomy and 1 each needed i-Stent and Ahmed glaucoma valve. Of the 208 patients in CLE group, 1 patient required trabeculectomy while 3 required surgical interventions for post-operative complications. The intraoperative complications in the CLE group included Posterior Capsular Rupture, Vitreous Loss, Iris prolapse and a broken haptic while the most common post-operative complication was Macular edema followed by flat AC, malignant glaucoma, corneal edema and macular hole. Irreversible loss of vision of more than ten ETDRS letters was seen in one patient in CLE group and three in the standard care (LPI) group. Most common post-procedure complication in the LPI group was IOP spike, but macular edema, malignant glaucoma, flat AC and retinal detachment were also seen.

Looking at the above parameters, the clinical relevance of the small difference between the groups in terms of IOP (1.18 mm Hg) is unclear since the degrees of appositional and synechial angle closure were not reported in most. The extent of pre-operative synechial angle closure is an important parameter and needs to be assessed to determine beneficial effect of lens extraction, requirement of future filtration surgery and the extent of IOP reduction.

Keeping this in mind, Walland and Thomas in a recent review have questioned the practice of clear lens extraction and advocate a stepped up approach of LPI as the first resort followed by lens extraction, after a month only for eyes with uncontrolled IOP. They point out that clear lens extraction as treatment for PAC or PACG is dependant on the extent of any synechial closure, and may not obviate the need for trabeculectomy particularly in medically uncontrolled angle closure glaucoma.

Recent report from India by Dada et al also advocate similar approach where clear lens extraction was done in 44 eyes which were uncontrolled on medical treatment (IOP>25mmHg) post LPI. Complete success noted as IOP<18mmHg without medications at 12 months follow up, was seen in 86% patients.

A case series of 5 patients by Barbosa et al wherein CLE was attempted in patients uncontrolled after LPI and medications also noted complete success in 3 patients only. Synechial closure resulted in one patient being unresponsive even to medications, hence emphasising the need for an individualised approach.

The need for future intraocular surgery in patients undergoing LPI may suggest that many people treated with this approach will be at risk of future cataract extraction. It has been similarly reported previously with filtration surgery as well wherein Gunning and Greve noted need for additional incisional surgery in 80% of trabeculectomy group and requirement of subsequent cataract surgery in 75% versus only 27% further surgeries in phacoemulsification group. It can be safely said that the need for some cataract operations within 3 years is not surprising and this finding should not to be interpreted as an increased occurrence of an unfavourable outcome in the laser iridotomy group.

The other aspect to consider, however, is the chances of intra-operative and post-operative complications. Although techniques for phacoemulsification have become highly advanced and specialised, operating in eyes with anatomically shallower AC and thick lenses can be a challenge and hence require highly experienced surgeons. A blanket advocacy of CLE approach may do more harm than good, especially in elderly eyes with low endothelial counts. Also, the mere existence of a very good operation is not an indication for surgery. Hence, the risk of severe complications after CLE must be taken into account from the perspective of individual patients.

The EAGLE study excluded PAC patients with IOP <30mmHg. Hence, these findings cannot be extrapolated to that group of patients. For fellow eyes with cataract, phacoemulsification seems a reasonable option but for eyes without cataract, no justification exists for clear lens extraction instead of LPI, despite non-opening of angle fully after a LPI, since natural course of disease progression and risk-benefit evaluation do not justify clear lens phacoemulsification. The same holds true for primary angle closure suspects (PACS). Despite popular belief, utility of even LPI is being questioned in such eyes with normal IOP by an ongoing study, the ZAP trial, which is looking at the natural course of the disease. For eyes with minimal visual acuity or visual field loss and none/minimal optic nerve damage, surgical intervention for a mere restoration of normal angle anatomy does not justify rendering the patient a pseudophagic. Tarongoy et al in 2009 concluded that although favourable clinical reports about role of lens extraction for treatment of PACG exist, its appropriateness remains unproven both after and in lieu of LPI. Similarly, extrapolation to advanced PACG may not be wise as these patients were excluded from EAGLE study.

However, as previously noted, CLE might be considered an alternative to filtration surgery as an initial surgical option in treating medically uncontrolled iridotomized PACG eyes without co-existing cataract. Clear lens extraction may be preferred in patients who do not
accept the risk of filtration surgery or are very vulnerable its complications.

Also, as previously noted, lens as the culprit has been documented in PACG patients; it might be thicker and more anteriorly placed. Lens vault (LV), defined as the amount of lens situated anterior to a plane between the scleral spurs, is another aspect to be considered. The presence of a large lens vault or a thick lens tilts the clinical decision towards lens extraction for controlling the glaucoma.

QUALITY OF LIFE PARAMETERS

The other aspect emphasised by the EAGLE study was the health status. This was measured with European Quality of Life-5 Dimensions (EQ-5D) questionnaire which measures 5 dimensions of health - Mobility, Self-care, Usual activity, Pain/Discomfort and Anxiety/Depression at three levels - No/Some/Extreme problems, and assigns a preference based utility score. Additionally, Glaucoma Utility Index was used which provides a descriptive profile in six dimensions, namely, central and near vision, lighting and glare, mobility, activities of daily living, eye discomfort, and other effects of glaucoma and its treatment, each at four levels. The mean health status score (0.08 [SD 0.12]) on the European Quality of Life-5 Dimensions (EQ-5D) questionnaire, was 0.052 higher (95% CI 0.015 to 0.088, p=0.005) after CLE than after LPI. The uncorrected visual acuity improved greatly for distance and near vision in the CLE group only, who became emmetropic with mean final refraction of 0.08 whereas those assigned to LPI remained hyperopic with mean final refraction of 0.92. Also the need for anti-glaucoma medications reduced to 0.4 in CLE group compared to 1.3 in the LPI group. Both these factors may have favourably affected the Glaucoma Utility Index and this might have been associated with improvements in the patient reported outcome questionnaires. Similar reduction in IOP lowering medications has also been noted by Dada et al in their study of CLE after LPI in uncontrolled cases.

INDIAN PERSPECTIVE

As a general perception, the findings of this trial could have a positive implication in the areas where angle closure is most prevalent, like in Asia. Places where health-care resources are scarce and patients might not have easy access to medications and monitoring, a yet unproven potential additional benefit with CLE could be that early intervention may prevent blindness due to PACG.

India although a rapidly developing economy, still has areas where healthcare access and monitoring is difficult and the high prevalence of angle closure disease may sometimes tilt the favour for CLE. However, the above findings should be tailored to a cautious individualised approach.

AN INTERNATIONAL PERSPECTIVE (J. PANARELLI MD)

Though cataract surgery has improved over the last several decades, it is still a surgical procedure which carries risk and the stakes are always high. My preference is to perform this procedure when the patients note a decline in vision thereby impacting their ability to perform activities of daily living. Results from recent studies suggest that cataract surgery may actually be a reasonable “treatment” for both open and closed-angle glaucoma. However, most glaucoma specialists prefer to follow the classic glaucoma treatment algorithm, i.e. instituting medical and/or laser therapy first and proceeding with traditional glaucoma surgery if the intraocular pressure still remains too high, depending upon the stage and severity of the disease.

Likewise, when I see any patient with narrow angles, I perform a laser iridotomy first. If the IOP is elevated, I begin medications and will consider iridoplasty, specifically in those patients with plateau iris syndrome or nanophthalmos. In cases where there is a considerable synechial angle closure and the IOP remains too high for the degree of disc damage, I proceed with a filtration surgery.

Even though the results of the EAGLE study are fascinating, there are several critical points that should be considered. The cumulative complication rate/need for additional glaucoma surgery was similar in both groups. Second, given the average age, mean visual acuity, and fact that the lens caused angle compromise and IOP elevation, not all patients likely had a “clear lens”. Finally, given the strict inclusion criteria, the results of this study are not necessarily generalisable to a broader set of patients.

Although multi-center, prospective, randomized clinical trials provide the highest level of evidence, many clinicians still prefer to do what is best in their hands, even if it is in contrast to the conclusions drawn from these studies. In a previous survey of the American Glaucoma Society (AGS), we learned that there are many factors associated with a clinical trial which influence whether or not it has an impact on practice patterns; these include study timing, design, conduct, and interpretation of results. Thus, even the “landmark” studies need to be evaluated critically, repeated at times to confirm the findings and be applied to patients similar to the population studied. Each patient is different and needs to be evaluated as such!

REFERENCES


**Notice for General Body Meeting**

The General Body Meeting of the Delhi Ophthalmological Society will be held during the Annual Conference on Sunday, April 8th, 2018 at 4:30 PM at the Ashok Hotel, Chanakyapuri, New Delhi.

The Agenda of the General Body Meeting shall be:

1. Confirmation of the minutes of the previous Annual General Body Meeting held on July 30th, 2017.
2. Adoption of the Annual report of Executive Committee presented by the Hony. Secretary.
3. Ratification of New Members.
5. Report of the Editor DJO.
6. Report from the Representatives to the AIOS.
7. Presentation of Awards and Momentoes.
8. Suggestions & Resolutions for the General Body Meeting.
10. Address of the outgoing President.
11. Installation of the incoming President.
12. Address of the incoming President.
13. Any other matter with the permission of the Chair.
14. Vote of thanks by the Secretary.

All members are requested to attend.

Thanking you,

Sincerely yours,

Prof. Kamlesh
President, DOS

Prof. Subhash C. Dadeya
Secretary, DOS
Glaucoma is a group of disorders characterized by a distinctive optic neuropathy that leads to progressive asymptomatic visual field loss. It is thought that gradual loss of vision in glaucoma is due to irreversible retinal ganglion cell damage which leads to optic neuropathy. Glaucoma is currently the leading cause of irreversible blindness. Neovascular glaucoma (NVG) is a type of secondary glaucoma and is a challenging condition to treat (Figure 1). The main causes of NVG are ischemic retinal conditions, such as proliferative diabetic retinopathy (PDR), central retinal vein occlusion (CRVO) and ocular ischemic syndrome (OIS). New vessels (NV) that are formed at the iris and anterior chamber angle can cause mechanical obstruction leading to open angle glaucoma and later contracture of the fibrovascular membrane at the angle result in progressive angle closure and intraocular pressure (IOP) elevation.

Anti Vascular endothelial growth factor (anti-VEGF) agents have an established role in the treatment of retinal vascular disorders and age-related macular degeneration due to their anti-angiogenic properties. They induce rapid regression of the anterior segment neovascularization that causes Neovascular Glaucoma. Due to the role of VEGF in fibrosis, the anti-VEGF agents have been widely used not only in NVG but also to modify the wound healing response in glaucoma filtration surgery. This article explains the role of anti VEGF agents in glaucoma in detail.

**ANTI-VASCULAR ENDOTHELIAL GROWTH FACTORS**

VEGF is a glycoprotein and has 5 main subtypes like VEGF-A, VEGF-B, VEGF-C, VEGF-D and placental growth factor (PIGF). VEGF-A is the dominant mediator of pro-angiogenic signaling. VEGF-A exists in five isoforms that differ in the average chain lengths (121, 145, 165, 189, and 206 amino acids). VEGF165 (45 kDa) is the predominant isoform and the key agent in neovascularization. The function of these molecules is primarily mediated by binding and activating two trans membrane tyrosine kinase receptors, VEGFR-1 and VEGFR-2. So on activation VEGF causes angiogenesis and wound healing due to increase in fibrosis.

The commonly used VEGF inhibitors are bevacizumab, ranibizumab and aflibercept in Ophthalmology.

Bevacizumab (BVZ, Avastin) is a full-size recombinant humanized IgG1 kappa monodonal antibody against all isoforms of VEGF. BVZ was approved by the US Food and Drug Administration (FDA) in 2005 for the treatment of colorectal and breast cancers, but it is also used extensively off-label in several ocular conditions (Figure 2).
Ranibizumab (RBZ, Lucentis) is an antibody binding fragment (Fab) of a recombinant humanized IgG1 kappa isotype murine monoclonal antibody against all isoforms of VEGF, thereby preventing binding of VEGF to its receptors VEGFR-1 and VEGFR-2. Owing to its simple structure and its higher affinity for VEGF, RBZ requires lower molar amounts than BVZ to neutralize an equal amount of VEGF. It was approved by the FDA in 2006 and is indicated in adults for the treatment of choroidal neovascularization due to age-related macular degeneration (AMD), diabetic macular edema (DME), macular edema secondary to retinal vein occlusion, and for the treatment of visual impairment due to choroidal neovascularization secondary to pathologic myopia.

Aflibercept (AFB, Eylea) is a glycosylated recombinant fusion protein produced from hamster ovary cells, AFB binds to all isoforms of VEGF-A with a higher affinity than BVZ and RBZ, also binding to VEGF-B and PIGF. It forms stable, inert, homogeneous complexes with VEGF that do not induce platelet aggregation or tissue deposits in the systemic circulation, unlike what has been hypothesized for heterogeneous multimeric immune complexes formed by BVZ and VEGF. It was approved by the FDA for the treatment of choroidal neovascularization and Diabetic Macular Edema. (in 2011 and 2014 respectively)

USES OF ANTI VEGF AGENTS IN GLAUCOMA

Anti VEGF agents are currently used to manage NVG and as an alternative to antifibrotic agents in glaucoma surgery. It has also been used in bleb needling.

ROLE IN NEOVASCULAR GLAUCOMA

The main pathogenesis in neovascular glaucoma is retinal vasculopathy causing hypoxia which causes an increase in vascular endothelial growth factors which in turn causes angiogenesis. When the level of hypoxia is more than the new vessels proliferate in the iris tissue also. When neovascularization develops in the iris and angle there is mechanical blockage of the trabecular meshwork causing increase in intraocular pressure or in later stages there is contraction of the fibrovascular membrane causing angle closure glaucoma also. Pan retinal photocoagulation was considered as the gold standard of neovascular glaucoma as it causes the hypoxic retina to become anoxic thereby reduces the VEGF load and the neovascularization. But it causes irreversible damage to the retina and field defects. In contrast, drugs such as the anti-VEGF’s do not damage the retina and may actually lower IOP. But the pharmacologic effect of anti-VEGF drugs eventually wears off, while the effect of PRP is permanent. Although there are beneficial effects including less anterior segment bleeding, the long-term outcomes with regard to visual acuity and IOP control are more dependent on definitive control of the underlying condition.

The effects of anti-VEGF agents for treating NVG are temporary, generally last 4–6 weeks. It is also known that anti-VEGF agents alone may not be sufficient to treat NVG caused by conditions with a prolonged natural history. Nonetheless, the combination of anti-VEGF and conventional treatments has the potential to be more effective than conventional treatments alone by virtue of a dual mechanism of action. As a protocol we give intravitreal anti-VEGF 0.1 ml, observe for a month and then do laser to reduce the new vessels.

Studies

Method and dose of administration has not been standard and has been tried differently by various authors. Waisbourd et al studied the efficacy of topically applied BVZ for the treatment of NVG. Eight patients were treated with topical BVZ (25 mg/mL) four times daily for 2 weeks. The authors observed a mean IOP reduction of 6.1 mmHg and noted that three patients had clinical regression of iris neovascularization. The intracameral administration of BVZ reduced the number of patients requiring surgical treatment of NVG, whereas some other patients became candidates for filtration surgery. Luke et al reported 10 cases with NVG who received intraocular injections of RBZ (0.5 mg/0.05 mL). According to the authors, RBV appeared to be beneficial owing to its anti-angiogenic property. Grover et al reported a considerable reduction in aqueous humor VEGF concentrations following an intracameral injection of BVZ.

ROLE IN GLAUCOMA SURGERY

Long term failure of glaucoma filtering surgery is mainly because of the excessive wound healing due to fibrosis. Diverse molecular and cellular processes such as collagen deposition, angiogenesis and the activation and proliferation of fibroblasts are implicated in the healing process which eventually obstructs aqueous outflow. The role of antifibrotic agents in traditional glaucoma filtering surgery is well known. With the use of 5-FU and MMC, trabeculectomy in particular became more successful at reaching target IOP. However they are commonly associated with bleb-related complications. VEGF has several roles in wound healing. While VEGF165 and VEGF121 more directly cause angiogenesis the isomer VEGF189 has more of an impact on fibrosis. And so multiple studies have evaluated the use of bevacizumab or ranibizumab as an alternative or adjunct to MMC at the time of trabeculectomy. The various
routes of administration include topical, subconjunctival, intracameral and intravitreal.

Studies

In a pilot study by sengupta et al24 38 patients were divided into three groups treated with conventional MMC application (0.03%), subconjunctival BVZ (1.25 mg/0.05 mL), or soaked sponges of BVZ (1.25 mg/mL). In both BVZ groups, bleb vascularity increased progressively over the 6-month follow-up.

ROLE IN BLEB NEEDLING

Some authors have tried bleb needling with anti VEGF and they have also used anti VEGF along with Express shunts25.

Side effects of anti VEGF agents

There are various local and systemic side effects of Anti VEGF agents.

The local side effects

Various adverse effects of anti-VEGF agents have been reported, the commonest being transient or sustained elevation of IOP26. The acute IOP elevation is due to blockage of trabecular meshwork by the large molecules of anti VEGF agents. Another author has hypothesized that the IOP rise could be because of trabeculitis and improper drainage. Other side effects could be vitreous hemorrhage, lens injury, retinal detachment, central retinal artery occlusion, morphologic changes in corneal fibroblasts and endophthalmitis27. They are associated with the procedure of giving intravitreal injection rather than the agent itself.

The systemic side effects

The possible side effects are hypertension, proteinuria, thromboembolic events like stroke, myocardial infarction, gastrointestinal perforation and even death. However, serum levels of anti-VEGF drugs after intravitreal injections are incomparably lower than after intravenous administration. In a Pan-American Collaborative Retina Study Group (PACORES)28 report on patients receiving intravitreal bevacizumab injections an acute blood pressure elevation was observed in 0.59%, myocardial infarction in 0.4%, cerebrovascular accidents in 0.5%, and death in 0.42%. In a meta-analysis by Ueta et al. the incidence of all cardiovascular accidents: transient ischaemic attacks, strokes, and other cerebral ischemic incidents was 2.2% in patients treated with intravitreal ranibizumab injections, versus 0.7% in the sham-treated ones.

CONCLUSION

Anti-VEGF therapy has become one of the more frequently applied treatment modalities in ophthalmology. Their effective use in NVG might lead to better outcomes. However, further studies are needed to establish definite treatment guidelines to use anti VEGF agents in NVG.

REFERENCES

Shibal Bhartiya¹ MS, Syril Dorairaj² MS,FACS

¹. Fortis Memorial Research Institute, Opp HUDA City Centre Gurgaon, Haryana, India
². Department of Ophthalmology, Mayo Clinic, 4500 San Pablo Road, Jacksonville, Florida, U.S.

Abstract: The current glaucoma surgery paradigm is now undergoing a renaissance with the introduction of several new technologies. Minimally invasive glaucoma surgeries (MIGS) are the buzzword in current glaucoma practice. Each of these new surgical methods comes with the promise of improved surgical efficiency and safety compared to the eternal gold standard, trabeculectomy. Most of these techniques, though still in the early stages of clinical testing, with few published peer-reviewed studies, have caught the imagination of glaucoma surgeons worldwide. This review is an attempt to critically evaluate what is commercially available worldwide, and discuss its possible application in the Indian context.

After decades of stagnation in innovation, glaucoma surgery is now undergoing a renaissance with the introduction of new technologies. Each of these new surgical methods comes with the promise of improved surgical efficiency and safety compared to the eternal gold standard, trabeculectomy. Most of these techniques, however, are still in the early stages of clinical testing, with few published peer-reviewed studies to support an established possible positioning in current glaucoma practice¹⁻⁵⁹. This review will attempt to list what is commercially available worldwide and possible positioning of these new methods in the Indian context.

Working Definition MIGS

In recent years, substantial innovation in surgical technique for managing glaucoma has sought to develop a procedure that provides IOP reduction comparable to that achieved with traditional surgery, but with a more favourable safety profile. Generally, these procedures avoid the formation of a bleb by shunting fluid across the obstructed trabecular meshwork (TM) into Schlemm’s canal, or into the suprachoroidal space. Overall, these procedures, termed minimally invasive glaucoma surgeries (MIGS), are safer than traditional glaucoma surgery, but have not consistently delivered comparable IOP reductions. More recently, in recognition of the bleb’s key role in achieving significant IOP reductions, bleb-based MIGS procedures have also been developed¹⁻⁵.

MIGS is known to be an evolving space with no well accepted definition. It includes a diverse group of “alternative” glaucoma surgeries that are intended to be safer, and induce considerably less tissue disruption than traditional procedures.

The American Glaucoma Society, in association with the FDA (Figure 1: FDA approved options of Ab interno MIGS in US in 2017) provides the following working definition for Minimally Invasive Glaucoma Surgery, popularly known by the acronym, MIGS:

Figure 1: MIGS FDA approved Ab-interno Options From left to Right: Xen, Cypass, KDB, Istent, Trabectome
IOP, or intraocular pressure, should be lowered by improving outflow of eye fluid.

The device or procedure can either be approached from inside the eye (ab-interno) or outside the eye (ab-externo).

There should be limited surgical manipulation of the sclera and the conjunctiva.

ADVANTAGES AND DISADVANTAGES OF MIGS

Most of these procedures are bleb independent (except for Xen and InnFocus) and are less invasive than the conventional glaucoma surgery. Faster visual rehabilitation and fewer complications mean a better quality of life for the patient. Most of the newer surgical procedures, euphemistically labelled as “Cataract plus” surgeries, have been devised to be used in conjunction with cataract surgery, these procedures have a higher patient acceptability.

Their stand-alone efficacy, except for NPDS (Non-Penetrating Deep Sclerectomy), in terms of IOP control is yet to be validated. MIGS have proven to be efficacious in decreasing the need for antiglaucoma medication, achieving target IOP for most cases of early and moderate glaucomas, with more predictable postoperative IOPs. However, in terms of comparison with trabeculectomy, with exception of NPDS, their efficacy leaves much to be desired.

Also, MIGS mean a much higher cost of surgery, since they involve either expensive instrumentation and/or implants. MIGS typically, with the exception of viscocanaloplasty and NPDS, have a relatively flat learning curve.

INDICATIONS OF MIGS

Patients with mild-moderate glaucoma, with:

- Primary open-angle glaucoma,
- Pseudoeudetiolation glaucoma, or
- Pigmentary dispersion glaucoma

In patients with glaucoma uncontrolled with maximum pharmacologic treatment or there are barriers preventing appropriate medication dosing, MIGS may be considered if

- Age greater than 18
- Patients with clinically significant cataract, for concomitant surgery

CONTRAINDICATIONS

Relative contraindications, which are to be evaluated for individual MIGS and on a case to case basis include:

- Angle-closure glaucoma,
- Secondary glaucoma: uveitic, neovascular
- Moderate-advanced glaucoma,
- Previous glaucoma surgery,
- Uncontrolled IOP.
- Other considerations include patients with previous refractive procedures as well as monocular patient (Also see Table 1)

CLASSIFICATION OF MIGS

MIGS can be classified according to the anatomical outflow pathway as well as surgical approach:

Subconjunctival filtration strategy:

- Ab externo approach
  - Ex-Press implant
  - Carbon dioxide (CO2) laser-assisted sclerectomy surgery (CLASS)
- InnFocus Micro Shunt
- Ab interno approach
  - XEN implant

Enhanced filtration into Schlemm’s canal (SC) strategy:

- Ab externo approach
  - Canaloplasty (Ellex catheter)– Stegmann canal expander (SCE)
- Ab interno approach (Figure 2)
  - iStent
  - High frequency deep sclerotomy (HFDS)
  - Ab interno trabeculotomy (Trabectome by NeoMedix or Ellex Catheter)
  - Hydrus implant
  - Kahook Dual Blade (New World Medical)

Suprachoroidal filtration strategy:

- Ab interno approach
  - CyPass implant
  - iStent supra implant
- Ab externo approach
  - Starflo implant
  - Gold Solx implant.

(Adapted from ISGS Textbook of Glaucoma Surgery, Ed: T Shaarawy, T Dada, S Bhartiya)

Mechanisms of Action and Salient Features:

**Trabectome:** The Trabectome (NeoMedix) was the first pro-cedure for MIGS ab interno trabecular ablation and got FDA approval in 2006. The trabectome is used to under gonioscopic guidance for a controlled electroablation of an arc of trabecular meshwork providing aqueous direct access to collector channels. The device simultaneously aspirates the debris, resulting in less postoperative inflammation.

**iStent Trabecular Micro-Bypass Stent:** (Figure 3) The iStent trabecular micro-bypass stent (Glaukos) is an ab-interno micro bypass stent which is placed in the Schlemm’s canal in the lower nasal quadrant. It provides a channel for direct
<table>
<thead>
<tr>
<th>Table 1: Indications and contraindications of newer glaucoma surgeries</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
</tbody>
</table>
| **ExPRESS Filtration device** | • Open Angle Glaucoma refractory to medical and laser treatment  
  • Open Angle Glaucoma with a failed filtration procedure  
  • Combined glaucoma and cataract procedure  
  • Sturge-Weber syndrome  
  • Aphakic glaucoma | • Angle closure glaucoma.  
  • Presence of ocular disease such as active uveitis, ocular infection, severe dry eye, severe blepharitis.  
  • Pre-existing ocular or systemic pathology that is likely to cause postoperative complications following implantation of the device |
| **Trabecular micro-bypass iStent** | • Early-to-moderate OAG  
  • Pigmentary glaucoma  
  • Pseudoexfoliative glaucoma, stand alone or in combination with cataract surgery. | • Presence of ocular disease such as uveitis, ocular infection  
  • Patients diagnosed with angle closure glaucoma |
| **Trabectome** | • Primary open-angle, pigmentary, and pseudoexfoliative glaucoma.  
  • OAG with a failed filtration procedure | Angle closure with or without peripheral anterior synechiae |
| **Canaloplasty** | • Early-to-moderate OAG  
  • Pigmentary glaucoma  
  • Pseudoexfoliative glaucoma | • Scarring from prior trabeculectomy  
  • Patients with obvious scarring in Schlemm’s canal due to prior medication use, laser, surgery or corneoscleral trauma at the limbus  
  • Anomalies in the anterior chamber angle |
| **Gold microshunt** | Failed trabeculectomy or Schlemm’s canal procedures | • Recent angle closure glaucoma episode  
  • Uveitic glaucoma, ICE syndrome, traumatic glaucoma, or NVG  
  • Other significant ocular disease, except cataract  
  • Active ocular infection  
  • Expected ocular surgery in next 12 months  
  • No suitable quadrant for implant |
| **Eyepass** | Early-to-moderate OAG | • Recent angle closure glaucoma episode  
  • Uveitic glaucoma, ICE syndrome, traumatic glaucoma, or NVG |
| **Cypass** | Mild to moderate POAG | • Narrow-Angle Glaucoma  
  • Secondary glaucoma |
| **Hydrus Microstent** | Mild to moderate glaucoma | • Narrow-Angle Glaucoma  
  • Secondary glaucoma |
| **InnFocus** | Refractory glaucoma | • Presence of ocular disease such as active uveitis, ocular infection.  
  • Neovascular glaucoma |
| **AqueSys/Xen Implant** | Refractory glaucoma | • Narrow-Angle Glaucoma  
  • Secondary glaucoma |
| **NPDS** | • Open-angle glaucoma  
  • Glaucoma in high myopia  
  • Pseudoexfoliative and pigmentary glaucoma  
  • Uveitic glaucoma  
  • Juvenile oag  
  • Glaucoma with elevated episcleral venous pressure | Neovascular glaucoma  
  Relative contraindications:  
  • Narrow-Angle Glaucoma  
  • Post-traumatic Angle-recession Glaucoma  
  • Status Post-Laser Trabecuoplasty |
| **CO₂ assisted DS** | Open-angle glaucoma  
  Glaucoma in high myopia  
  Pseudoexfoliative and pigmentary glaucoma  
  Uveitic glaucoma  
  Juvenile OAG  
  Glaucoma with elevated episcleral venous pressure | Neovascular glaucoma  
  Relative contraindications:  
  • Narrow-Angle Glaucoma  
  • Post-traumatic Angle-recession Glaucoma  
  • Status Post-Laser Trabecuoplasty |

trans-trabecular aqueous outflow from anterior chamber to collector channels. Currently, the device is indicated for use in conjunction with cataract surgery and if one stent does not produce the desired outcome, the iStent is titratable, although implanting multiple devices is an off-label use. The next generation iStent is yet to get FDA approval, and is currently being evaluated for use in association with cataract surgery and as a solo procedure. The iStent Inject comes loaded with two stents, which can be inserted a few clock hours apart in the same procedure. In trials, this device has maintained the safety and efficacy profile of the first-generation iStent.

**Kahook Dual Blade (KDB):**
The KDB is a surgical knife designed to facilitate goniotomy. The KDB device has a sharp distal tip that pierces the TM and enters Schlemm’s canal. As the instrument is advanced along the trajectory of Schlemm’s canal, the TM is elevated on the instrument’s ramp and guided onto 2 parallel blades. Unlike a standard goniotomy knife that simply incises the TM, leaving contiguous anterior and posterior flaps, the KDB excises a strip of TM, leaving a direct opening for aqueous to pass from the anterior chamber into Schlemm’s canal. Thus, the KDB procedure removes the tissue at the site of aqueous outflow obstruction in open-angle glaucoma, restoring the natural aqueous outflow pathway without the formation of a filtering bleb producing more sustained IOP control.

**Xen Glaucoma Treatment System:**
(Figures 4, 5) The Xen Glaucoma Treatment System (Allergan) got FDA approval in 2016, and aims to lower IOP by creating a subconjunctival drainage pathway. The implant, a hydrophilic tube composed of a porcine gelatin cross-linked with glutaraldehyde, is approximately 6 mm long with an inner diameter of about 45 mm. It is said to provide approximately 6 to 8 mm Hg of flow resistance, which essentially eliminates postoperative hypotony.

Xen Glaucoma Treatment System: (Figures 4, 5) The Xen Glaucoma Treatment System (Allergan) got FDA approval in 2016, and aims to lower IOP by creating a subconjunctival drainage pathway. The implant, a hydrophilic tube composed of a porcine gelatin cross-linked with glutaraldehyde, is approximately 6 mm long with an inner diameter of about 45 mm. It is said to provide approximately 6 to 8 mm Hg of flow resistance, which essentially eliminates postoperative hypotony.

The needle tip exits the sclera ±3 mm from the limbus before delivery of the Xen45 Gel Stent, preferably in the superonasal quadrant, to deliver the implant in the subconjunctival space. After implantation, the stent softens in about 2 minutes and conforms to the shape of surrounding tissue. This ensures aqueous egress directly from the AC into the subconjunctival space.

The mechanism of action of the Xen glaucoma implant is similar to that of full-thickness glaucoma surgeries like trabeculectomy and shunts, which bypass all potential outflow obstructions. The tubular implant maintains the microfistula between the anterior chamber and the subconjunctival space with spontaneous healing of the surrounding tissues. An iridotomy is not required, and this can potentially minimise surgical trauma, subsequent inflammation and fibrosis.

Of the MIGS devices available worldwide, only the Xen implant is slated for the India market within the coming year, following DCGI clearance.

**CyPass:** (Figure 6) CyPass (Alcon) is a biocompatible polyamide tube 6.35-mm in length with a 300-μm lumen. It is placed in the supraciliary and suprachoroidal space...
### Table 2: IOP Outcomes of published studies for MIGS

<table>
<thead>
<tr>
<th>Author (year of study)</th>
<th>% IOP reduction and % medication reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trabectome alone</strong></td>
<td></td>
</tr>
<tr>
<td>Minckler et al (2005)</td>
<td>38% IOP reduction</td>
</tr>
<tr>
<td>Minckler et al (2006)</td>
<td>41% IOP reduction</td>
</tr>
<tr>
<td>Minckler et al (2008)</td>
<td>35% IOP reduction</td>
</tr>
<tr>
<td>Ting et al (2012)</td>
<td>44% IOP reduction with 28% medication reduction in PXG; 34% IOP reduction and 21% medication reduction in POAG</td>
</tr>
<tr>
<td>Ahuja et al (2013)</td>
<td>35% IOP reduction</td>
</tr>
<tr>
<td>Maeda et al (2013)</td>
<td>29% IOP reduction</td>
</tr>
<tr>
<td><strong>Trabectome with CE/IOL</strong></td>
<td></td>
</tr>
<tr>
<td>Francis et al (2008)</td>
<td>16% IOP reduction</td>
</tr>
<tr>
<td>Minckler et al (2008)</td>
<td>18% IOP reduction</td>
</tr>
<tr>
<td>Ting et al (2012)</td>
<td>35% IOP reduction with 30% medication reduction in PXG; 22% IOP reduction and 31% medication reduction in POAG</td>
</tr>
<tr>
<td>Ahuja et al (2013)</td>
<td>22.8% IOP reduction</td>
</tr>
<tr>
<td><strong>Trabectome with or without CE/IOL</strong></td>
<td></td>
</tr>
<tr>
<td>Jordan et al (2013)</td>
<td>26% IOP reduction with 43% medication reduction</td>
</tr>
<tr>
<td></td>
<td>28% IOP reduction with 45% medication reduction</td>
</tr>
<tr>
<td><strong>iStent with CE/IOL</strong></td>
<td></td>
</tr>
<tr>
<td>Fea (2010)</td>
<td>17.3% IOP reduction with 80% medication reduction in the stent/CE/IOL group (9.2% IOP reduction and 31.6% medication reduction in the CE/IOL group)</td>
</tr>
<tr>
<td>Samuelson et al (2011)</td>
<td>8% IOP reduction with 87% medication reduction in the stent/CE/IOL group (5.5% IOP reduction and 73% medication reduction in the CE/IOL group)</td>
</tr>
<tr>
<td>Craven et al (2012)</td>
<td>8.6% IOP reduction with 88% medication reduction in the stent/CE/IOL group (5.0% IOP reduction and 73% medication reduction in the CE/IOL group)</td>
</tr>
<tr>
<td><strong>Multiple iStents with CE/IOL</strong></td>
<td></td>
</tr>
<tr>
<td>Fernández-Barrientos et al (2010) (two iStents)</td>
<td>27% IOP reduction with 91% medication reduction in two-stent/CE/IOL (16% IOP reduction with 42% medication reduction in CE/IOL)</td>
</tr>
<tr>
<td>Belovay et al (2012) (two vs three iStents)</td>
<td>20% IOP reduction with 64% medication reduction in the two-stent/CE/IOL group, vs 20% IOP reduction with 85% medication reduction in three-stent/CE/IOL</td>
</tr>
<tr>
<td><strong>Multiple iStents (second-generation iStent inject) alone</strong></td>
<td></td>
</tr>
<tr>
<td>Voskanyan et al (2014)</td>
<td>29% IOP reduction from medicated baseline data on follow-up medication not specified</td>
</tr>
<tr>
<td>Fea et al (2014)</td>
<td>48% IOP reduction in the two-stent group (47% in the two-medications group)</td>
</tr>
<tr>
<td>Klamann et al (2015)</td>
<td>33% IOP reduction with 60% medication reduction in POAG (P&lt;0.001); 35% IOP reduction with 55% medication reduction in PXG (P&lt;0.001)</td>
</tr>
<tr>
<td><strong>Hydrus with CE/IOL</strong></td>
<td></td>
</tr>
<tr>
<td><strong>ELT alone</strong></td>
<td></td>
</tr>
<tr>
<td>Babighian et al (2010)</td>
<td>30% IOP reduction with 62% medication reduction in ELT (21% IOP reduction and 60% medication reduction in the SLT group)</td>
</tr>
<tr>
<td>Töteberg-Harms et al (2013)</td>
<td>23% IOP reduction (P&lt;0.001) with 38.9% medication reduction (P&lt;0.001)</td>
</tr>
<tr>
<td><strong>Cypass alone</strong></td>
<td></td>
</tr>
<tr>
<td>García-Feijoo et al (2015)</td>
<td>35% IOP reduction with 36% medication reduction</td>
</tr>
<tr>
<td><strong>Cypass with CE/IOL</strong></td>
<td></td>
</tr>
<tr>
<td>Hoeh et al (2013)</td>
<td>Patients with medicated baseline IOP ≥21 mmHg had a 37% IOP reduction and a 50% medication reduction. IOP-controlled patients had a 71% medication reduction (P&lt;0.001)</td>
</tr>
</tbody>
</table>

**Notes:** This table summarizes the main IOP outcomes of each study for a MIGS device. This format is limited by the variation in study design. Abbreviations: CE/IOL, cataract extraction/intraocular lens implant; ELT, excimer laser trabeculotomy; IOP, intraocular pressure; MIGS, minimally invasive glaucoma surgery; n/a, not available; OAG, open-angle glaucoma; Pig, pigmentary glaucoma; POAG, primary open-angle glaucoma; PXG, pseudoexfoliation glaucoma; SLT, selective laser trabeculoplasty. 

Adapted from Minimally invasive glaucoma surgery: current status and future prospects Richter et al, 2016
space to increase uveal scleral outflow by creating a small cyclodialysis. The FDA approved the CyPass Micro-Stent in 2016, making it the first FDA-approved MIGS procedure that targets alternative uveal scleral outflow. It is designed for transcorneal placement and fenestrations along the device allow aqueous to egress throughout its length. The negative pressure gradient in the suprachoroidal space results in aqueous outflow and IOP reduction.

**Hydrus Microstent:** The Hydrus Microstent (Ivantis) is SC scaffolding device, which aims to restore the conventional outflow into the Schlemm canal, avoiding the risk for hypotony because of the resistance encountered by the physiological episcleral venous pressure. The 8-mm stent is made from a highly flexible, biocompatible alloy of nickel and titanium (Nitinol), resides in the lumen of Schlemm canal without obstructing collector channel ostia located along the posterior wall. It is in Phase 3 FDA trials.

**Gold microshunt:** The Solx Gold Shunt (Solx), an ab externo suprachoroidal trans-limbal shunt, draining aqueous into the suprachoroidal space. Aqueous flows both, through the channels in the body of the shunt as well as around its body, acting like a controlled cyclodialysis.

**Eyepass:** This bidirectional shunt also diverts aqueous from the anterior chamber directly into Schlemm’s canal.

**InnFocus Microshunt:** The InnFocus Microshunt (Santen) is a minimally invasive, plateless glaucoma drainage microshunt made from an inert biomaterial called SIBS (polystyrene-block-isobutylene-block-styrene). The device shunts aqueous humor from the anterior chamber to the sub-Tenon capsular space. The MicroShunt differs from the Xen 60 Gel Stent since it is implanted ab externo, requires a conjunctival incision, with potentially more scarring than with the Xen.

**Ab Interno Canaloplasty Using the iTrack 250A Microcatheter, ABiC:** ABiC opens up the whole outflow system and viscodilates all sites involved in the control of aqueous outflow. The procedure is performed with an illuminated microcatheter (iTrack 250A; Ellex) that is inserted via a corneal microincision. It restores the natural outflow pathway with minimal tissue trauma by viscodilation and leaves no foreign body (tensioning suture or stent) in the eye. ABiC is also the only MIGS procedure that addresses collector channel blockages as well.

**Excimer laser trabeculostomy:** Excimer laser trabeculostomy (ELT) is a form of ab interno trabeculotomy, that precisely ablates the trabecular

---

### Table 3: Complications of newer glaucoma surgeries

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>ExPRESS Filtration device</td>
<td>• External blockade</td>
</tr>
<tr>
<td></td>
<td>• Dislocation in anterior chamber</td>
</tr>
<tr>
<td>Trabecular micro-bypass iStent</td>
<td>• Peripheral anterior synechia, rarely</td>
</tr>
<tr>
<td>Trabectome</td>
<td>• Transient hyphema</td>
</tr>
<tr>
<td></td>
<td>• Iridodialysis</td>
</tr>
<tr>
<td></td>
<td>• Cycodialysis</td>
</tr>
<tr>
<td></td>
<td>• IOP spike</td>
</tr>
<tr>
<td>Canaloplasty</td>
<td>• Microhyphema(Figure 7)</td>
</tr>
<tr>
<td></td>
<td>• Early and late IOP elevations</td>
</tr>
<tr>
<td></td>
<td>• Woundhemorrhage</td>
</tr>
<tr>
<td></td>
<td>• Suture extrusion</td>
</tr>
<tr>
<td></td>
<td>• Descemet membrane detachment</td>
</tr>
<tr>
<td></td>
<td>• Hypotony</td>
</tr>
<tr>
<td>Gold microshunt(GMS)</td>
<td>• Mild hyphema</td>
</tr>
<tr>
<td></td>
<td>• Hypotony</td>
</tr>
<tr>
<td></td>
<td>• Choroidal effusion, haemorrhage or detachment</td>
</tr>
<tr>
<td></td>
<td>• Shunt migration</td>
</tr>
<tr>
<td>Eyepass</td>
<td>• Hypotony</td>
</tr>
<tr>
<td></td>
<td>• Perforation of TM</td>
</tr>
<tr>
<td>NPDS</td>
<td>• Perforation of Trabeculodescemetic membrane</td>
</tr>
<tr>
<td></td>
<td>• Failure</td>
</tr>
<tr>
<td></td>
<td>• Hyphema</td>
</tr>
<tr>
<td></td>
<td>• Iris prolapse</td>
</tr>
<tr>
<td></td>
<td>• Hypotony</td>
</tr>
<tr>
<td></td>
<td>• Descemets detachment</td>
</tr>
<tr>
<td>CO2 laser DS</td>
<td>• Perforation of Trabeculodescemetic membrane</td>
</tr>
<tr>
<td></td>
<td>• Failure</td>
</tr>
<tr>
<td></td>
<td>• Hyphema</td>
</tr>
<tr>
<td></td>
<td>• Iris prolapse</td>
</tr>
<tr>
<td></td>
<td>• Hypotony</td>
</tr>
<tr>
<td></td>
<td>• Inflammation</td>
</tr>
<tr>
<td>CyPass</td>
<td>• Descemets detachment</td>
</tr>
<tr>
<td></td>
<td>• Implant migration</td>
</tr>
<tr>
<td>Xen Implant/AqueSys</td>
<td>• Wound leak/Dehiscence</td>
</tr>
<tr>
<td></td>
<td>• Hyphaema/Vitreous hemorrhage</td>
</tr>
<tr>
<td></td>
<td>• Hypotony</td>
</tr>
<tr>
<td></td>
<td>• Aqueous misdirection</td>
</tr>
<tr>
<td></td>
<td>• Failure and Needing Recurrent needling</td>
</tr>
<tr>
<td></td>
<td>• Implant migration</td>
</tr>
<tr>
<td>InnFocus</td>
<td>• Wound leak/Dehiscence</td>
</tr>
<tr>
<td></td>
<td>• Hyphaema</td>
</tr>
<tr>
<td></td>
<td>• Hypotony</td>
</tr>
</tbody>
</table>

Recent Trends and advances

This procedure uses a XeCl (308-nm) excimer laser coupled to an intraocular fiber optic delivery system to create long-term anatomic openings that connect the anterior chamber directly to Schlemm canal. The photodissolution of trabecular meshwork tissue into gas enables pneumatic canaloplasty.

**NB:** The following surgeries do not fit into the current definition of MIGS, but have been traditionally classified in this group, since they are relatively newer surgeries. They are being mentioned in this review for the sake of completion.

**Non-Penetrating Glaucoma Surgeries:** Aqueous egress is known to occur at the level of Schlemm's Canal (SC) and its efferents and the selective removal of the inner wall of SC and the adjacent trabecular meshwork, leaving intact the innermost trabecular meshwork layers decreases the resistance to aqueous outflow. The residual membrane, formed by the anterior and posterior trabecular meshwork, the internal endothelium of Schlemm's canal and Descemet's membrane in deep sclerectomy or viscocanalostomy, retains a degree of residual outflow resistance, making this surgery safer. Since the anterior chamber (AC) is not entered, these group of surgeries are called non-penetrating glaucoma surgeries.

**CO₂ Laser Assisted DS:** CO₂ laser energy ablates the underlying sclera layer by layer until the roof of SC is exposed. At that point fluid percolates in the thinned tissue and prevents further ablation, thus preventing a full thickness perforation. The laser thus is the fancy knife that makes the surgery safer, easier to perform, with decreased rates of perforations into the AC.

**Canaloplasty:** Canaloplasty and viscocanalostomy are procedures that rely on dilatation of the SC to decrease outflow resistance. The tensioning suture within the SC, similar to the action of pilocarpine, as well as helps in maintaining a patent canal lumen.

**ExPress:** The ExPress Glaucoma Filtration Device controls IOP by allowing a limited outflow of aqueous humor into the intrascleral space and thereafter into the subconjunctival space, with a mechanism of action similar to trabeculectomy. It makes a trabeculectomy more standardised with decreased complications.

**EVOLVING TRENDS**

MIGS can potentially address several problems that plague current day glaucoma management. These include problems of patient compliance and adherence, life costs of glaucoma medications, quality of life concerns including ocular toxicity of glaucoma medications. In addition, the minimally invasive nature of most of these procedures means that that the conjunctiva remains available for any future incisional surgeries.

**CONCLUSION**

Whenever a new procedure is evaluated, it is important to choose one that is easy to learn, safe, efficacious, and applicable to a broad population of patients and stages of disease, and has proven long-term outcomes. It is definitely safer and less invasive than traditional surgery and is characterized by minimal external dissection, shorter operating time, better safety profile, and patients' rapid postoperative recovery.

Several well designed clinical trials have reported a significant decrease in IOP over periods of up to 24 months along with a significant decrease in medication usage, with minimal adverse events. These procedures are being positioned a viable option for patients with mild-moderate glaucoma, in patients with IOPs uncontrolled on medications or in those who have poor medication compliance.

However, on critical evaluation, MIGS may not find widespread popularity in the Indian population on several of these counts.

**Most of these minimally invasive surgical procedures are also minimally efficacious:** with no data available for their efficacy in advanced glaucomas.

Most of these procedures mean a much higher cost of surgery, since they involve either expensive instrumentation and/or implants. Viscocanaloplasty and NPDS have a very steep learning curve, and that of the other MIGS is described to be relatively flat. But, in the current scenario, with the general ophthalmologist being trained in trabeculectomy, the acceptability of MIGS given the learning curve may also be doubtful.

Table 1 briefly outlines the published MIGS studies with regard to IOP lowering efficacy, as well as percentage reduction in glaucoma medications following surgery.

Table 2 lists the documented complications of MIGS.

Table 3 enlists the indications and contraindications for each of the MIGS.

**REFERENCES**

Recent Trends and Advances


Correspondence to: Dr. Shibal Bhartiya, Fortis Memorial Research Institute, Gurgaon, Haryana, India.
How to Diagnose and Monitor Glaucoma with Accuracy in Patients of LASIK or Cornea Refractive Surgery

Dr. Charu Khurana, Dr. Kiran Kirtani, Dr. Hemlata Gupta
Centre For Sight Group of Eye Hospitals, New Delhi, India

Abstract: Evaluation and management of glaucoma in patients scheduled for refractive surgery or post-refractive surgery is a challenging task. Variation in corneal shape, thickness and bio-mechanical factors after refractive surgery makes measurement of IOP tricky. In addition, patients with myopia and astigmatism may have large or tilted discs with peri-papillary atrophy which makes interpretation of OCT and Visual Field changes difficult. This article aims to help the clinician understand how to handle these patients better by keeping a high index of suspicion, modifying techniques of IOP measurement and introducing newer instruments which give an accurate estimate of the IOP after refractive surgery. All these need to be used in conjunction with a good clinical examination so we may understand the glaucoma status of our patients better and treat them as best as possible.

Almost 40 million patients have undergone refractive surgery in the last 20 years and form a sizeable proportion of the population visiting an ophthalmologist. The global prevalence of glaucoma is steadily increasing and is estimated to reach about 76 million patients by 2020. At some point these population groups intersect and form a diagnostic and management challenge for us.

In addition myopia and hyperopia are considered independent and significant risk factors for glaucoma. Myopia is associated with a 3 to 6 fold increase in incidence of glaucoma due to decreased scleral rigidity and increased vulnerability of the optic nerve to pressure induced damage due to stretched lamina cribrosa and thinned out retinal nerve fibres. Hyperopic patients are more prone to narrow angle glaucoma. With the modification of the corneal shape, thickness and bio-mechanical properties because of the LASIK procedure, evaluation and monitoring of these 'high-risk' patients poses a considerable challenge for a glaucoma specialist.

What follows next is a brief description of the factors one needs to keep in mind when evaluating a potential refractive surgery patient for glaucoma and how best to evaluate a patient with history of refractive surgery for glaucoma.

**PRE-OPERATIVE ASSESSMENT**

1) Family history of glaucoma increases the risk of developing ocular hypertension or glaucoma especially when a first degree relative is affected by about 2-4 times. Eliciting a positive family history of glaucoma during a LASIK work up is an important additional risk factor.

2) Goldman Applanation tonometry (GAT) measurements are a must and should be repeated a few times to have a baseline for future evaluations. Any patient with a high IOP should be completely evaluated for glaucoma including gonioscopy, visual fields and imaging of peri-papillary RNFL with OCT or GDx or HRT before being considered for LASIK.

3) Myopia is considered to increase the risk of glaucoma significantly especially with high myopia (>6.0D) but the Blue Mountains Eye Study has stated that even low myopia (between -1 to -3 D) increases the odd ratio to 2.3 times and moderate myopia (between -3 to -6D) increases the odds ratio to 3.3 times. The Beaver Dam Eye Study showed that, after taking into account the effects of age, sex, and other risk factors, persons with myopia were 60% more likely to have glaucoma than those with emmetropia.

4) Hyperopes are at higher risk of angle closure glaucoma and must obtain a gonioscopy especially when associated with a shallow anterior chamber. Occurrence of angle closure attack has been reported after LASIK which was successfully managed by laser iridotomy. Possible reasons behind the pupillary dilatation which may trigger an attack of angle closure glaucoma include use of local anesthetic drops, the suction ring, steroid drops, emotional stress, dark room and mechanical deformity of anterior segment structures. Prophylactic laser iridotomy should be performed for patients with narrow angle before LASIK correction.

5) Large discs, tilted discs and peri-papillary atrophy all increase the risk of developing glaucoma but may also make the evaluation of glaucoma tricky as the imaging tools have limited ability to differentiate these patients from true glaucoma. In such patients it is important to take baseline clinical photographs and obtain baseline visual fields and RNFL measurements so that progression if any can be monitored accurately.

6) High Cup disc ratio especially vertical CD ratio merits further investigations for glaucoma.

7) Thin central corneas not only limit the refractive procedures possible but are also independent risk factors for...
Recent Trends and Advances

This issue.

GDx machines with enhanced corneal color perception or contrast sensitivity of the retinal nerve fibers. The new birefringence and are not real damage the GDx machines, but these effects are LASIK with the SLP technology used by individuals.

Changes or progression can be monitored be followed up closely and any early changes or progression can be monitored individually.

INTRA-OPERATIVELY

During the LASIK procedure suction pressure of 60-80 mm Hg is applied to fix the eye with a suction ring which leads to a transient IOP rise during corneal flap creation. While anecdotal reports of ischemic optic neuropathy during LASIK have been reported, per se LASIK is not known to affect the structure and function of the optic nerve or visual fields, color perception or contrast sensitivity.

Some studies have reported a reduction of the nerve fiber layer after LASIK with the SLP technology used by the GDx machines, but these effects are probably due to the change of the corneal hirerigence and are not real damage of the retinal nerve fibers. The new GDx machines with enhanced corneal compensator (ECC) seem to overcome this issue.

However to be on the safer side we do prefer a PRK procedure in high risk patients or those on medications or with previous filtration blebs. At the same time newer procedures like small incision lenticule extraction (SMILE) and other time newer procedures like small incision lenticule extraction (SMILE) and other newer generation femto-lasers create a much smaller suction pressure (20-35 mm Hg) and maybe considered safer for high risk patients as compared to standard LASIK.

POST-OPERATIVELY

1) The corneal thickness is reduced during refractive surgery leading to an underestimation of the measured IOP especially by applanation tonometry. This makes the estimation of the true IOP difficult especially in these vulnerable eyes and hence makes the evaluation and management tricky. Various formulas have been reported to compensate for the reduced corneal thickness and various correction factors have been recommended but the relationship is neither simple nor linear. The post-op reduction is not only due to thinning of cornea but also due to change in curvature and instability of corneal flap in LASIK and removal of Bowman’s membrane in PRK.

An interesting algorithm has been proposed by Kohlihas et al to calculate actual IOP after myopic LASIK.

IOP (real) = IOP (measured) * (540-CCT) / 71 + (43-K-value)/ 1.7 + .75 mm Hg.

Where CCT is the central corneal thickness postoperatively and K is the average of keratometry readings postoperatively. However, there is no single universally accepted formula to accurately calculate post-op IOP.

Other recommendations include:

a) Measuring the IOP in the peripheral cornea where corneal tissue may not be as affected.

b) Using pneumotonometer which approximates a smaller area of the corneal surface than the Goldmann tonometer and though it also records a lower IOP but the underestimation may be lower than GAT.

c) A Tonopen based on the Mackay-Marg principle is less influenced by the thinning of the stroma and the reduction of the corneal curvature and maybe used to get accurate measurements from the peripheral cornea.

d) The PASCAL Dynamic Contour Tonometer (DCT, Figure 1) is considered fairly accurate for measuring the IOP especially in thin corneas both after Lasik and PRK as it is based on contour matching and is not influenced by corneal thickness or the viscoelastic properties of the cornea including corneal hysteresis (CH) and Corneal resistance factor (CRF). While the GAT provides an indirect calculation of the IOP, converting the force exerted for the flattening of the cornea to pressure, the Pascal DCT measures the IOP directly transcorneally with a piezoelectric sensor, avoiding systemic errors that may be produced by GAT.

The concave surface of the contour matched tip of the DCT touches but allows the cornea to assume a shape (close to its steady-state shape) in which no tangential and bending forces are acting within the area of the cornea touching the tip. If the apex of the cornea is tension free, the pressure acting on both of its sides (inside and outside) must be exactly equal. The presence of a miniaturized piezoelectric pressure sensor flush inside the surface contour of the tonometer’s tip allows measurement of the IOP. Variations in any corneal properties over a wide range of values do not influence this pressure measurement and hence is useful in post-refractive surgery patients with altered bio-mechanical properties. The chosen contour of the DCT tip will furnish correct measurements (defined as measurements with a systematic error of less than 0.5 mm Hg) for corneas with a radius of between approximately 5.5 and 9.2 mm and a corneal thickness ranging from 300 to 700 µm. Most corneas will fall within this range but outside these limits errors may increase.

e) The Corneal Visualization Scheimpflug Technology instrument
Recent Trends and Advances

Khurana C. et al. How to Diagnose and Monitor Glaucoma

www.dos-times.org

63

(Corvis ST tonometry: CST; Oculus, Wetzlar, Germany), is a new non-contact tonometry device integrated with an ultra-high-speed Scheimpflug camera which enables the direct visualization of corneal movement during the application of a rapid air-puff and helps measure the IOP, CCT and a large number of biomechanical properties which have an impact on the IOP. The CST system is designed to gather 4330 frames per second within a 100 ms period and record dynamic IOP in a range 1 to 60 mm Hg. The movements of the cornea are then displayed on the built-in control panel in ultra-slow motion and output includes the IOP value, central corneal thickness, and corneal biomechanical properties (applanation time, applanation length, applanation velocity and details of highest concavity) (Figure 2). Since the change in the deformation pattern after refractive surgery due to stromal ablation and flap formation is also measured, this instrument should be a useful adjunct to measure the IOP in such patients.

Some studies have also reported that measurement of IOP with Schiotz tonometry may be used in conjunction with other instruments to give a fairly accurate estimate of the IOP as the IOP measured with Schiotz is higher than that obtained with GAT in post-refractive surgery patients.

The biomechanical properties of the cornea also undergo a significant change because of corneal thinning and corneal flap formation after LASIK and have an impact on IOP measurement. The Ocular Response Analyzer (ORA) is a non-contact tonometer that measures Corneal Hysteresis (CH) and also the corneal response factor (CRF) in addition to 2 IOP readings termed IOPg and IOPcc (Figure 3). The first IOPg is supposed to match with GAT while the IOPcc corrects for the corneal biomechanical properties (CH and CRF) and gives the corrected IOP. Patients with glaucoma or at risk of glaucoma usually have a lower CH.

The Ocular Response Analyzer has a built-in eye tracking software which automatically positions the instrument’s sensor over the patients’ eyes. Once the ORA is in place, it directs a stream of air toward the eye that first flattens (applanates) and then indents the cornea. At the moment of applanation, the infrared light reflected by the cornea aligns with the detector. This event is recorded as peak (P1) on the ORA’s signal plot. As the device continues to direct air toward the eye, the cornea becomes concave, the light disperses, and the applanation signal decreases. The light re-aligns with the infrared detector after the air pulse is discontinued and the cornea passes through a second applanation event (recorded as P2 on the signal plot). At the end of the test, the cornea returns to its baseline convex shape. The ORA provides 4 values, 2 IOP values IOPg and IOP cc and 2 corneal biomechanical values. The first IOP value is an estimate of Goldmann IOP (IOPg) and corresponds to the IOP value at the first applanation point in the ORA waveform (P1). The second IOP value, IOPcc, is an estimate of IOP corrected for the biomechanical properties of
the cornea. The two biomechanical values provided by the ORA are called corneal hysteresis and the corneal resistance factor. Corneal hysteresis is a quantification of the cornea’s ability to absorb and/or dissipate energy (viscous damping). It is calculated as the difference in pressure between the two corneal appplanation events (P1 minus P2) in the waveform. The corneal resistance factor is also derived from these two pressure values but in a more complex calculation that provides a combined estimate of both the viscous and elastic nature of the corneal tissue.

Both the Corvis ST (discussed earlier) and the 10Pc derived from the ORA are supposed to give a more accurate estimate of the IOP as well as the changed biomechanical values due to stromal ablation and flap formation in post-LASIK patients and may become more commonly used in years to come19.

3) Steroid responsiveness is another issue that may occur following refractive surgery. Steroid responders maybe high, low or intermediate responders depending on whether they are homozygous positive, homozygous negative or heterozygous in the gene inheritance pattern as postulated by Becker and Armanly20. Approximately 18 to 36% of the general population are corticosteroid responders implying that they will develop a IOP rise within 4 to 6 days of initiating steroid therapy while 5% of the general population are high responders implying that they may develop a significant pressure spike within a few days of initiating steroid therapy21,22. In addition myopia is also a significant risk factor and the combination of the two gives a much higher incidence of steroid induced glaucoma in patients undergoing refractive surgery. Therefore, patients with myopia, diabetes, family history of glaucoma and glaucoma suspects with their added increased risk of steroid responsiveness need to be monitored closely.

In addition the low IOP measured due to corneal ablation makes it easy to miss such a diagnosis. As a general rule we measure IOP on every visit and normally expect IOP to be low after refractive surgery. If the IOP is in the high teens a diagnosis of steroid induced glaucoma should always be kept in mind. The incidence of increased IOP after surface ablation has been reported to range from 11% to 25% of patients. The incidence can be as high as 25% in patients using dexamethasone or similar strong corticosteroids compared to patients using fluoromethalone (incidence of 1.5-3% of patients).

As discussed above, one may get falsely low (or normal) IOP when measured with GAT and hence either a Tonopen or pneumotonometer in the peripheral cornea may give a better estimate. If available use of the newer devices like DCT or ORA or CST may be used.

The clinical picture with high IOP postoperatively varies from mild corneal haze with milky vision to stromal swelling, fluid accumulation under the flap to frank interface edema which may mimic a diagnosis of DLK. This is critical as the treatment of the two conditions is opposite. While DLK needs intensive steroids, Pressure induce stromal keratitis (PISK) will need stoppage of steroids and treatment with aqueous suppressants21.

4) Fluid accumulation in the LASIK interface or Interface fluid syndrome (IFS) leads to falsely low IOP estimation by GAT as the fluid acts as a cushion. When suspected, IOP should be re-checked with Pascal’s Tonometer or Corvis ST and treatment in the form of pressure lowering agents initiated. Anecdotal reports of ischemic optic neuropathy due to missed glaucoma are present in literature and warn us that high clinical suspicion and use of more accurate IOP measuring devices must be done especially when a patient is not improving normally after LASIK24.

5) Choice of anti-glaucoma medications is based on the level of IOP. In general beta blockers and carbonic anhydrase inhibitors (both topical and oral) should be initiated. Alpha 2 agonists also stabilize the pupil and prevent mydriasis, so maybe additionally beneficial in patients experiencing glare. Remember that IOP should be normally low after refractive surgery as compared to pre-op estimates. Any IOP which is normal or in high teens especially when the patient is not having a smooth recovery should be re-checked.

**FOLLOW UP**

Postoperatively, continue to keep these high risk patients under follow-up. Consider visual fields 6 months to a year later especially if the patient has responded with a high IOP after refractive surgery. Patients with high myopia and large discs or peri-papillary atrophy will need to be compared carefully with their preoperative records to monitor for any change. Incidence of glaucoma increases with age, so these patients will continue to be glaucoma suspects in the future. Posterior pole imaging using OCT/ HRT or GDx will be most beneficial when compared to their preoperative baseline values since patients with myopic or tilted discs are usually not a part of the standard database of these machines. Use clinical judgment combined with more accurate devices like ORA or Corvis ST to monitor their IOPs along with clinical photographs to detect early changes. Remember good vision may not always be ‘healthy vision’ and some of these patients maybe having a gradual, painless visual loss due to undetected high pressures, so follow up meticulously.

**PEARSLS**

- Treat patients with family history, large cup-disc ratios, tilted or large discs with peripapillary atrophy, high myopia, and borderline IOP as high risk patients and perform detailed baseline evaluation including visual fields, posterior pole imaging with OCT or HRT/GDX, clinical photography and 24 hour IOP measurements.
- Prefer a PRK which does not use a suction pressure or a femto-laser (such as iLasik or SMILE) which causes lesser IOP rise during a refractive procedure25. In case of previous filtering blebs, PRK or surface ablation would be the procedure of choice.
- Monitor IOP carefully using devices other than GAT which may underestimate the IOP. Pascals Tonometer, ORA and Corvis ST are more accurate for IOP measurement but if not available use a tonopen on the peripheral cornea to get a better estimate of the IOP.
- Keep a high clinical suspicion of PISK if the patient has interface haze/edema or inflammation which may appear similar to DLK and treat carefully using aqueous suppressants and withdrawal of steroids.
- Remember higher incidence of steroid responsiveness in these patients compared to general population.
- Follow up with visual fields, imaging and photography and careful comparison with preoperative records. Follow up IOP
measurements may not always be accurate especially when measured with GAT. Clinical judgment is paramount.

REFERENCES


**R**ecent trends and advances

**Dr. Rita Dhamankar, Dr. Vijay Shetty, Dr. Suhas Haldipurkar, Dr. Nancy Sehdev**

*Laxmi Eye Institute, Panvel, Maharashtra, India*

**Abstract:**

**Purpose:** To co-relate internal bleb morphology and bleb wall features on anterior segment optical coherence tomography with bleb function (intraocular pressure) at 1 month, 3 months, 6 months post-trabeculectomy.

**Materials and methods:** A prospective cohort of patients (96 eyes) who underwent trabeculectomy with or without cataract surgery were included. Postoperatively, blebs were analysed using anterior segment OCT and slit lamp photography at 1, 3 and 6 months. Bleb parameters assessed on AS-OCT included bleb height, bleb wall reflectivity and bleb pattern. These morphological features were correlated with intraocular pressure. 1 µm increase in bleb height leads to 0.02 mmHg reduction in mean IOP with a significant p value of 0.002 (95% confidence interval being -0.039 to -0.009). Bleb is considered functional if IOP is less than 16mmHg without medication. 15 of patients underwent 5-Fluorouracil subconjunctival injection to reverse the reflectivity obtained from AS-OCT.

**Conclusion:** AS-OCT can be used as an efficient tool to decide on managing a bleb successfully, by identifying the AS-OCT picture for different stages of bleb healing. Eg- identifying early failure and giving subconjunctival 5-fluorouracil injection which helps in salvaging a failing bleb. Similarly, needling a bleb that is encysting will open up the bleb.

**T**rabeculectomy has been widely accepted as the procedure of choice in the surgical management of glaucoma since its introduction by Cairns in 1968. The outcome of trabeculectomy largely depends on the formation of a functioning filtration bleb. Further, the ability of the bleb to remain functional determines the maintenance of desired intraocular pressures and the long-term success of surgery. In recognition of the importance of bleb appearance in relation to surgical outcome and complications, a number of classification systems have been proposed to characterise bleb morphology based on slit lamp grading. But slit lamp assessment remains essentially subjective and qualitative. The internal morphology of filtering blebs, which could play an important part in determining surgical outcome, cannot be evaluated under slit lamp.

More recently, anterior segment optical coherence tomography (AS-OCT) has been introduced as a useful imaging device in objective evaluation of filtering blebs. AS-OCT provides a high resolution cross-sectional optical imaging of the anterior segment structures via a non-invasive and noncontact procedure, and can provide internal visualization of the blebs. The different patterns of intra bleb morphology identified by AS-OCT in the early postoperative stages are related to the bleb function which is assessed on the basis of intraocular pressure. Both optical coherence tomography (OCT) and ultrasound biomicroscopy (UBM) provide real-time cross-sectional images of the angle and anterior segment.

**OCT ADVANTAGES VERSUS UBM**

- Higher resolution
- Faster scan rate
- Noncontact method, allowing immediate postoperative use

**NEED OF THE STUDY**

There are very limited studies that have used imaging for identifying features of blebs in their early development period after trabeculectomy, which may predict success of these blebs in the long term.

**MATERIALS AND METHODS**

A prospective cohort study was designed to study bleb morphology in patients undergoing trabeculectomy with or without cataract surgery. Study question is can the bleb morphological features which predicts its functionality in late stage be assessed early using imaging techniques and be useful for preoperative guidance for bleb revision? Aim of the study is to co-relate internal bleb morphology and bleb wall features on anterior segment optical coherence tomography with bleb function (intraocular pressure) at 1 month, 3 months, 6 months post-operatively and objectives are to study the bleb morphology using AS-OCT in early postoperative period and to co-relate bleb wall thickness, bleb wall reflectivity, and bleb pattern on AS-OCT with intraocular pressure. Inclusion criteria includes all consenting patients diagnosed to have primary open angle glaucoma, primary angle closure glaucoma or secondary glaucoma undergoing trabeculectomy with or without cataract surgery. Patients with history of any surgery including conjunctival dissection like retinal detachment surgeries, pterygium surgeries, squint surgeries and patients with re-trabeculectomy done were excluded from the study. A previous study by Khamar and colleagues found that the prevalence of
Recent Trends and Advances

Dhamankar R et al. Structural and Functional co-relation of Bleb

Also, photos were taken at 10X magnification and maximum illumination. They were fit into a frame of 250x250 megapixels on Adobe photoshop 7. Two tangents were drawn on either side of bleb from points where blood vessel appear to raise above the surface of bleb. Angle between two tangent was noted and named as Bleb Angle.
Recent trends and advances

Dhamankar R et al. Structural and functional co-relation of Bleb

Table 1: Showing mean intra-ocular pressure pre-operatively and at all post operative visits

<table>
<thead>
<tr>
<th>Follow-up visit</th>
<th>Mean Intra-ocular pressure</th>
<th>Standard deviation</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-operative</td>
<td>30.76</td>
<td>6.85</td>
<td>20-50</td>
</tr>
<tr>
<td>At 1 month</td>
<td>15.14</td>
<td>3.14</td>
<td>8-24</td>
</tr>
<tr>
<td>At 3 months</td>
<td>12.95</td>
<td>1.97</td>
<td>8-16</td>
</tr>
<tr>
<td>At 6 months</td>
<td>11.89</td>
<td>1.61</td>
<td>8-16</td>
</tr>
</tbody>
</table>

Table 2: Showing mean bleb height at 3 post operative visits

<table>
<thead>
<tr>
<th>Follow up visit</th>
<th>Mean bleb height</th>
<th>Standard deviation</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 1 month</td>
<td>82.92</td>
<td>20.42</td>
<td>40-151</td>
</tr>
<tr>
<td>At 3 months</td>
<td>94.44</td>
<td>22</td>
<td>54-182</td>
</tr>
<tr>
<td>At 6 months</td>
<td>98.53</td>
<td>23.64</td>
<td>54-184</td>
</tr>
<tr>
<td>At 6 months</td>
<td>11.89</td>
<td>1.61</td>
<td>8-16</td>
</tr>
</tbody>
</table>

Table 3: Showing mean bleb angle at 3 post operative visits

<table>
<thead>
<tr>
<th>Follow up visit</th>
<th>Mean bleb height</th>
<th>Standard deviation</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 1 month</td>
<td>137.50</td>
<td>13.93</td>
<td>100.9-168.2</td>
</tr>
<tr>
<td>At 3 months</td>
<td>143.21</td>
<td>13.79</td>
<td>110.9-173.4</td>
</tr>
<tr>
<td>At 6 months</td>
<td>148.59</td>
<td>13.32</td>
<td>120.6-175.8</td>
</tr>
<tr>
<td>At 6 months</td>
<td>11.89</td>
<td>1.61</td>
<td>8-16</td>
</tr>
</tbody>
</table>

Table 4: Showing no of eyes with different types of bleb pattern at 1,3 and 6 months

<table>
<thead>
<tr>
<th>Bleb pattern</th>
<th>No. of eyes at 1 month</th>
<th>No. of eyes at 3 months</th>
<th>No. of eyes at 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffuse</td>
<td>95</td>
<td>90</td>
<td>77</td>
</tr>
<tr>
<td>Cystic</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Encapsulated</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 5: No of eyes with different grades of BMA

<table>
<thead>
<tr>
<th>Follow up visit</th>
<th>No of eyes with Grade 3 BMA</th>
<th>No of eyes with Grade 4 BMA</th>
<th>No of eyes with Grade 5 BMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 1 month</td>
<td>1</td>
<td>26</td>
<td>69</td>
</tr>
<tr>
<td>At 3 months</td>
<td>0</td>
<td>9</td>
<td>81</td>
</tr>
<tr>
<td>At 6 months</td>
<td>0</td>
<td>2</td>
<td>75</td>
</tr>
</tbody>
</table>

Table 6: Showing no of eyes with different grades of Bleb Central Area at 3 follow-up visits

<table>
<thead>
<tr>
<th>Follow up visit</th>
<th>No of eyes with Grade 3 BCA</th>
<th>No of eyes with Grade 4 BCA</th>
<th>No of eyes with Grade 5 BCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 1 month</td>
<td>1</td>
<td>11</td>
<td>84</td>
</tr>
<tr>
<td>At 3 months</td>
<td>0</td>
<td>0</td>
<td>90</td>
</tr>
<tr>
<td>At 6 months</td>
<td>0</td>
<td>0</td>
<td>77</td>
</tr>
</tbody>
</table>

Morphology of bleb on AS-OCT showed multiform reflectivity in all blebs at all 3 follow up visits

Hospital and Laxmi eye institute, Panvel, Maharashtra. In this study, patients are selected by non blinded randomization. If any progression of the disease is detected, accordingly medical or surgical management was initiated to prevent the further damage. Enrolment of patients was done over a period of 12 months with three follow ups on 1month, 3months and 6 months. Preoperative assessment includes- Best corrected visual acuity - noted using snellen’s visual acuity charts, slit lamp examination using Haag Streit Model was done to note findings of anterior segment, intraocular pressure- calculated using Goldmann applanation tonometer which was calibrated every month, posterior segment examination was done using Volk 90D lens,gonioscopy was done using Goldmann’s four mirror gonioscope and RP Centre grading for gonioscopy used to comment on the angles, visual field assessment was done using Humphrey field analyser (30-2). Atleast 2 reliable fields were assessed before making diagnosis of glaucomatous field defect. Postoperatively, on 3 post operative visits (1 month, 3 months, 6 months) assessment included.

Visual acuity assessment and intraocular pressure measurement using same techniques as mentioned before. Anterior segment photographs of the bleb taken using Haag Streit model-patient were asked to look down and with the upper lid elevated photos were captured and compared with standard photographs provided with Moorfields Bleb Grading System.

Patients were asked to look down, and the upper lid gently elevated to expose the bleb as much as possible, taking care to avoid exerting any pressure on the globe or bleb. Scanning was performed with both vertical and horizontal linear scans at the centre of bleb. Bleb wall reflectivity was classified as uniform reflectivity or multiform depending on presence or absence of hyper-reflective areas in the bleb wall itself. In uniform reflectivity there are no fluid filled hypo-reflective spaces in the subconjunctival space. It is seen as smooth, hyper-reflective wall. In multiform reflective wall, there is presence of small multiple fluid filled spaces seen as hypo-reflective areas in the conjunctiva or bleb wall. Bleb wall thickness is defined as the distance between the first reflective signal from the conjunctiva to the top of the subconjunctival fluid space, or the suprasceral fluid space if the former is not present. As bleb wall thickness may vary along the scan, only the minimum distance will be measured. Diffuse filtering blebs are characterised by multiple subconjunctival signal void areas corresponding to pockets of fluid collections and low to moderate intra-bleb reflectivity. Cystic blebs are
Table 7: No of eyes with different grades of bleb height

<table>
<thead>
<tr>
<th>Follow up visit</th>
<th>No of eyes with Grade 1 BH</th>
<th>No of eyes with Grade 2 BH</th>
<th>No of eyes with Grade 3 BH</th>
<th>No of eyes with Grade 3 BH</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 1 month</td>
<td>15</td>
<td>31</td>
<td>46</td>
<td>4</td>
</tr>
<tr>
<td>At 3 months</td>
<td>32</td>
<td>54</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>At 6 months</td>
<td>11</td>
<td>66</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

After the above analysis was done, co-relation between IOP and different bleb parameters on AS-OCT and slit lamp was obtained.

Table 8: Showing no of eyes with different grades of bleb height

<table>
<thead>
<tr>
<th>Follow up visit</th>
<th>No of eyes with Grade 1 BH</th>
<th>No of eyes with Grade 2 BH</th>
<th>No of eyes with Grade 3 BH</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 1 month</td>
<td>18</td>
<td>77</td>
<td>1</td>
</tr>
<tr>
<td>At 3 months</td>
<td>46</td>
<td>44</td>
<td>0</td>
</tr>
<tr>
<td>At 6 months</td>
<td>67</td>
<td>10</td>
<td>0</td>
</tr>
</tbody>
</table>

Graph 1: Showing significant co-relation between Bleb height on AS-OCT and IOP at 3 follow up visits. We found that 1 µm increase in bleb height leads to 0.02 mmHg reduction in mean IOP with a significant p value of 0.002 (95% confidence interval being -0.039 to -0.009).

Graph 2: Showing a positive co-relation between IOP and percentage of eyes with Grade 5 BMA at 3 follow up visits. We found that as the percentage of Grade 5 BMA increases, mean IOP decreases by 0.98 mmHg with p value of 0.022 (95% confidence interval being -1.02 to -0.14).

Graph 3: Showing positive co-relation between Bleb Angle on slit lamp photograph and IOP. We found that 1 degree increase in slit lamp angle leads to -0.015 reduction in mean IOP with a p value of 0.23 and 95% confidence interval being -0.039 to -0.009.

**DATA ANALYSIS**

We calculated the means and standard deviation for continuous variables and proportions for categorical variables. The means were compared using t-tests and proportions were measured using chi-square tests. Also, we used logistic regression to predict odds of surgical success at 1 month, 3 months, and 6 months with the observations of AS-OCT at the same follow-ups using predictor variables which includes bleb wall reflectivity (uniform/multiform), bleb pattern (diffuse, cystic, non-functioning flat bleb) and thickness of bleb wall.

**OBSERVATION AND RESULT**

Total 96 eyes were included. Mean age was 54.92±7.70 (Range:16-72 years) Data for 1 month, was available for all 96 eyes. Data for 3 months was available for 90 eyes and 6 months data is available for 77 eyes because of loss to follow up. After the above analysis was done, co-relation between IOP and different bleb parameters on AS-OCT and slit lamp was obtained.

In 15 of our patients we observed rise in intra-ocular pressure. AS-OCT showed reduction in bleb wall reflectivity. Intervention in terms of 5 Fluorouracil injection was done and reversal of reflectivity was seen on AS-OCT.

**DISCUSSION**

The main challenge in the management of filtration surgery is the preservation of the aqueous humour outflow through the scleral ostium and the bleb in order to maintain a good IOP control. Therefore, a careful postoperative clinical evaluation is strongly recommended because the bleb filtering ability may decrease over time. In several cases, the slit-lamp appearance may not be indicative of the bleb functionality because the clinical analysis is a qualitative assessment affected by the intra- and inter-observers variability. Therefore, clinical assessment cannot permit a timely identification of signs of
Recent Trends and Advances

Dhamankar et al. Structural and Functional co-relation of Bleb filtration failure. AS-OCT may contribute to overcome these problems by allowing a detailed structural assessment of bleb-wall layers, bleb cavity, and scleral opening. Moreover, this methodology provides essential biometric parameters such as the bleb wall reflectivity and thickness, which may help the clinician in distinguishing between functioning from nonfunctioning blebs. In addition, AS-OCT proved valuable in the early identification of signs of failure, critical for the bleb management. This is essential since bleb management procedures are much more effective when administered very early. Therefore, a postsurgical follow-up that also considers the routine use of AS-OCT with the clinical evaluation is recommended in order to obtain detailed information concerning bleb functionality.

Previously, other studies have also concluded in their findings that multiform walls (i.e. Areas of hypo reflectivity) in the early bleb may have better bleb function at six months which is consistent with findings of our study.

A limitation of a previous study done by Khamar et al was that they had not co-related clinical morphologic features of the bleb, such as bleb vascularity, with the anterior segment OCT features which we have done and came out with significant co-relations between various bleb parameters and IOP.

In closing, a combined diagnostic approach that comprehends the standard clinical evaluation and an imaging technique such as the AS-OCT may improve the clinician’s ability in the understanding of bleb functionality, in planning the correct timing for bleb management procedures, and in the evaluation of their efficacy.

CLINICAL SIGNIFICANCE DERIVED

AS-OCT can be used as an efficient tool to decide on managing a bleb successfully, by identifying the AS-OCT picture for different stages of bleb healing. Eg: identifying early failure and giving subconjunctival 5-fluorouracil injection which helps in salvaging a failing bleb. Similarly, needing a bleb that is encysting will open up the bleb.

LIMITATIONS

One of the shortcomings of AS-OCT in assessing filtering blebs is that it does not provide microscopic information (as all imaging modalities), which is essential for detecting the very early signs of failure, such as the stromal collagen deposition and the reduction of aqueous humour filled epithelial microcysts. Also, we did not have many failed blebs as had been seen in previous studies, structural changes of failing blebs could not be more elaborately studied and co-related clinically.
Tube Shunts- Our Experience

Dr. Suneeta Dubey, Dr. Deepti Mittal, Dr. Madhu Bhoot

Dr. Shroff’s Charity Eye Hospital, New Delhi, India

Abstract: In the past decade or so, there has been a significant increase in the number of patients being diagnosed with secondary glaucoma which are refractory to medical management. Undoubtedly, the tube implant surgery plays an imperative role in managing such challenging cases of glaucoma. This article throws light on the important indications, contraindications and technique of performing a tube surgery along with its complications. In the end, we would like to share our experience of 165 eyes which underwent tube surgery from January 2003 to March 2017 and some valuable pearls of performing this surgery in different clinical scenarios.

Glaucoma is one of the leading causes of blindness worldwide. Refractory glaucoma is the term used to define any kind of glaucoma that does not respond to medical or conventional surgical management. Trabeculectomy has been the most commonly performed glaucoma surgery for all types of glaucoma, however the success rate remains low in cases of refractory glaucomas despite use of antifibrotic agents and various modifications. In the present era, Tube implants or Glaucoma drainage devices (GDDs) have emerged as a promising and perhaps indispensable surgical tool for the management of refractory glaucoma. Glaucma drainage devices have proven to be more efficacious in reducing intraocular pressure in refractory glaucoma.

Contemporary glaucoma implants are of two types-valved and non-valved. The Ahmed and Krupin implants are valved, whereas the Baerveldt and Molteno implants are nonvalved. Valved implants open at a specific IOP level, thus having a lower chance of post-operative hypotony. Nonvalved implants require few modifications in surgical technique like ligature of the tube in order to prevent hypotony in the immediate postoperative period. Valved implants are easy to perform and provide immediate control of intraocular pressure (IOP) postoperatively. Furthermore, the endplates of the implant can be made of various biomaterials like silicone and polypropylene. Presently, silicone implants are preferred due to lower incidence of hypertensive phase and thinner lower edge thickness and tapered profile thus, promoting better flexibility and easier insertion of the tube. Polypropylene implants are no longer used.

AGV is a shunt device with a built in Venturi valve which opens at a specific level of IOP thus reducing the chances of hypotony in the early post-operative period. It is being extensively used for the treatment of refractory glaucoma cases like neovascular glaucoma (NVG), post penetrating keratoplasty glaucoma, post vitreo-retinal surgery glaucoma and other secondary glaucomas.

Among the various models available for AGV – FP7 is the one which is most commonly used for adults and FP 8 for paediatrics, the two differing in the surface area of endplate.
Recent trends and advances

Dubey S et al. Tube Shunts- Our Experience

www.dos-times.org

73

GDDs are generally reserved for difficult glaucoma cases in which conventional filtering surgery has failed or is likely to fail. However, in most of the secondary glaucoma cases, it can be considered as the first choice of surgery.

Contraindications

• Compromised corneal endothelial function
• Excessively fibrosed conjunctiva
• Severe scleral or corneo-scleral limbus thinning

INDICATIONS

Figure 4: 2-3 mm of the tube inside anterior chamber

Figure 5: Anterior part of the tube is covered with donor scleral patch graft

Figure 6: Meticulous closure of conjunctiva and tenon’s capsule

Figure 7: Tube in sulcus in post penetrating keratoplasty glaucoma and extensive PAS

Figure 8: Horizontal placement of tube in silicone oil induced glaucoma-decreases risk of clogging of tube by silicone oil

Figure 9: Hypotony with shallow AC

Figure 10: Plate extrusion
**Surgical technique**

**A. Preoperative assessment**
- Meticulous patient selection and thorough ophthalmic evaluation is required to assess the placement of implant/tube.
- Superotemporal quadrant is the most preferred site, however, in cases of extensive conjunctival scarring like in post vitreoretinal surgery one should place the implant in the quadrant with least scarring.
- In case of NVG, preoperative management of primary condition leading to neovascularization (Systemic causative factors) should be achieved as progression of basic pathology- fibrovascular proliferation can lead to failure of treatment- blockage of tube. Regression of neovascularization of iris and/or angle can be achieved by panretinal photocoagulation (PRP) or AntiVEGF agents atleast 3- 5 days before surgery.

**B. Surgical steps**
- Surgery can be performed under peribulbar or general anesthesia.
- Superotemporal quadrant is generally chosen for the placement of plate of the implant unless there is some contraindication.
- Superior rectus bridle suture or corneal traction suture or both can be applied for better exposure of the surgical site.
- A fornix-based conjunctival flap and tenon’s capsule dissected to allow insertion of the plate of the implant into sub-tenon’s space 8 -10 mm behind the corneal limbus.
- The valve of the implant is primed with balanced salt solution.
- The plate is fixed to the sclera with 9–0 black nylon sutures.
- The tube is shortened to the desired length with its sharp bevel facing anteriorly to allow 2–3 mm of tube in anterior chamber.
- Insert tube in AC (0.75mm), observe position, avoid touching cornea, iris or lens. Tube should be introduced parallel to the plane of the iris.
- Anterior chamber (AC) paracentesis wound is created at the peripheral cornea and sodium hyaluronate 1% (Healon) injected to prevent collapse of the AC after sclerotomy.
- To prevent tube movement, a radial groove is made in the sclera at the proposed site & the edges of the groove retracted using mild cautery.
- The tube of the implant enters the AC parallel to the iris plane through the sclerostomy made with a 23 gauge syringe needle.
- The tube is fixed to the sclera with 9–0 black nylon suture.
- The anterior part of the tube is covered with a donor scleral patch graft/cornea/processed pericardium which is then fixed to the sclera with 9–0 black nylon sutures (Alternatively, in cases of non-availability of donor tissue, tube can be placed beneath a sclera flap to prevent tube extrusion).
- The conjunctiva is closed with 8–0 polyglactin suture.
- The sodium hyaluronate in the AC is then removed.

**Postoperative care**
- Intensive steroid, antibiotic and cycloplegic drops are to be instilled daily. The antibiotic drops are stopped at 2 weeks postoperatively, and steroid drops are tapered gradually over 8-12 weeks.
- In pseudophakic patients with secondary glaucomas and extensive peripheral anterior synchiae, especially post-penetrating keratoplasty glaucoma, the tube can be placed in the ciliary sulcus. For sulcus placement of tube, enter 1.5-2 mm posterior to limbus. During withdrawal inject visco to push iris anteriorly and IOL posteriorly.
- Concurrent anterior or pars plana vitrectomy is performed in aphakic patients and in patients in whom pars plana insertion of tube is planned.
- In cases of silicone oil induced glaucoma, inferior or horizontal placement of tube helps to prevent tube getting clogged postoperatively. Silicone oil removal should be performed before planning implant surgery.

**Complications**
- Besides the unique complication profile seen with implant procedures, some of the complications encountered in tube surgery are similar to those seen with trabeculectomy.
To summarize, Tube implants have become mainstay for immediate IOP control in difficult and refractory glaucoma cases. However, a multidisciplinary approach is required to deal with these complicated cases. Advent of newer materials, coatings and designs have improved the results greatly. Consideration should be given to expanding the role of tube implants in the surgical management of glaucoma.
Glaucoma is characterised by progressive loss of retinal ganglion cells. The nerve fibre loss results in characteristic changes in the optic nerve head. Structural documentation of the retinal nerve fibre layer (RNFL) and the optic nerve head (ONH) therefore, is an integral part of diagnosis and follow up of glaucoma. Optical coherence tomography (OCT) allows for high resolution measurements of the retinal nerve fibre layer and the optic nerve head. The technology is currently used widely in the diagnosis and follow up of patients with Glaucoma.

As in the use of any technology, the knowledge of the strengths and limitations of the technique, and recognition of artefacts and errors in image acquisition and accurate interpretation is important. Large anatomical variations exist in the size and shape of the optic nerve head, in the normal population. This means that any structural assessment cannot be used in isolation to distinguish between "normal" and "abnormal". A thorough understanding of the possible artefacts helps in accurate interpretation and utilization of this imaging modality in the diagnosis and management of patients with Glaucoma.

ONH SIZE AND ONH AND RNFL IMAGING BY OCT

The optic nerve head is variable in size, and shape. Also most machines have an automated marking of the end of the optic canal by the machine identifying the end of the Bruch's membrane.

The determination of the disc border is made by the automated marking of the Bruch's membrane opening (BMO). The Minimum Rim Width (MRW) is the least perpendicular drawn to the ILM from the BMO. Additionally, before the acquisition in the Glaucoma Module of the Spectralis, the fovea-BMO center axis is first determined. Data acquisition is relative to this axis, and this ensures that measurements are distributed according to the anatomy of the individual eye. All these factors can introduce artefacts and errors in the analysis and the ability to distinguish between a normal and glaucomatous disc.

Imaging errors which make the BMO difficult to identify e.g. Peripapillary atrophy, myopic posterior staphyloma, Incomplete Posterior Vitreous Detachment (iPVD), will cause erroneous marking of the ONH borders and rim width analysis will also be erroneous.

Imaging in Large ONH, is likely to introduce false positives in ONH MRW analysis, and on the other hand, imaging in a small ONH can miss small defects and lead to false negatives, in the analysis of MRW.

Detection of the fovea-BMO axis may be erroneous in eyes with posterior staphyloma and high myopia.

The Cirrus HD OCT ONH analysis is not supported by a normative database if disc area less than 1.3mm² or greater than 2.5 mm².

Larger discs have thicker RNFL measurements. This may be due to the fact that they may contain more nerve fibers, or it may be an artifact of a fixed measurement circle around a larger disc. Because larger discs start with thicker RNFL measurements, they must suffer more damage before registering as abnormal on OCT and therefore have lower sensitivity for early glaucoma detection. Smaller Disc size, on the other hand is associated with OCT RNFL False Positives, due to higher distance of the calculation circle from the disc margin. Therefore one must
exercise caution in interpreting RNFL thickness for disc larger than 3mm² and disc smaller than 2mm².  

**Example 1:**
- iPVD interfering with the imaging of the ONH
**Example 2:**
- Inaccurate BMO detection by the machine influencing the MRW calculation.

- Imaging of the RNFL and ONH, examples of other errors and artefacts:

1) **Image quality**

   - The minimum acceptable image quality on the different OCT technologies are:
     - Cirrus OCT >6
     - RTVue OCT >30
     - Spectralis OCT > / = 20

   - Scan quality affects OCT performance, even when within manufacturer recommended limits. The effect of the scan quality is greater on RNFL than ONH and GCC. Low signal strength causes artefactual thinning of the retinal nerve fiber layer (RNFL).

   - Cataract is a major culprit that can lead to a low signal strength. Dry eye and ocular surface abnormalities can also cause poor image quality.

   - **Example 3:** Poor image quality on Cirrus HD OCT.

2) **Segmentation errors**

   - Segmentation algorithms allow identification of the anterior and posterior limits of the RNFL scan. Errors in the algorithm can cause errors in measurement of RNFL thickness.
Example 4: Error in identification of the anterior limit of the RNFL due to peripapillary epiretinal membrane.

Example 5: Error in identifying the posterior limit of the RNFL in a patient with High Myopia.

Example 6: Incomplete segmentation due to absent data of RNFL due to vitreous opacity.

3) Decentration of scans on the ONH:
Spectralis OCT scans are considered de-centered when the center of the optic nerve head is more than approximately 10% off the center of the peripapillary circular scan. When the scans are de-centered on the ONH, the interpretation of the RNFL thickness will be inaccurate. Accurate centration is essential for the measurement and analysis of RNFL thickness.

Example 7: Inaccurate centration of the RNFL circle around the disc causing errors in RNFL analysis.

4) Artefacts due to shadowing:
If a portion of the scan data is missing due to shadowing due to a vitreous opacity, or prominent blood vessel, or myelinated nerve fiber layer, the missing data poses problems for analysis and interpretation of the OCT images.

Example 8: Shadowing of ONH scans due to vitreous opacity

Example 9: Shadowing due to blood vessel

Example 10: shadowing due to Myelinated Nerve fibers.

5) Errors in RNFL thickness estimations due to other anatomical structures or pathology.
Presence of prominent or thick blood vessels, Myelinated nerve fibers and prominent ERM can cause erroneously thick estimates of the RNFL.

Example 11: Myelinated NFL causing apparent increase in NFL thickness

Example 12: Blood vessel causing apparent increase in thickness and back shadowing.

Example 13: Traction causing apparent increase in thickness/ MRW

6) Errors due to imaging of eyes with Peripapillary atrophy, and tilted discs, and high myopes.
The presence of peripapillary atrophy interferes in the estimation of RNFL thickness. Estimation of RNFL thickness in eyes with extensive PPA is likely to be inaccurate. Also high myopia and its associated features such as posterior staphylomas can cause poor
images, and segmentation artefacts, and estimation of RNFL thickness is likely to be inaccurate.

**Example 14:** Unilateral pathological myopia with tilted disc. Low scan quality and segmentation artefacts.

**Example 15:** High myopia with PPA, segmentation artefacts.

**Example 16:** Other examples of PPA and low quality images and erroneous RNFL and MRW assessments.

7) **Truncation of scans leading to missing data for analysis.**

Errors during acquisition of the scans where part of the RNFL image is truncated, or cut off due to inaccurate optimization of the scans, or truncation due to staphylomas in myopes can lead to errors in RNFL estimation.

**Example 19:** Truncation of scan due to poor alignment during acquisition.

8) **Artefacts due to blinking.**

If the patient blinks during acquisition of the scans, a portion of the data in the ONH cube is missing. This is indicated by a dark or black band on the reflectance image on the printout. This can lead to errors in RNFL thickness estimation and such scans should be discarded.

Blink artefacts can be avoided, if the patient is allowed to blink during the alignment process, and is asked to blink firmly once and keep the eye open during the acquisition. Lubricant eye drops may also be used prior to the scan.

**Example 20:** Missing data due to blinking during scan acquisition.

9) **Errors due to micro movements of the eye during acquisition**

Small movements of the eye can lead to errors in acquisition of the ONH images. The errors are seen as a horizontal break in the image on the black and white images of the scans, or a shadow images of the disc, or blood vessel. This can lead to errors in measurement of disc and RNFL parameters.

**Example 21:** Error due to micro movements of the eye during acquisition.

**Example 22:** Shadow image of ONH and blood vessels due to movement of eye during acquisition.

Liu et al in their study of 2313 consecutive Spectralis Glaucoma scans found that at least one artefact could be identified in 1030 or 46.3% of scans. De-centration error was the most common artifact (27.8%), followed by posterior vitreous detachment artifacts (14.4%). Visual acuity of less than 20/40 (p<0.0001), presence of moderate to severe cataracts (p<0.0001), advanced stage of glaucoma (p<0.0001), and a diagnosis of open angle glaucoma (p=0.0003) were associated with increased prevalence of artifacts.

Similar results have been found in studies with the Cirrus HD OCT Glaucoma scans as well.

Automation of the neuroretinal rim parameter measurement is a significant advance, in OCT over the other imaging
Techniques

80

Example 23: “Green disease” - normal scan in the presence of a RNFL defect.

Table 1 gives a step by step approach to avoid misdiagnosing OCT scans of the ONH and RNFL.

The technician and the interpreting ophthalmologist should be aware of all possible artefacts and these should be considered while interpreting the OCT images. The physician should go back to the original scans on the machine, and check the quality, and segmentation, before deciding on the interpretation of doubtful scans. Diagnosis of Glaucoma should NEVER be solely based on a single imaging result.

Table 1: Step by step protocol to avoid misinterpretation of OCT in Glaucoma

<table>
<thead>
<tr>
<th>Step</th>
<th>Protocol</th>
</tr>
</thead>
</table>
| 1.   | Confirm the name and age of the patient  
|      | - Measurements are made against age matched controls |
| 2.   | Check signal strength  
|      | - Signal strength ≥7 out of 10 is preferable (for Cirrus OCT)  
|      | - > 20 for Spectralis |
| 3.   | Check if there are any blink related or movement related errors |
| 4.   | Look for vitreous opacities and epiretinal pathologies which can influence RNFL measurements in the scan. |
| 5.   | Check refractive error and, if available, axial eye length  
|      | - Axial eye length is particularly helpful for patients who are pseudophakic or who have had refractive surgery |
| 6.   | Interpretation of the optic disc OCT  
|      | - Examine the thickness and probability retina maps for the presence of rectangular areas of absolute RNFL loss that do not match the anatomical distribution of RNFL arcuate bundles. Non anatomical areas of loss typically indicate errors in segmentation  
|      | - Compare the fundus image and thickness maps to ensure that the identification of the disc border and cup by OCT corresponds to the clinical estimation.  
|      | - Examine the TSNIT RNFL plot and make note of whether the location of the peaks correspond to the peaks from the normative database.  
|      | - Look for presence of tilted discs and peripapillary atrophy and be aware of the artefacts possible. |
| 7.   | Recognize that ocular disease can create errors in segmentation |
| 8.   | CORRELATE WITH CLINICAL EXAMINATION OF THE DISC AND RETINA AND VISUAL FIELDS. |


modalities, but has its share of artefacts too.

**RED AND GREEN DISEASE**

False positive and False negatives are a definite possibility in OCT scans related to Glaucoma. Kim et al analyzed the RNFL of 149 eyes from 77 healthy adults with spectral domain OCT and found a false-positive rate of 26.2%.

The false diagnosis of Glaucoma based on the “red” color code in the statistical comparison with the normative database, is known as “Red Disease”. Focal RNFL defects are usually averaged out when the sectoral RNFL maps are analyzed and compared to the normative database. The false diagnosis as “normal” in a patient with RNFL loss, due to the “green” color coding in the comparison maps, is called “green” disease. One should not take OCT results at face value, seeing red automatically prompting a diagnosis of Glaucoma, or green falsely reassuring that everything is normal.

**Example 23: “Green disease” - normal**

REFERENCES

H

uman nature is such that it is not at all keen to bring about change and seeks great amount of solace and comfort in maintaining status quo, more so glaucoma specialists than most. However as has been well said before – change is the only constant in this world. Desire for change is the force that metamorphosed mutilating intra-capular cataract surgery into phaco and femtosecond laser assisted cataaract surgery; similarly, in corneal transplants, with capability of replacement in layers, forgoing the need for penetrating keratoplasty.

Glaucoma traditionally has been a disease where cautious step-wise approach to management is the norm. It is initially treated medically, proceeding to surgery only following failure of medical treatment. Management is not in that order in angle closure disease wherein it is laser (peripheral iridotomy) that is done first and subsequent management is substantially dictated by the amount of synaechial angle closure and damage to the optic disc. That is why morbidity due to angle closure disease is known to be high and in a developing country like ours, as access to healthcare is not only poor, but also delayed, it increases several-fold.

Nonetheless, thus far, trabeculectomy, since its description in the late 1960’s, has been the mainstay of surgical treatment in both open as well as closed angle glaucoma. The guarded filtration technique, as described by Cairns, was an improvement on the full thickness filtration procedure, with unquestionable efficacy specially when adjuvant anti-fibrotics are used. However, it continued to be plagued by unique sight-threatening complications, including and not limited to hypotony and its sequelae and life-long risk of infection. Perhaps this risk of morbidity was the prime determinant of its use mostly in medically resistant, usually advanced glaucoma. Drainage implants or tubes, also considered traditional surgery, with all its incumbent risks, hitherto reserved for refractory glaucomas, are increasingly making in-roads into the management of primary glaucomas following publication of long-term results in the Tube vs. Trab study. With the presentation of the results of the Primary Tube vs Trab study time will determine whether this trend will continue or not.

Perhaps spurred by a desire to find suitable alternatives with fewer sight threatening complications, non-penetrating glaucoma procedures were described in the 1990s which produced minimal blebs. Safer it is, but only with a moderate intraocular pressure (IOP) lowering effect. It is indicated in open angle glaucoma and has a steep learning curve; thus, favourable results have been reproducible only in small pockets around the world.

The Express Glaucoma Filtration Device (GFD, Alcon Laboratories, Fort Worth, TX, USA) implanted under a modified trabeculectomy- like scleral flap, restricts outflow by standardizing wound size and retarding flow by channelling it through a cylindrical implant. It too created a bleb, with fewer complications when compared to trabeculectomy. However, it appears that its main contribution was to usher in a generational change in the design of glaucoma surgical devices, epitomised by the development of multiple ab-interno (inside-out) and ab-externo (outside-in) devices and procedures (Table 1), developed by industry and refined in collaboration with ophthalmologists/glaucoma specialists.

These newer devices and procedures, so called minimally invasive glaucoma surgery (MIGS) – unlike their predecessors, are bleb-independent and hence have a better safety profile. However IOP reduction is modest at best and they are thus indicated in early-to moderate open angle disease; these devices do not have relevance in synaechial angle closure, unless the angle opens post laser peripheral iridotomy (LPI). A literature search yields approximately 25-59%9-11 angles that continue to remain occludable post LPI. Thus, there is unmet need in angle closure disease.

Recent evidence from The EAGLE study12 suggests that lens extraction (clear) alone may be sufficient for control of angle closure disease. However, angle closure exists in various forms and phacoemulsification alone does not seem to resolve the pure plateau mechanism of angle closure due to high ciliary body insertion.

Plateau iris is apparent clinically as a relatively deep central anterior chamber, planar iris, and a “double-hump” appearance on gonioscopy, despite the presence of a patent LPI. Anatomically, plateau iris is defined as anteriorly positioned ciliary processes (UBM) that push the peripheral iris forward, resulting in irido-trabecular proximity. Ultrasound
Biomicroscopy studies performed before and after lensectomy demonstrate that irido-ciliary apposition seems to persist in plateau iris syndrome (PIS) despite lens extraction (Figure 1).

Endocyclophotocoagulation (ECP) is one such minimally invasive procedure that may be deployed in angle closure as angle status is inconsequential in the delivery of laser. It has been used with moderate success in open angle, paediatric and refractory glaucomas. In a modification of ECP, endocycloplasty (ECPL) has recently been described and combined with Phacoemulsification, it is gathering momentum in PIS.

**Table 1: Some of the MIGS devices and procedures**

<table>
<thead>
<tr>
<th>Ab-interno</th>
<th>Trabecular micro bypass</th>
<th>iStent (Glaukos, CA, USA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trabeculotomy</td>
<td>Trabectomy (NeoMedix, Tustin, USA), Kahook Dual Blade (New World Medical, CA, USA)</td>
<td></td>
</tr>
<tr>
<td>Suprachoroidal stent</td>
<td>Cypass (Transcend Medical, CA, USA)</td>
<td></td>
</tr>
<tr>
<td>Subconjunctival implant</td>
<td>Xen (AqueSys Inc., CA, USA), InnFocus (InnFocus Inc, FL, USA)</td>
<td></td>
</tr>
<tr>
<td>Intracanalicular scaffold</td>
<td>Hydrus (Ivantis Inc., Irvine, CA, USA)</td>
<td></td>
</tr>
<tr>
<td>Endocyclophotocoagulation</td>
<td>ECP (Endo Optiks, NJ, USA)</td>
<td></td>
</tr>
<tr>
<td>Ab-externo</td>
<td>Suprachoroidal micro shunt</td>
<td>SOLX (GMS, Mass, USA), Starflo (iSTAR Medical, Belgium)</td>
</tr>
<tr>
<td>Canaloplasty</td>
<td>iTrack-250A (iScience Interventional, CA, USA), ABiC (Ellex, Aus), Glauclolight (DORC, The Netherlands)</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1:** UBM: persistence of irido-ciliary apposition, before and after lensectomy in PIS (with kind permission from Dr. Iqbal Ike Ahmed, MD)

**Figure 2A:** Endoscopy pre-ECPL, post phaco - except for 1 clock hour (arrows), the rest of the angle in the inferior 180 degrees appears closed.

**Figure 2B:** Endoscopy post phaco-endocycloplasty - scleral spur is visible throughout inferior 180 degrees.

**Surgical Technique of Phaco-ECPL**

It involves Phacoemulsification and IOL surgery, performed prior to endocycloplasty.

We prefer a clear corneal incision for ease of access and its self-sealing properties. The same incision is typically used for both phacoemulsification and endocycloplasty.

After phaco is completed and the IOL is in the bag, we fill-up the anterior chamber with a cohesive visco-surgical device and introduce the endoscope in the AC to visualize the angle.

Following this, we inject cohesive ophthalmic visco-surgical device to expand the ciliary sulcus and create space for the endoscopic probe. The 20-gauge curved ECP probe (Endo Optiks, Little Silver, NJ), which consists of a fiberoptic camera and a diode laser is placed through the main incision. We set the laser to continuous-delivery mode with 250 to 500 mW of power. We visualize the ciliary processes by passing the curved probe behind the iris and into the sulcus. A red aiming beam is aligned with the posterior aspect of the ciliary processes. It is important to start lasering at the posterior tail aspect of the ciliary processes and to observe the processes retreat posteriorly (Figure 3). The goal of laser is shrinkage and not destruction so the endpoint of laser treatment is marked by adequate shrinkage and whitening of the ciliary process, strictly avoiding “pops”. The latter occur due to application of too much energy;
Moreover, overtreatment may lead to excessive postoperative inflammation and a breakdown of the blood-aqueous barrier and its sequelae.

The endoscope is re-introduced into the AC, to visualise the angle yet again. In this case, in stark contrast to the view after phaco alone (Figure 2A), immediately prior to endocycloplasty, appositionally closed angle opens up to scleral spur in the inferior 180 degrees (Figure 2B).

We have performed intra-operative anterior segment OCT to demonstrate change in angle recess. Images were obtained after phaco (and before ECPL) and again after ECPL. ASOCT has been done in several cases (Figure 4,5,6). All of them show increase in angle recess.

Cyclo-ablation pulls the entire ciliary process, including its anterior head, posteriorly. It thereby widens the anatomic angle and flattens the peripheral iris, along with IOP control, due to the photocoagulative effect on ciliary processes (decreased aqueous production). Currently, no treatment definitively addresses angle closure secondary to plateau iris syndrome. Our preliminary results suggest that endocycloplasty in combination with phacoemulsification and an IOL implantation directly impacts on this underlying morphological anomaly. Anterior segment OCT provides direct evidence of this.

**OUR EXPERIENCE**

We conducted a pilot study of 10 eyes of 9 patients who were treated with combined phacoemulsification and ECPL for angle closure disease and did not restrict the procedure to PIS alone. We have a median follow-up of 18 months; median IOP significantly decreased from 20 to 15.5 mm Hg, and the median number of glaucoma medications significantly decreased from 3 to 0 and decimal VA significantly improved from 0.55 to 1.

Encouraged by our success in this study, a prospective, randomised study was conducted comparing this procedure with the current standard of phaco-trab in all those subjects that had standard indications for combined surgery. We recruited 42 patients in this pilot study; twenty in each group, as 2 patients in phaco-ECPL were excluded due to non-adherence with laser protocol. At median 6 months’ follow-up, there was no difference in IOP, anti-glaucoma medication and vision in either group; however, the phaco-ECPL group had a much lower rate of complications.

None of the patients in either of the studies developed hypotony or lost vision due to ECPL. The ECP collaborative study group (in 5824 eyes), too, have reported very low complication rates (0.12% hypotony, 0.09% choroidal haemorrhage).

Both our pilot studies (publication pending) have successfully demonstrated the ability of ECPL in controlling IOP in angle closure disease, when combined with phaco surgery.

Thus, in a head-to-head comparison with phaco-trabeculectomy, currently the gold standard procedure, phaco-ECPL is quicker surgery, with faster recovery, and appears to be equally efficacious without the incumbent serious complications related to trabeculectomy in angle closure disease. It need not be restricted to PIS; it has been effective in synaechial angle closure as well. Studies hitherto have mainly concentrated in open angle or refractory glaucomas.

Furthermore, it can be repeated if required and if it is still not effective,
it does not preclude, or compromise, future trabeculectomy as conjunctiva is unscathed. It can be easily combined with cataract surgery by anterior segment surgeons and usually adds no more than 5-10 minutes to a phaco procedure.

Direct visualisation of ciliary processes for precise delivery of laser helps to avoid pain, excessive inflammation, hypotony, phthisis and visual loss related to trans-scleral delivery of the same.

This technology is readily available but expense may be a consideration, especially in a developing country like ours. However, it should be considered as a one-time capital expenditure, just like a phaco machine. The possibility of acquiring an endoscope alone and coupling it with a pre-existing diode laser machine, if available, can also be contemplated, driving down expenditure.

Cost not with standing, when seen from the perspective of the patient, this freely-available, relatively new technology not only improves their quality of life, with none or fewer anti-glaucoma medications, but also faster visual rehabilitation with fewer post-operative visits.

CONCLUSION

To conclude, removal of the lens is advocated early in angle closure disease and when it is combined with ECPL, it has the ability of further widening the angle recess, along with IOP control, with minimal side-effects. The benefit of any glaucoma procedure reducing intraocular pressure needs to be weighed against its adverse events. Creation of a bleb in trabeculectomy, efficacious though it may be, is the source of most serious sight threatening complications.

So, change we (glaucoma specialists) must. Trabeculectomy had to step back once before, with the advent of the so-called ‘chemical trabeculectomy’ when prostaglandin analogues were made available in the last decade of the last century. It is standing at a cusp, yet again, likely to be dethroned from its primacy in the overall surgical management of glaucoma, as safer surgical alternatives are made possible, even in angle closure disease. Winds of change indeed.

REFERENCES

SELECTIVE LASER TRABECULOPLASTY (SLT) – A NOVEL THERAPY

Dr. Mayuri B Khamar MS, Dr. Sonal Juneja MS, Dr. Priyanka Patel DNB
Raghudeep Eye Hospitals, Gurukul, Memnagar, Ahmedabad, India

Abstract: Background: Selective Laser Trabeculoplasty (SLT) has been used effectively in Caucasian eyes having Primary Open Angle Glaucoma (POAG) and Ocular Hypertension (OHT). Its effect in pigmented eyes is not known.

Purpose: To determine effectiveness of SLT in Indian eyes with POAG or OHT.

Material & method: A prospective, non-randomized, interventional study included 65 eyes (47 patients) that completed 2 years follow up were taken for analysis. Standard technique of SLT was performed (360-degrees). Main outcome measures were reduction in IOP, no of drugs at 1 day, 1 month, 6 months, 1 year, 2 years.

Results: Pre-SLT mean IOP was 18.99 ± 3.05 mm Hg which dropped to 15.61 ± 4.25 mm Hg at 12 months and 16.04 ± 3.57 at 2 years (p<0.01). IOP reduction of >15% from baseline was found 50.77%, 66.67%, 49.23% eyes at 6 months, 1 year and 2 years. Mean number of medications dropped from 1.40 ± 1.012 pre-treatment to 0.63 + 1.08, 0.70 + 1.06, 0.51 + 0.85 at 6 months, 1 year and 2 years (p<0.01). Pre-SLT 11 (16.9%) patients were not using any drug. Post SLT 40(66.7%), 34 (59.6%), 44(67.7%), were not on treatment at 6 months, 1 year and 2 years.

Conclusion: SLT is effective in reducing IOP and number of medications in Indian eyes with POAG and OHT. However, effect does show a wear off over time.

Medical therapy is the mainstay of treatment for primary open angle glaucoma. However, there are number of concerns regarding chronic medical therapy like poor compliance, side effects, wide fluctuations in IOP due to trough effects and worsening the prognosis of glaucoma surgery due to ocular surface induced changes. To overcome these problems Selective Laser Trabeculoplasty (SLT) has come as a novel therapy.

Selective Laser Trabeculoplasty is a laser procedure used to lower intraocular pressure in patients with primary open angle glaucoma and ocular hypertension. It is safe and cost-effective treatment modality with no compliance issues. It produces its effect by selective absorption of energy in pigmented trabecular meshwork, sparing the adjacent structures from thermal damage with minimal morphological alteration in the tissues post treatment.

BACKGROUND
Since many decades, lasers have been known to play a major role in management of glaucoma. The general concept which is prevalent, is that it is used after failure of medical treatment. The efficacy of Argon Laser Trabeculoplasty (ALT) got established after Glaucoma Laser Trial. ALT became popular as a second line of treatment for open angle glaucoma or as an adjunct to medical therapy. However, ALT lost its popularity due to its limited efficacy in controlling IOP in long term follow up, peripheral anterior synechia (PAS) formation and coagulative damage of trabecular meshwork.

Anderson and Parrish in 1893 demonstrated the concept of ‘photothermolysis’ which gained wide popularity in dermatology. This modality involved application of laser to selective cell population. Based on this concept in the field of glaucoma, a laser modality was developed which can target selectively the pigmented trabecular meshwork without affecting the neighbouring population. Hence came forth the genesis of ‘selective laser trabeculoplasty’ (SLT).

Selective laser trabeculoplasty (SLT) was launched in 1998 by Latina et al. It uses a frequency-doubled, Q-switched, 532 nm Nd:YAG laser which is able to deliver energy at short pulse duration of 3nsec with a spot size of 400μm. Pulse duration is too short (limits the conversion of electromagnetic energy to thermal energy) to generate heat and cause thermal damage.¹

Comparison of ALT and SLT is summarised in Table 1. This
information provides an insight to opt SLT as a repeatable treatment modality for IOP reduction.

MECHANISM OF ACTION

A number of theories have been proposed regarding the mechanism of laser trabeculoplasty. The main theory attributed to SLT is biological and cellular. The laser application selectively stimulates the pigmented trabecular meshwork cells causing various changes like release of cytokines, it induces cell division, upregulates metalloproteinases, increases porosity of endothelial layers of TM and Schlemm’s canal and recruits macrophages into the TM zone. These changes result in remodeling of extracellular matrix and hence increases aqueous outflow from the eye with minimal damage to the tissue.

It has been demonstrated on light microscopy and transmission electron microscopy that SLT breaks down the melanin granules and ruptures the lysosomal membranes in the melanin containing cells without damaging adjacent non-pigmented cells ultrastructurally, suggesting its work at cellular level.

PATIENT SELECTION

Almost all patients with abnormally elevated IOP (POAG and OHT), who may benefit from IOP reduction, are suitable candidates for SLT treatment. Patients with any type of open angle glaucoma, and those who confirm to the following criteria, are suitable candidates:

- Require lowering of IOP as either primary or secondary therapy
- Non-compliance to drug therapy
- Have difficulty in administering eye drops
- Suffer from drug induced side effects
- Complain of reduced quality of life due to the need to administer eye drops daily
- Failed drug therapy
- Failed ALT treatment, or if ALT ceased to reduce the IOP sufficiently
- Failed SLT treatment, or if SLT ceased to reduce the IOP sufficiently
- Pigmentary or pseudoxfoliation glaucoma (Proceed with caution as there is a risk of post-SLT IOP spike)
- Normal tension glaucoma
- Ocular hypertension

Indications for SLT:

a) Open Angle Glaucoma
   - Primary Open-Angle Glaucoma
   - Ocular Hypertension

b) Combination or replacement therapy:

For cases where target IOP is not achieved with medical therapy, diurnal curve has high fluctuations, one or more drugs are not tolerated and compliance issues.

c) Failed ALT

d) Voluntarily chosen by the patient as an alternative to or in combination with medical therapy

e) Post-filtration surgery patients requiring additional treatment

SUGGESTED SLT TREATMENT PROTOCOL

Counselling is must regarding lifetime follow up visits. Baseline investigation of optic disc changes, visual field and diurnal variation of IOP should be done. Washout period of topical anti-glaucoma treatment (two to three weeks depending upon the drug) should be given. Oral medications should be given to control IOP during washout period. Before performing SLT pilocarpine 2% eye drop should be instilled 2-3 times. This helps in pulling iris away from angle giving good visibility.

Using Latina SLT Gonio lens 3600 angle should be treated in clockwise manner with a spot size of 400 microns and energy range between 0.6 mJ to 1.4 mJ with number of spots ranging 80-100 per session with pulse duration of 3 nsec. Treatment end point is suggested by appearance of “cavitation-bubbles”. Post operatively the non-steroidal anti-inflammatory eye drop should be given. Do not use steroid eye drops as it may potentially interfere with the SLT mechanism.

Monitor IOP after 1 hour of procedure. 5% cases may show IOP spike. IOP should be checked on day one, one week, 1 monthly till 3 months and then 3 monthly. Diurnal variation of IOP should be performed after 3 months to note any IOP fluctuations. Disc and visual field evaluation can be repeated yearly. Repeat SLT can be done after 3-4 months of treatment if required.

Special caution should be taken in cases of pigmentary glaucoma, where one quadrant at a time or 90 degrees should be treated with low energy settings (< 0.6mJ). Post operatively aggressive use of NSAIDs in needed. Also, cases of advanced glaucoma with tubular field of vision or temporal island of visual field should be

- Pigmentary Glaucoma
- Pseudoxfoliative glaucoma

---

**Table 2: Demographic data**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>N= number of patients</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>61</td>
<td>30</td>
<td>92</td>
<td>57.39</td>
<td>14.917</td>
</tr>
<tr>
<td>Female</td>
<td>4</td>
<td>48</td>
<td>74</td>
<td>61.5</td>
<td>10.755</td>
</tr>
</tbody>
</table>

**Table 3: Mean IOP and number of anti-glaucoma medications before and after SLT**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Baseline</th>
<th>6 months</th>
<th>1 year</th>
<th>1.5 years</th>
<th>2 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>61</td>
<td>30</td>
<td>92</td>
<td>57.65</td>
<td>14.663</td>
</tr>
<tr>
<td>Female</td>
<td>4</td>
<td>48</td>
<td>74</td>
<td>61.5</td>
<td>10.755</td>
</tr>
</tbody>
</table>

**Table 4: Change in IOP (mmHg)**

<table>
<thead>
<tr>
<th>Difference (mm of Hg)</th>
<th>No. of eyes at 1 year</th>
<th>No. of eyes at 1.5 years</th>
<th>No. of eyes at 2 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 2</td>
<td>17</td>
<td>21</td>
<td>27</td>
</tr>
<tr>
<td>2.1-4.0</td>
<td>10</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>&gt;4-6</td>
<td>12</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>&gt;6</td>
<td>18</td>
<td>11</td>
<td>13</td>
</tr>
</tbody>
</table>
treated cautiously needing close follow up.

EFFECT OF SLT ON IOP

SLT lowers IOP significantly on day 1 due to induced low grade uveitis. The maximum lowering is seen at 8 weeks. Rarely the lowering is seen at 3 months. So, wait for at least 3-4 months before repeating the SLT IOP lowering effect of SLT wears off over time. IOP reduction of around 20-25% (4-6 mmHg) reported in the short term follow up (up to 6 months).

Jindra et al have shown that a 31% mean IOP reduction (5.9 + 3.2 mm Hg); in 35-50% of eyes IOP was controlled with no additional IOP-lowering interventions whereas 50-65% required some treatment at five years after SLT as a primary treatment. They also reported that post SLT more than 50% of patients did not require medications.*

It has been shown that major factor influencing the success of SLT is baseline IOP only, higher the IOP at treatment greater the reduction.

COMPLICATIONS

Conjunctival redness and injection, blurred vision, ocular discomfort, are possible complications after SLT. Rarely IOP spike of 5-7 mm of Hg is seen after procedure. Failure to achieve the target IOP may need re-treatment. SLT has not been shown to be suitable for the following conditions:
- Pediatric glaucoma.
- Juvenile glaucoma.
- Primary or secondary narrow-angle glaucoma.
- Inflammatory or Uveitic glaucoma.
- Any disease process or malformation that blocks the angle.
- Unclear view of the trabecular meshwork (TM).

Why SLT should be used as a primary treatment?

SLT is effective, safe, painless and fast procedure which can be completed in 5-10 minutes. It can be repeated with minimum risk. It is also effective in lowering the IOP even in post ALT patients.

It is easy to perform and well tolerated by the patients. Some ophthalmologists prefer doing 180 considering the previous effects of ALT but it has been shown in studies that both 180 and 360 approaches are successful as an initial therapy.

The development of SLT has provided us with a new, exciting option in the treatment of glaucoma. It has been shown to be as effective as medical therapy. SLT can have a tremendous impact on patient’s quality of life by decreasing the dependency on the topical treatment.

Our Experience in Indian pigmented eyes:

The objective of our study was to assess the potential efficacy and safety of selective laser trabeculoplasty as a primary treatment modality for lowering the intraocular pressure in cases of Primary Open Angle Glaucoma and Ocular Hypertension. The major outcome measure was percentage of reduction in intraocular pressure and reduction in number of anti-glaucoma medications before and after SLT.

MATERIAL AND METHODS

A prospective interventional study was performed on 65 eyes (47 patients) who underwent SLT in our outpatient department. The study adhered to the principles of the Declaration of Helsinki. Informed consent was taken from all the patients after explaining the procedure and approval by the institutional review board was obtained prior to the study commencement. The authors declare no financial or conflicting interests.

The cases of Primary Open Angle Glaucoma and Ocular Hypertension either newly diagnosed or currently on medical therapy were included. Number of anti-glaucoma medications patients were using pre-SLT were recorded. Baseline IOP was measured for each patient using Goldmann Applanation Tonometer and IOP was also recorded before performing the SLT.

All recruited patients received a single session of SLT. To achieve miosis, Pilocarpine 2% eyedrop was instilled every 15 minutes for 2 times. Under effect of topical anaesthesia, Latina gonio lens was placed on eye. Laser was delivered in affected eye with an initial energy of 0.8 mJ (0.6 mJ-1.2 mJ) (LUMENIS SLT machine). The power was titrated up or down until bubble formation was just visible. All eyes were treated 360° in Trabecular meshwork using standard approach. Approximately 80-100 shots were delivered to treat each eye. The procedure was performed by single glaucoma specialist (Dr. Mayuri Khamar) in all cases and both eyes were treated in the same laser session for those with bilateral disease. Post-operative non-steroidal anti-inflammatory eye drops and anti-glaucoma eye drops were given for a period of one week.

Post SLT intraocular pressure was measured after 1 hour and then patients were followed up at one day, one week, three months, six months, 1 year and then 6 monthly upto 2 years. At each follow up IOP was measured using Goldmann Applanation Tonometer. Diurnal variation of IOP was done every 3 months for each patient and visual fields and optic nerve head OCT were repeated every 1 year.

RESULTS

Sixty-five eyes of 47 patients (29 unilateral and 18 bilateral cases) were enrolled. Out of 65 eyes, 60 were males and 4 were females. 54 were on less than 2 anti-glaucoma medications and remaining 11 patients were on no medical therapy. Mean age was 57.65 ± 14.66 years (range 30-92 years) (Table 2). All subjects were Indians with pigmented TM and open angle configuration. Mean (pre-study) baseline IOP with current medication in all patients was 18.99 ± 3.05 mmHg.

Mean IOP (mmHg) reduced to 15.67 ±3.50, 15.61 ± 4.25, 15.74 ± 3.40, 16.04 ± 3.57 at 6 months, 1 year, 1.5 years and 2 years post SLT. Percentage reduction in IOP of more than 15% was seen in 33 eyes (51%) after 6 months, 38 eyes (66.67%) after 1 year, 29 eyes (52.73%) after 1.5 years and 32 eyes (49.23%) after 2 years of SLT procedure. Also, percentage reduction from baseline IOP was 16.85%, 17.79%, 17.11%, 15.53% at 6 months, 1 year, 1.5 years and 2 years respectively (Table 3).

Mean number of drugs reduced from baseline (pre-SLT) 1.40 ± 1.012 to 0.63 ± 1.089, 0.70 ± 1.068, 0.55 ± 0.878, 0.51 ± 0.85 at 6 months, 1 year, 1.5 years and 2 years after SLT.

Difference in intraocular pressure of more than 6mmHg post SLT was observed in 18 eyes (42.8%) after 1 year, 11 eyes (26.19%) after 1.5 years and in 13 eyes (30.9%) after 2 years. Whereas difference of less 2mm of Hg was observed in 17 eyes (26.15%), 21 eyes (32.30%) and 27 eyes (41.5%) at 1year, 1.5 years and 2 years (Table 4).

Lee JW et al in their study reported an absolute success in IOP reduction of 22% at 12 months and our study showed a similar IOP reduction of 18% by 1 year in Indian eyes.

CONCLUSION

Argon Laser Trabeculoplasty (ALT)
was deployed as an alternative to anti-

glaucoma medications with significant IOP reductions. However, it can lead to coagulative damage and trabecular scarring and henceforth lost its clinical value in terms of IOP reduction with respect to time.

SLT is a laser-based treatment modality that is gaining worldwide popularity as a means of primary line of management. SLT employs a low energy, nanopulse technology with minimal thermal damage to the trabecular meshwork and hence repeatability does not act as a barrier in cases which fail to respond with initial treatment or in cases with area of treatment being 180 degrees or less.1,2

To conclude, our study emphasizes that SLT can be considered as an alternative primary treatment for primary open-angle glaucoma and ocular hypertension cases and it may provide long-term benefits if good compliance is achieved with proper counseling and follow-up of the cases.

REFERENCES


Correspondence to:
Dr. Mayuri B Khamar
Director, Glaucoma Center,
Raghudeep Eye Hospitals, Gurukul,
Memnagar, Ahmedabad, India
Photo Essay

**ND-YAG Laser Cystostomy for Iris CYST with Secondary Angle Closure Glaucoma Following Phacoemulsification**

Shalini Mohan MS, DNB, Mohit Khattri MS, Raj Nath Kushwaha MS, Sonali Bhalla MS, S.K. Sachan MS

*Glaucoma Services, Department of Ophthalmology, GSVM Medical College, Kanpur, U.P, India*

**Abstract:** This is a case report of a 52 years old female, referred due to non improvement in best corrected visual acuity (BCVA) in her right eye (OD). There was a history of phacoemulsification six months back in the same eye. The detailed slit lamp evaluation revealed lobulated, pigmented, cystic mass arising from the iris and filling half of the anterior chamber. Gonioscopy showed closed angles corresponding to the cyst and intraocular pressure (IOP) was 38 mm Hg OD. A diagnosis of angle closure glaucoma (ACG) secondary to iris cyst with pseudophakia was made. The cyst was confirmed on Ultrasound biomicroscopy (UBM). It was treated by Nd-YAG Laser cystostomy following which it drastically reduced in size. The eye was quiet on all visits and cyst recurrence was not seen till one year follow up. IOP dropped to 16 mm Hg on timolol (0.5%, twice daily) and the BCVA improved to 6/6 from 6/18. The conclusion was drawn that iris cysts can also be seen rarely after phacoemulsification surgery and can cause secondary ACG. Nd-Yag Laser photodisruption can be used effectively to manage these cases. To our knowledge, this is the first published case report in which iris cyst following phacoemulsification surgery lead to secondary ACG.

**Key words:** Iris Cyst, Phacoemulsification, secondary ACG, Nd-YAG laser.

A 52 year old female presented with diminution of vision in her right eye since two months. She underwent phacoemulsification with IOL implantation for immature senile cataract in her right eye 6 months back and had uneventful postoperative recovery until 2 months back when she noticed blurring of vision. She was referred due to non improvement of vision with change of glasses. There was no history of trauma or any other surgery to the eye and no complaints of pain, redness, lacrimation.

On examination, the right eye was pseudophakic with a BCVA of 6/18. There was a large, lobulated, pigmented, cystic mass arising from the iris (2 o’clock to 8.30 o’clock) and filling half of the anterior chamber, leading to pupil ovalization (Figure 1). Gonioscopic examination OD revealed closed inferior angles (about 200 degrees) with significant pigmentation, corresponding to the site of lesion. The angles could not be seen to open up on indentation gonioscopy as the iris cyst was hiding the visualization of angles. IOP by Goldmann applanation tonometry (GAT) was 38mm Hg OD, with normal fundus examination. Ultrasound biomicroscopy demonstrated a large thin- walled cystic lesion of the inferior iris encroaching upon the angles and abutting the corneal endothelium. It had no hyperechoic areas or opacities (Figure 2).

Left eye had an immature senile cataract with a BCVA of 6/24, normal fundus, open angles on gonioscopy and IOP of 16mm Hg on GAT.

A diagnosis of right angle closure glaucoma secondary to iris cyst, with pseudophakia was made and patient was started on topical anti-glaucoma medications (timolol 0.5% and brimonidine 0.2% twice daily) in her right eye. The IOP lowered...
to 24 mm Hg OD at 2 weeks. However, diminution of vision persisted due to pupillary encroachment by the cyst.

The patient underwent Nd-YAG Laser cystotomy after a written and informed consent. Five laser shots were given at the cyst wall with settings less than those used for iridotomy (i.e. 3–5 mJ), as the cyst wall was thinned out, stretched and ballooned. This lead to the rupture of the cyst wall and release of pigments in anterior chamber. Post laser, the patient was started on topical steroids (Prednisolone acetate 1% 6 times, tapered over 6 weeks) and oral acetazolamide (250 mg thrice daily for 2 days), along with continuation of timolol and brimonidine. Patient was reviewed after 1 day, 1 week, 1 month and then 3 monthly. The cyst drastically reduced in size (Figure 3) at 6 weeks follow up with a quiet eye, round pupil and BCVA of 6/6 OD. IOP dropped to 16 mm Hg on one topical anti-glaucoma medication (timolol 0.5%, twice daily). Gonioscopic examination revealed closed angles only in inferior angle and angles opened up in other quadrants. No recurrence of the cyst or IOP spikes were noted upto one year post treatment.

**DISCUSSION**

The patient in discussion presented with secondary angle closure glaucoma caused by an anterior chamber cyst arising out of the epithelium of the iris1. The prior surgical intervention (phacoemulsification with intraocular lens implantation) might have predisposed the eye for cyst formation. Since the cyst was peripheral, it went unnoticed until it grew big enough to cause pupillary encroachment with secondary angle closure and subsequent rise in IOP. Although this association is well known, Shields has emphasized the uncommon nature of visual complications and glaucoma on progression2.

Management strategies however, are still not clearly defined for these cysts. Surgical excision might be troublesome due to associated complications like inflammation, hemorrhage and hypotony3. Trans-corneal cyst aspiration and alcohol lavage has been tried with success although it is an invasive procedure4. Other invasive procedures like injection of sclerosing agents, diathermy applications, electrolysis etc. have also been tried in various settings. Laser cystotomy as a less invasive procedure has been described in few discrete case reports with successful results, less complications and complete regression5-9.

The response to laser in our patient was good, with regression of the cyst, improvement in BCVA and reduction in need for anti-glaucoma medications. The angles on gonioscopic examination opened up, which probably lead to reduced IOP and subsequent reduction in antiglaucoma medications. The addition of one medication to control IOP could be explained due to closed inferior angles and pigmentation of angles that lead to obstruction of pores of trabecular meshwork and IOP rise. The patient was closely followed to rule out recurrence.

This case report highlights the rare occurrence of iris cysts after phacoemulsification and association with secondary angle closure glaucoma. To our knowledge, this is the first case report in which iris cyst following phacoemulsification surgery caused secondary angle closure glaucoma. This emphasizes the need for proper wound construction and closure, minimal iris manipulation and avoiding conjunctival incarceration in the wound and side ports. Nd-YAG Laser photodisruption of the cyst is an effective treatment modality in such clinical scenarios, both in terms of cyst collapse as well as treating the angle closure and high IOP caused by the same.

**Figure 3:** Regression of the cyst following Nd-YAG laser cystotomy.

**REFERENCES**


**Correspondence to:**

Dr. Shalini Mohan
Associate Prof, Officer Incharge: Glaucoma Services, Department of Ophthalmology, GSVM Medical College, Kanpur, U.P., India
CHOROIDAL HYPOPERFUSION: GAME CHANGER IN OCULAR ISCHEMIC SYNDROME INDUCED NEOVASCULAR GLAUCOMA

Dr. Arshi Singh MBBS, Dr. Umesh Chandra Behera MS
L V Prasad Eye Institute, Patia, Bhubaneswar, Odisha, India

Abstract: Purpose: To report a case of low tension neovascular glaucoma in ocular ischemic syndrome.
Case report: A 63-year-old diabetic, hypertensive male developed rubeosisiridis OD while recovering from branch retinal venous occlusion OU. Patient had prior history of left sided hemiparesis 4 months ago. The fundus finding of venous dilatation, fluorescein angiography finding of choroidal hypoperfusion with prolonged arterio-venous transit time in right eye only with persistent normal intraocular pressures led to clinical diagnosis of rubeotic glaucoma secondary to ocular ischemic syndrome(OIS). Imaging studies by colour doppler imaging of carotid vasculature and magnetic resonance angiogram confirmed OIS with severe occlusion of right common carotid artery. Panretinal photocoagulation (PRP) prior to advised carotid endarterectomy led to an unusual response.
Conclusions: Lack of hypertensive response despite florid NVI, asymmetry in retinal findings of two eyes should alert the ophthalmologist to OIS etiology. Fluorescein angiography and carotid imaging are essential in managing such cases. Multidisciplinary treatment with tight follow up to prevent unforeseen ocular and systemic complications is required.
Key words: Ocular ischemic syndrome; Neovascular glaucoma; Carotid stenosis; Stroke; Choroidal hypoperfusion.

Ocular ischemic syndrome after compromised retrobulbar circulation manifests with retinal findings of arterial narrowing, venous dilatation sans tortuosity, rubeosis iridis, ischemic optic neuropathy and progression of cataract. Ocular ischemic syndrome is the third common cause of neovascular glaucoma after vascular occlusions and diabetic retinopathy.

We report a case where both branch retinal vascular occlusions and diabetic retinopathy confounded the picture of a patient of Ocular ischemic syndrome (OIS) presenting with rubeosis iridis. Lack of ocular hypertensive response despite extensive rubeosis iridis and choroidal hypoperfusion on fluorescein angiography led us to conclude ciliary hypoperfusion as the reason for normal pressures.

The case report highlights the importance of fluorescein angiography in evaluation of low tension neovascular glaucoma for treatment planning.

CASE REPORT

A 63 year old male with controlled diabetes and hypertension of 8 years duration was under our care for mild non proliferative diabetic retinopathy, supero-temporal minor branch retinal vein occlusion in both eyes with cystoid macular edema in the left eye. Anterior segment findings during the follow up revealed grade 2 nuclear sclerosis in both eyes with best corrected visual acuity of 20/60 OU. On a routine follow up visit, rubeosis iridis was noted in right eye iris stroma (Figure 1). Vision in right eye had dropped to 20/80 with clear cornea, pupil was sluggish to light and there was no progression of cataract. Intraocular pressure (Goldmann applanation tonometry) measured at different times was in mid-teens (12-14mmHg) OU. Gonioscopy revealed zipping of angle due to pulse clock hours of peripheral anterior synechiae in right eye.

Figure 1: Slit lamp capture of the right eye shows radiating iris new vessels at pupil in ocular ischemic syndrome.

Anterior segment findings in left eye were unremarkable.

Dilated fundus examination revealed narrowed arterioles, dark dilated engorged venules in right eye (Figure 2a) versus relatively normal vasculature in left eye (Figure 2b). Few small dot and blot haemorrhages with no retinal neovascularisation were noted. Fluorescein angiography was performed (Figure 2c) and it documented delayed (110 seconds) and patchy choroidal filling with prolonged arterio-venous transit time (20 seconds) in right eye. Retinal capillary non-perfusion and telangiectatic collateral vessels in the distribution of the tributaries of the occluded venule in macular area was present (Figure 2d). There was no delay in filling of dye in left eye; capillary non-perfusion corresponding to the branch vein occlusion was seen at macula.

Detailed questioning elicited history of an episode of left sided hemiparesis, 4 months prior to this visit. Patient was a non-smoker and at no time did he give history of pain in the eye.

Keeping in view this significant history of cerebrovascular...
Symptomatic carotid endarterectomy advised right carotid endarterectomy in right eye was established. Patient was diagnosed with ocular ischemic syndrome, which explained the stroke event. Perfusion in right hemisphere of brain, Right CCA along with resultant reduced slices. It reported near total occlusion of angiogram (MRA) with ocular and brain led to conducting magnetic resonance correlate this with the episode of stroke event, hemodynamic co-morbidities of diabetes and hypertension, ruberosis iridis along with asymmetrical fundus perfusion, a vasco-occlusive disorder was suspected. Complete hemogram including ESR, lipid profile, coagulation studies and blood sugar profile was performed and was reported as normal. Echocardiography showed sclerotic aortic valve with mild aortic regurgitation, good left ventricular function with no regional wall akinesia. Blood pressure on anti-hypertensive medications was recorded as 130/90mmHg.

The differential perfusion in two eyes incited a search for ocular blood flow investigations. Colour Doppler imaging of carotid vessels confirmed thrombosis of right sided internal and common carotid artery (CCA). An attempt to correlate this with the episode of stroke led to conducting magnetic resonance angiogram (MRA) with ocular and brain slices. It reported near total occlusion of Right CCA along with resultant reduced perfusion in right hemisphere of brain, which explained the stroke event.

Based on clinical and imaging results, diagnosis of ocular ischemic syndrome in right eye was established. Patient was advised right carotid endarterectomy in concordance with North America Symptomatic carotid endarterectomy trial guidelines (NASCET) and antiplatelet therapy was advised along with strict control of hypertension and diabetes.

A prophylactic panretinal photocoagulation (PRP) of right eye was conducted in 2 episodes at 2-week interval, to prevent likelihood of ocular hypertension exacerbation post endarterectomy.

Pan retinal photocoagulation result was unusual in that no regression of iris new vessels occurred and visual acuity reduced further to 2/60 at 1 month follow up post laser. Repeat gonioscopy at this point showed worsening of angle zipping with 360 degree peripheral anterior synechiae (PAS), with IOP still in the normal range at 16mmHg. The vision loss was presumed to be secondary to posterior ischemic optic neuropathy.

Despite close follow up of 9 months, secondary glaucoma did not supervene and IOP remained stable at 16mmHg. At the last follow up ectropion uveae and total cataract were the prominent anterior segment changes. Posterior segment examination was obscured by cataract, B scan ultrasonography however showed normal posterior segment images.

DISCUSSION

Ocular ischemic syndrome is a result of reduced blood flow in the retrobulbar vessels secondary to stenosis or occlusion of ipsilateral common carotid artery and/or internal carotid artery and rarely ophthalmic artery. A chronic arterial occlusive disorder, it manifests with gradual visual loss, often accompanied with orbital pain. Ocular hypoperfusion results in anterior and post segment hypoxia manifesting in ruberosis iridis, angle neovascularisation culminating in neovascular glaucoma. Most common clinical manifestation is ruberosis iridis seen in 66-87%, which usually result in neovascular glaucoma. It is the third common cause of neovascular glaucoma after central retinal vein occlusions and diabetic retinopathy.

However, in some situations despite the presence of NVI, rubecotic glaucoma may not manifest, as was seen in this case. The explanation for lack of IOP rise is uveal hypoperfusion affecting ciliary body resulting in reduced aqueous production. Therefore occurrence of neovascularization of iris, angle zipping with unexplainably normal IOP should alert the ophthalmologist towards poor ocular perfusion as the etiology.

Retinal changes comprise of narrowed retinal arteries and dilated retinal veins, mid - peripheral retinal hemorrhages, perifoveal telangiectasia, microaneurysms, cherry red spot and cotton wool spots. Fluorescein angiography is diagnostic with delayed and patchy choroidal filling being most specific and arteriovenous transit time prolongation being most sensitive sign of ocular ischemia.

Ocular ischemic syndrome represents the sequel of diffuse atherosclerotic disease; systemic associations with diabetes, hypertension and hyperlipidemia being very common. This association results in cerebrovascular accidents as was seen in this case. A large cohort study of 80 eyes of ocular ischemic syndrome, reported 17 and 22% patients having stroke/transient ischemic attack and myocardial infarction respectively, either prior or after onset of the ocular condition. These complications account for an extremely high mortality rate of almost 40% being reported over a 5-year period in patients presenting with this condition.

Management of this multisystem disease involves a systemic exam to rule out hemodynamic disturbances especially in the carotid vasculature. Colour Doppler imaging quantitates hemodynamic characteristics of carotid and retrobulbar
circulation, with the latter viewing ocular end arteries like central retinal and posterior ciliary arteries. Hypoperfusion is confirmed by reduction in peak systolic velocity and increase in vascular resistance in central retinal and short posterior ciliary arteries, the latter have been reported to have a direct correlation with visual outcomes.

Treatment options are both causal and targeted for the glaucoma. Targeted therapy options are intravitreal injection of anti VEGF drugs like bevacizumab, pan retinal photocoagulation in clear media or cyclophotocoagulation in hazy media. Trabeculectomy or tube shunt implants may be used once the ruberosis resolve. Anti glaucoma drugs can be used as additional measures, with pilocarpine and prostaglandins being avoided. Use of mydriatics has been recommended by some. Causal treatment involves restoration of ocular perfusion eg. by carotid endarterectomy along with anti-platelet therapy, without which 90% of such eyes become legally blind within a year.

Panretinal photocoagulation (PRP) response is often suboptimal, as was seen in this case, since ruberosis is the response to global uveal ischemia and PRP merely reduces retinal ischemia. Therefore requirement for PRP needs to be judiciously weighed in the absence of significant retinal ischemia.Panretinal photocoagulation course is known to be stormy and transient increase in IOP exacerbating disc hypoperfusion leading to anterior ischemic optic neuropathy has been reported. The unusual PRP complication of accelerated synechial closure as seen in this patient is less easy to understand and could represent an aberrant response due to subclinical, transient inflammation induced by laser or undetected anterior chamber shallowing subsequent to anterior shift of lens iris diaphragm in these cases. A tight follow up post PRP in such cases and prophylactic use of atropine could help circumvent this rare complication.

Since neovascular glaucoma risk increases with length of time elapsed, maintenance of normal IOP should not lull the physician as 68% eyes develop rubeotic glaucoma after a 12 month period. This necessitates a longer follow up in rubeotic non-glaucomatous eyes. Another aspect worth mentioning is high incidence of bilateral disease in almost 20% cases, mandating dose monitoring of the relatively healthy eye.

Ocular ischemic syndrome manifesting as rubeotic glaucoma or ruberosis with normal pressures, depending on ciliary perfusion, represents the tip of an iceberg of atherosclerotic pathology affecting multiple systems. It requires close multidisciplinary treatment by the neurologist, physician and cardiologist with the ophthalmologist often being the one to diagnose the condition by picking up the patient presenting with vision loss and ruberosis iridis.

**CONCLUSION**

A strong suspicion of compromised perfusion in normotensive neovascular glaucoma could facilitate early diagnosis and treatment of this blinding condition. Panretinal photocoagulation in this type of rubeotic glaucoma is not the panacea and options for its use should be judiciously weighed in absence of significant posterior segment neovascularisation, especially when choroidal hypoperfusion is significant. Ophthalmologists in this setting need to play an important role in early diagnosis and in coordinating systemic evaluation of patients as OIS is often the presenting sign of serious cerebrovascular and ischemic heart diseases. Consult with physicians to treat co-morbidities is essential and prognostication for ocular morbidity and patient survival needs to be done.

**REFERENCES**

Clear Lens Phacoaspiration with Posterior Chamber Intraocular Lens Implantation as Treatment of Choice in Pupillary Block Glaucoma Due to Microspherophakia

Dr. Madhu Bhadauria MS, FMRF, Dr. Misba Shams MS
RIO Eye Hospital Sitapur U.P. India

Abstract: This is a case report of a 16 year old female who presented with complaints of diminution of vision and headache. Her intraocular pressure was high with very shallow AC and angle closure. Post Yag Laser peripheral iridotomy, slit lamp examination revealed small spherical clear crystalline lens in both eyes. This article discusses a treatment option for patients presenting with secondary angle closure glaucoma due to microspherophakia.

Key Words: Microspherophakia, Angle closure Glaucoma, Phacoemulsification.

Microspherophakia is a rare disorder which is characterised by a small, spherical crystalline lens with a small lens diameter, increased antero-posterior thickness and visualization of the lens equator on full mydriasis1. The condition is supposed to occur due to faulty development of the zonules2. In later stages, subluxation and dislocation is common. It leads to high myopia and faulty accommodation may occur. Glaucoma is the most common sight threatening complication of the condition3.

CASE REPORT

A 16 year old girl presented to our OPD with complaints of diminution of vision in both eyes which was also associated with throbbing headache for two years. Her best corrected visual acuity (BCVA) was 6/18 OD (-2.0DS/-2.5DC@90°) and 6/12 OS (-2.5DS/-2.0DC@90°); she was reading N8 with Jaegers chart held close to face. Intraocular pressure (IOP) was 44mmHg in RE and 42 mmHg in LE by GAT. Anterior chamber was shallow with a convex iris configuration (Figure 1) and patent peripheral laser iridotomy bilaterally. Relative afferent papillary defect (RAPD) was present in RE. Gonioscopy revealed closed anterior chamber angle where no angle structures were visualised, with 360° synechial angle closure OU.

A small circular crystalline lens with increased antero-posterior thickness and phacodonesis was seen on mydriatic examination (Figure 2a,b). Fundus examination revealed increased vertical cup disc ratio (CDR) in both eyes. The discs were of 1.5mm diameter with RE vertical CDR of 0.9 (Disk Damage Likelihood Score of 6) and 0.5 in LE (Disk Damage Likelihood Score of 4). RE shows diffuse RNFL loss and LE showed wedge shaped RNFL defect in supero-nasal and supero-temporal quadrants (Figure 3). The Humphrey Visual field 24-2 threshold test in RE showed severely depressed fields with mean deviation (MD) of -24.36 and double arcuate scotoma, LE visual field shows early glaucomatous damage with MD of -5.8 (Figure 4a, b).

Optical biometry measured axial length (AL), antero-posterior lenticular thickness (LT) and anterior chamber depth (ACD) of 21.44mm, 4.05mm and 2.36mm respectively in the right eye; and 21.17mm, 4.00mm and 2.20mm respectively in the left eye. Her keratometry reading were k1 44.82D at 94°, k2 44.41 at 4° in RE and k1 42.51 at 71°, k2 44.06@161° in LE. On subsequent follow ups, her brother was also diagnosed with microspherophakia and angle closure glaucoma.
IOP in both eyes was uncontrolled medically on topical and systemic antiglaucoma therapy (brimonidine eyedrops 0.2% BD, bimatoprost 0.03% HS, oral acetazolamide 250mg TDS). The patient was atropinised to deepen the anterior chamber. A clear lens phacoemulsification with monofocal PCIOL was planned for both eyes at separate sitting. The surgeries were uneventful with post operative BCVA of 6/9 and 6/6 (Figure 5a,b), and IOP of 16 and 15mmHg in RE and LE respectively. It was maintained on topical therapy of dorzolamide drops 2%, timolol drops 0.5% and bimatoprost drops 0.01%. Visual fields, optic nerve head examination via slit lamp biomicroscopy (+90 D) and OCT-RNFL have shown no progression of disease over a one year follow-up postoperative.

**DISCUSSION**

Microspherophakia is a rare condition and is commonly associated with systemic disorders such as Weill Marchesani syndrome, Marfan, Klinefelter, Alport, Peters, Lowe syndrome, hyperlysinaemia and homocystinuria. Our patient had no systemic findings suggestive of syndromic association. She was of average built and height with a stable mental status. No cardiovascular, muscular or skeletal abnormality was seen. A similar presentation in her brother is suggestive of familial microspherophakia. Glaucoma uncontrolled after peripheral iridotomy and maximal medical therapy warranted surgical intervention, clear lens extraction with PCIOL implantation in our patient. Postoperative, though we still had to continue her on anti glaucoma medication which could be due to her synechial angle closure, her IOP was well controlled. We believe that an early clear lens extraction with PCIOL implantation can be a viable option in the treatment of angle closure glaucoma secondary to microspherophakia.

The management of angle closure glaucoma secondary to microspherophakia is debatable. Bhattacharjee H et al. have reported restoration of good vision and sustained normal IOP after phacoemulsification and PCIOL implantation in a 19-year-old boy with microspherophakia, high myopia and angle closure glaucoma. Yang et al. described both phacoemulsification with PCIOL with CTR and lensectomy with scleral-fixated PCIOL help reduce IOP and restore better visual acuity in patient suffering from angle closure glaucoma due to microspherophakia. KPS Malik et al. reported a case of bilateral angle closure glaucoma due to microspherophakia which was treated with lensectomy and scleral fixation of PCIOL giving a good visual acuity and IOP control to the patient. Simsek T et al. also reported a similar case with bilateral angle closure glaucoma due to microspherophakia who initially underwent a laser peripheral iridotomy and then a clear lens extraction leading to a controlled IOP post surgery without the need of any further anti glaucoma medication. However, Senthil et al. reported good success rate following primary trabeculectomy in patients with secondary angle closure glaucoma with microspherophakia; although post operative shallow AC was a frequent complication, requiring lensectomy in 2 of these 5 cases for resolution.
The protocol for treatment of secondary angle closure glaucoma due to microspherophakia is not clear currently. In our case, a clear lens phacoemulsification with PCIOL implantation gave satisfactory results regarding visual acuity and IOP control, though long term follow-up is required to ascertain an appropriate treatment protocol for such patients.

CONCLUSION

The protocol for treatment of secondary angle closure glaucoma due to microspherophakia is not clear currently. In our case, a clear lens phacoemulsification with PCIOL implantation gave satisfactory results regarding visual acuity and IOP control, though long term follow-up is required to ascertain an appropriate treatment protocol for such patients.

REFERENCES


Correspondence to:
Dr. Madhu Bhadauria
Director
RIO Eye Hospital Sitapur U.P. India
Abstract: An unusual case of 34 years old male with undiagnosed normal tension glaucoma complicated with CRAO right eye, found to have 22% fall in systolic blood pressure and 15% fall in diastolic blood pressure between awake and sleep and significant fall of blood pressure at different times of the day. Use of antiglaucoma drugs decreased intraocular pressure Control of systolic and diastolic blood pressure fluctuations was found.

Key Words: Normal tension glaucoma, CRAO, Blood pressure fluctuations.

A 34 year old male presented with sudden onset painless diminution of vision in his right eye of 3 hours duration. There was no associated headache, jaw claudication, scalp tenderness, weight loss or loss of appetite, flashes, floaters, pain, paraesthesia, numbness or neurological defects, migraine, cold hands or feet. There was no history of ocular or systemic trauma. The patient was not hypertensive or diabetic and was not on any systemic or topical medication.

At the time of presentation, he was found to have vision of hand movements close to face, right eye and 6/6 left eye, RAPD right eye, entire retina was pale and oedematous and with cherry red spot in the macula (Figure 1A,B). Optic cups were large in both eyes, suggestive of glaucoma but the intraocular pressures were normal. Other than the large optic cup, the left eye was found to be normal. Systemic examination was normal.

Initial investigations, revealed Haemoglobin to be 22.3 gm% with hematocrit of 56%. He was provisionally diagnosed as a case of Polycythemia with central retinal artery occlusion right eye and was treated with ocular massage right eye, tablet Diamox and phlebotomy within four hours of becoming symptomatic.

Two days later, his vision had improved to counting fingers at 2 feet right eye and left eye was 6/6. Ocular findings were RAPD right eye with gross pallor of the retina and a cherry red spot (Figure 2). No box carring of vessels or any emboli were seen. His intraocular pressures were repeatedly normal.

Fluorescein angiography revealed delayed filling of vessels with lack of filling in the superonasal vessel in right eye. Left eye angiography was normal (Figure 3A,B).

Mild oedema of inner retinal layers in the right eye in OCT and MRI brain revealed subacute infarcts in the right posterior centrum ovale and fronto parietal sub cortical white matter.

Systemic investigations of Bone marrow biopsy (BM/816/16) showed trilineage hematopoiesis. BM biopsy showed panmyelosis for which a JAK2 mutation study was ordered. JAK2 mutation analysis was negative. EPO was 3.38mIU/mL. He was treated with Hydroxyurea, Venesection, Ecosprin and Folic acid.

He was given Tablet Diamox for one month with topical beta blockers for his ocular condition. Only topical beta blockers was continued till he was reviewed five months later at which time, his right eye vision had improved to 6/9 with -0.5 D at 180, left eye was 6/6 unaided. Right eye: RAPD Grade 1, clear cornea, normal anterior chamber gonioscopy grade 4 open angles, optic disc was pale with a cup disc (CD) ratio of 0.8:1 with pallor of the supero-nasal part of the retina. Lt eye anterior segment was normal except for angle recession in all four quadrants. Optic disc left eye had cup disc ratio of 0.8:1 with normal retinal background. Intraocular pressure was normal on repeated examinations.

Humphrey’s perimetry with 24-2 SITA Standard of the right eye showed an inferior arcuate scotoma with a superior...
nasal step, MD-16.41 dB P< 0.5% PSD 12.79 dB P< 0.5%, VFI 60%. The defect was reproducible (Figure 4A).

Left eye showed Seidel’s scotoma, MD – 2.76 dB; P < 2% PSD 2.69dB P< 2% (repeated for reproducibility) VFI 96% (Figure 4B).

Diurnal variation of intraocular pressure ranged from: Rt eye 16-18 mm Hg, Lt eye 14-18 mmHg

Ambulatory blood pressure monitoring for 24 hours revealed 22% fall in systolic blood pressure and 15% fall in diastolic blood pressure. His measurement data showed low blood pressure at the following times of the day and night.

Blood pressure readings at other times were normal.

Patient’s treatment was changed from topical Timolol 0.5% to Eye drops Dorzolamide 2% three times a day only.

One month later ambulatory blood pressure was repeated twice which showed significant reduction of blood pressure fall with systolic drop of 0% and diastolic drop of 3%.

Six months after his CRAO right eye were:

- BCVA 6/6 each eye
- IOP (AT) 14 mmHg
- CCT 540 µ, 544µ

Right eye: Anterior segment was normal, Optic disc was normal in shape and size, CD Ratio 0.8:1 thin neuroretinal rim, dull foveal reflex.

Left eye: Anterior segment normal, posterior segment had normal optic disc but with a CD ratio of 0.8:1 Narrow neuroretinal rim, normal foveal reflex.

His investigations were: Hb 14.7%, Haematocrit 45.3%.

Diagnosis of Normal tension glaucoma with Polycythemia with CRAO Rt eye.

**DISCUSSION**

Our patient, a young healthy male, suffered sudden loss of vision of the right eye with the diagnosis of CRAO, was treated within four hours of onset of symptoms, with ocular massage and tablet Acetzolamide. He regained his vision completely in six months time but perimetric and fundus picture had

---

**Table 1**

<table>
<thead>
<tr>
<th>Time</th>
<th>Systolic BP</th>
<th>Diastolic BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>17:02</td>
<td>91</td>
<td>54</td>
</tr>
<tr>
<td>20:31</td>
<td>76</td>
<td>56</td>
</tr>
<tr>
<td>2:02</td>
<td>80</td>
<td>55</td>
</tr>
<tr>
<td>3:00</td>
<td>92</td>
<td>62</td>
</tr>
<tr>
<td>4:00</td>
<td>88</td>
<td>63</td>
</tr>
<tr>
<td>5:00</td>
<td>91</td>
<td>65</td>
</tr>
<tr>
<td>6:02</td>
<td>85</td>
<td>54</td>
</tr>
<tr>
<td>9:02</td>
<td>92</td>
<td>60</td>
</tr>
</tbody>
</table>
Patyal S et al. Normal Tension Glaucoma with CRAO

features of normal tension glaucoma.

The aim of presenting this case is to highlight:
a) Presence of two pathologies causing a field defect confounding the diagnosis.
b) Role of ambulatory blood pressure in determining blood pressure falls which decreased blood flow to the optic nerves.

Age group of persons affected by CRAO is generally in the 60s whereas our patient was in his mid thirty’s as this depends on the etiology of CRAO. Incidence of CRAO in the young (under 30 years of age) is known to be 1 in 50,000, the youngest reported case being in a 40 day old female neonate with shock and diffuse intravascular coagulation with bilateral ophthalmic artery occlusion1.

Our patient had a CRAO right eye due to a systemic etiology which also resulted in subacute infarcts in the brain, was diagnosed by clinical findings,
management of which resulted in gradual improvement of vision from hand movements close to face to BCVA OF 6/6 in six months time. The presentation of CRAO with sudden diminution of vision without any associated features is known to occur and has been found in 94% of patients in young patients in an Indian setting.

The etiology of CRAO in patients older than 60 years and patients of younger age is vastly different. In the retrospective analysis of CRAO done by Ratra et al in young patients, the commonest etiology of this condition was hypercoagulable states, chief causes of which were hyperhomocysteinemia and hyperlipidemia. Polycythemia accounted for only 3.1% of the cases. The etiology of CRAO in western literature has been found to be due to hypercoagulable states and cardiac abnormalities. Our patient had altitude related polycythemia as he had stayed in high altitude a few months prior to his present location.

The fundus picture in the right eye in our patient consisted of complete pallor of the retina with cherry red spot in the macula. No other retinal findings were visible. Amongst the known fundus findings in young patients with CRAO are cherry red spot (71.4%), retinal oedema (82.1%), box carring /arterial attenuation (75%), disc pallor (35.7%), disc oedema (7.1%), retinal /disc haemorrhages (10.7%), NVD/NVE (1.6%), RPE changes at macula (7.1%), visible embolus (3.6%).

Brown et al, in a retrospective analysis of 27 patients younger than 30 years of age, found subtle optic buried drusen of the optic nerve head and congenital preapillary arterial loop in the fundi of affected patients.

Visual improvement is known to occur in less than 10% of cases of CRAO. While the conventional management of an acute case of CRAO consists of ocular massage, Carbogen inhalation, sublingual isosorbide dinitrate, Intravenous Acetazolamide/ Mannitol, anterior chamber paracentesis, hyperbaric oxygen therapy, none is known to be really effective. Ocular massage of the affected eye may mechanically dislodge an embolus and restore retinal circulation. Blood supply may also improve by immediate reduction of intraocular pressure which can be obtained with Acetazolamide or IV Mannitol. Our patient’s ocular status improved with conservative treatment. Attempts at recanalization have been made by catheterization of the ophthalmic artery and locally infusing Urokinase or recombinant tissue plasminogen activator at the site of obstruction.

In our patient, perimetry of the right eye could not be done at the presentation of illness due to impaired vision of the right eye. On continuing treatment of the patient with tablet Acetazolamide and Timolol 0.5% eye drops and systemic treatment with Tablet Ecosprin 150 mg and tablet folic acid 5 mg once a day, as prescribed by the haematologist, the patient’s vision improved significantly to BCVA of 6/6 in six months.

The retinal arterial block was found on fluorescein angiography done five days after the presentation, in the superonasal vessel in the right eye could have produced an inferotemporal field defect. Repeated perimetry showed a much larger field defect which had crossed the vertical meridian in the right eye and also a field defect in the left eye, causing a dilemma in diagnosis. Bilaterality of field defects which crossed the midline, with optic nerve heads findings suggestive of glaucoma raised the suspicion of a dual pathalogy in this patient. Narrow neuroretinal rims with large deep optic cups, reproducible field defects in both eyes, normal intraocular pressures including diurnal, pointed the diagnosis towards normal tension glaucoma though both eyes did not show any Drance’s haemorrhages, arterial attenuation or pigment changes around the optic discs.

Since it is known that there is a greater drop in mean diastolic blood pressure at night in Normal tension glaucoma and patients with visual field deterioration had significantly lower minimum night time diastolic blood pressure ambulatory blood pressure was done. This investigation showed a significant dip in the systolic and the diastolic blood pressures both during varying times of day but especially in the early hours of the morning implying decreased blood flow to the optic nerve. On decreasing the intraocular pressure with topical Dorzolamide which is known to act nocturnally, perfusion pressure must have improved resulting in decreased decrease in systolic and diastolic blood pressures seen by repeated ambulatory blood pressure recording.

To conclude, this young male suffered a CRAO of the right eye due to Polycythemia. He also had normal tension glaucoma with drop in systolic and diastolic blood pressures which normalised with treatment.

VISUAL FIELDS
Reye: Inferior arcuate scotoma with a superior nasal step, MD -16.41 dB P< 0.5% PSD 12.79 dB P< 0.5%, VFI 60%.
Lt eye: Seidel’s scotoma, MD – 2.76 dB P < 2% PSD 2.69 dB P< 2% VFI 96%.

REFERENCES
Abstract: A summary of different gadgets available for screening and recording fundus photographs for OPD patients using a simple smart phone. The information for affordable and DIY adaptors used for fundus photography and improvised version, which are coupled with smart phone apps to record and edit the records is described here.

Glaucoma is a progressive disorder, requiring repeated investigations such as visual field analysis and OCT, to assess disease progression. A baseline fundus photograph, for glaucoma cases is invaluable to diagnose the disease, to document and confirm progression during follow up, to correlate with field changes and to determine both course and management of the disease.

Fundus photograph provides a definitive record for both patient and treating ophthalmologist; comparison of cup-disc ratio over years becomes easy with its help. However, the expense involved in purchase of a fundus camera, makes this tool difficult to use in daily practice.

Smart phones have become a common gadget in current times and changed the way we work and think. For every basic thing, we share images and text on Whatsapp and emails. In past few years smart phone has been used as a major tool for investigatory procedures. Fundus photography by smart phone has made it easy for ophthalmologist to document different retinal conditions and also educate patients about disorders. All this is done at a fraction of the cost of expensive fundus imaging equipment.

This article shares use of android (smart) and iOS phones to perform fundus photography with or without Adaptors.

NO ADAPTOR

The inbuilt phone camera along with the LED light source is used for imaging. The camera is used for recording a video and taking a picture with the LED light providing illumination. While making a video snapshots can also be taken at the best view seen. The user has to view the fundus on the phone screen. Good hand eye coordination is required as best image is formed on the focal point (of 22cm for 20D aspheric lens). Since the LED light source is very strong, patients often become uncomfortable and good rapport is required with patient.

ADAPTOR AND ASPHERIC LENS

The phone and aspheric lens (power 20D) are fixed at opposite ends of adaptor. When distance between camera and lens reaches focal distance of lens, the image gets recorded on the smart phone. Adaptor use provides a better control for imaging and both live recording or snap shots can be taken. This method is useful in screening camps and peripheral centers especially rural ones.

DIY Adaptors

These are economical alternatives, which can be self-designed. The DIYret CAM uses PVC pipes and can be used both for slit lamp or fundus photograph. Two, different sized adaptors can be made by varying length of the PVC pipe.

Phone sleeve and PVC pipe along with 20 D aspheric lens.

This adaptor uses a 22 cm long pipe which has a small ridge at distal end, to prevent the 20D lens sliding out of while capturing pictures. The LED brightness can be reduced by using butter paper, micro-pore tape to reduce glare perceived by patients (Figure 1).

THREE-DIMENSIONAL PRINTER

This helps to align a 20D lens with phone's camera. It is more expensive due to limited availability and cost of 3D printing. An example is Paxos Scope, patented and marketed by DigiSight Technologies, USA. This adaptor has a variable intensity external LED light source, which can be adjusted to patient's comfort level. It has a universal, adjustable mounting system and can be mounted any smart phone. Paxos Scope also comes with an app, developed by DigiSight that aids in storing images thereby maintaining records.

MIIRetcam

This hand-held adaptor holds a 20 D lens on one end, with a docking adaptor for phone on the other side. The concept of 22 mm distance between aspheric lens and camera distance is applied here too. It is not slit-lamp dependent. Compared to DIY adaptor, it is slightly costlier but still in affordable range. It has a downloadable app, the iOS version allows one to reduce flash light intensity of smart phone, which sadly is not available in the android version of the app. The pictures can be directly printed or emailed to patient or to higher centers for cross reference by a specialist. The quality of print out is dependent on printer quality. High end printers give a professional finish similar to high end Fundus cameras. After some hand coordination and

Figure 1: PVC pipe adaptor
learning curve, pictures can be taken up till oraserrata7 (Figure 2).

Fundus on Phone (Remedio Innovative Solutions Private Limited, Bengaluru, India)

This slit lamp mountable fundus camera is light and portable. It has a docking slot for the smart phone, which can be easily adjusted for any type of smart phone camera, either central or edge place camera. The device’s camera has a 45° field of view, a 33-mm working distance, +20D to −20D adjustment, and an optical magnification of 12×. The light source is in built and is either white or pale-yellow LED powered by a 1500 mAh Li-ion battery. It is chargeable and has battery life of approx. 5-7 hours. Picture quality is determined by the phone camera and best option is anything more than 10 megapixel. The downloadable phone app provides ease in storage of patient’s data, each photograph has identification data printed on it, which aids in record keeping. The app helps in creating a PDF, making file sharing via e-mail easy. Printing the same PDF gives a paper copy for patient’s future reference or for a second opinion.

It comes in two models, mydriatic and non-mydriatic, the latter being more expensive. A trained technician can take good fundus pictures and share with ophthalmologist, thus enabling screening of large number of patients.

Presently the author is using Fundus on camera mydriatic model, which is cheaper than the non-mydriatic version (Figure 3). The smart phone used is iphone 5 S and the picture quality is good. One can make a PDF and get a print out in the same sitting. The light intensity is kept a lowest possible, which can be increased if required. The touch screen of phone allows zooming in and out, and is used to the advantage so the disc image can be captured.

The Retina photographs taken for screening and making diagnosis for diabetic retinopathies are comparable to any conventional retinal photography methods used8 (Figure 4,5).

Note: while sharing the patient information with colleagues on internet / whatsapp, one has to keep in mind the patient–doctor confidentiality if consent is not obtained9. It is better to have a simple; self formatted printed consent form for each patient where in permission to share the data is taken from the patient.

REFERENCES

3. Raju B, Raju N, Akkara JD, Pathengay

Correspondence to: Dr. Shruti Sharma Nee Pandey
Consultant
Parma Nethralya, Bawana, Delhi, India

Buy or Sell
If you want to sell your used Ophthalmic Equipments at Good Price
OR
If you are Interested to Purchase Second hand Ophthalmic Equipments at Reasonable Prices in Good Condition
Please Contact: Manoj Pandey

Venus Surgitech
B-503, Plot No. 23, Sector-6, Dwarka, NEW DELHI-75
Ph.: 011-43557387, 9350257387
Email: pandeymanoj67@yahoo.co.in
Q1. Mechanism of glaucoma in following condition is:
   a. Pretrabecular membrane overgrowth
   b. Obstruction of trabecular meshwork
   c. Obstruction of schlemm canal
   d. Elevated episcleral venous pressure

Q2. Which of the following is not a form of non-conventional perimetry (uses a different stimulus than SAP)?
   a. Hidelberg Edge Perimetry (HEP)
   b. High-pass resolution perimetry (HRP)
   c. Octopus perimetry
   d. Flicker perimetry

Q3. Rubeosis iridis is frequently seen in all except?
   a. CRVO
   b. Diabetic retinopathy
   c. Fuch's heterochromatic cyclitis
   d. Nanophthalmos

Q4. The following procedure is used to manage which of the following bleb related complication?
   a. Encapsulated filtering bleb
   b. Hypotony with deep anterior chamber
   c. Hypotony with flat anterior chamber
   d. Leaking filtering bleb

Q5. All of the following are potential complications of tube shunt procedures except?
   a. Diplopia
   b. Hypotony
   c. Corneal edema
   d. Corneal neovascularisation

Q6. Which of the following is not seen in the following type of glaucoma?
   a. Krukenberg spindle
   b. Inverse pupillary block
   c. Reverse pupillary block
   d. Iris transillumination defects

Q7. Which of the following gene is most commonly associated with this form of familial glaucoma?
   a. PAX6
   b. CYP1B1
   c. PITX2
   d. FBN1
Q8. Which of the following drugs is not known to aggravate acute angle closure attack?
   a. Fluoxetine
   b. Ipratropium bromide
   c. Topiramate
   d. Echotriphate

Q9. Which of the following is not a suprachoroidal filtration implant device?
   a. iStent
   b. Ex-Press implant
   c. CyPass implant
   d. Gold Solx implant

Q10. Which of the following are the parameters used for SLT?
   a. 50µ spot size / 0.1 sec exposure / 500-1200 mW power / 50-100 spots
   b. 200-500µ spot size / 0.3-0.6 sec exposure / 200-400 mW power / 20-24 spots
   c. 400µ spot size / 3 nsec exposure / 0.4-1.2 mJ power / 50-100 spots
   d. 100µ spot size / 0.1 sec exposure / 500-1000 mW power / 50-100 spots

Q8. Which of the following drugs is not known to aggravate acute angle closure attack?
   a. Fluoxetine
   b. Ipratropium bromide
   c. Topiramate
   d. Echotriphate

Q9. Which of the following is not a suprachoroidal filtration implant device?
   a. iStent
   b. Ex-Press implant
   c. CyPass implant
   d. Gold Solx implant

Q10. Which of the following are the parameters used for SLT?
   a. 50µ spot size / 0.1 sec exposure / 500-1200 mW power / 50-100 spots
   b. 200-500µ spot size / 0.3-0.6 sec exposure / 200-400 mW power / 20-24 spots
   c. 400µ spot size / 3 nsec exposure / 0.4-1.2 mJ power / 50-100 spots
   d. 100µ spot size / 0.1 sec exposure / 500-1000 mW power / 50-100 spots

Compiled by:
Guru Nanak Eye Centre, Maharaja Ranjit Singh Marg, New Delhi

Dr. Nikhil Gotmare MBBS
ACROSS
4. Pathway utilized by shortwave automated Perimetry (13)
8. Calculation of Target Pressure (6)
9. Chennai Glaucoma Study used .... Classification (5)
10. Study by the name of a Bird (5)
12. Mercury 2 Trial test combination of....... with Latanoprost (10)
14. Second Thursday of.... Is celebrated as World Sight Day (7)

DOWN
1. Glaucoma drainage surgery utilizing sîp of iris tissue within corneal or limbal incision (13)
2. Anticonvulsant which can cause acute angle closure glaucoma (10)
3. Associated with ash leaf spots (11)
5. Embryology of schlemms canal resembles.......(10)
6. Ophthalmologist associated with "Glaucoma-days" and Glaucoma-Bus"(6)
7. Mutation associated with Aniridia (4)
11. Corneal epithelial iron line at the edge of filtering bleb (5)
13. ab-interno Minimally Invasive Glaucoma surgery (6)
Nominations are invited from the Delhi Members of the Delhi Ophthalmological Society for the posts of Vice President (1 Post). The duly filled nomination form should reach the Secretary’s Office on or before February 15th, 2018 (2:00 pm).

Dates to Remember:
- Nominations filing Opens: January 20, 2018
- Nominations filing Closes: February 15, 2018, 2:00 pm
- Last Date of withdrawal of Nomination: March 8, 2018, 5:00 pm
- Date of Election: April 8, 2018

Please refer to the Constitution at www.dosonline.org for more details.

FOR KIND ATTENTION OF ALL VOTING DOS MEMBERS

Please ensure that your correct address (Office and Residential) is made available to the DOS Secretariat latest by February 15th, 2018 (5:00 PM). You can check & update your address online at www.dosonline.org.

RESOLUTIONS / SUGGESTIONS FOR GENERAL BODY MEETING

DOS members are requested to send us their Suggestions / Resolutions to be discussed in the General Body Meeting to be held on April 8th, 2018. These will be discussed first in the Executive Meeting and then forwarded to the General Body Meeting. Last date of receipt of suggestions/resolutions is 15th February, 2018 (2:00 PM).

LIFE TIME ACHIEVEMENT AWARD - 2018

Recommendations and Suggested Names are invited for the Life Time Achievement award:

General Conditions
1. Maximum of TWO Awards in a year may be awarded.
2. Any Member of the Society who is eligible for the Award shall be entitled to be considered for the same.
3. Recommendations can be sent by one of the following:
   a) Any of the Past Awardees
   b) Any of the Past Presidents
   c) At least 5 members of the Executive Committee
   d) At least 15 Delhi Members of DOS.
4. Recommendations should be sent to the Secretariat, DOS.
5. The person should have significant Life Time Achievements in the field of Ophthalmology.
6. Recipient of the Award shall be selected and recommended by the Award Sub-committee, which has to be ratified by the Executive.
7. The Award sub-committee can ask for the Biodata and latest photograph of the individuals recommended.

Eligibility
1. The Member should be at least 65 years of age
2. Active participation in Society for 20 years
3. Contribution in improvement of standard of Ophthalmology in India
4. Award will carry a citation.

The Recommendations and Suggested Names must be received in DOS Secretariat not later than on 15th February, 2018 (5:00 PM).

Prof. Kamlesh
President, DOS
Prof. Subhash C. Dadeya
Secretary, DOS

Address for all Correspondence:
Prof. Subhash C. Dadeya
Secretary, Delhi Ophthalmological Society,
Room No. 205, 2nd Floor, OPD Block, Guru Nanak Eye Centre,
Maharaja Ranjit Singh Marg, New Delhi – 110002
Ph : +91-11-23210810, 65705229 Email: dosrecords@gmail.com, Website: www.dosoline.org
DR. P.K. JAIN ORATION & DR. S.N. MITTER ORATION-2018

Nominations are invited for the above orations. The nominee should be a voting member of the Delhi Ophthalmological Society.

Selection Procedure
Nomination should be signed by one of the following:
1. Any of the Past Awardees
2. Any of the Past Presidents
3. At least 5 members of the Executive Committee
4. At least 15 Delhi Members of DOS.

The nomination must include an introductory paragraph justifying the nomination, a biodata of the nominee, a statement to the effect that the nominee would accept the Oration, if awarded and would deliver an oration of his choice at the Annual Conference of the DOS.

The topic should be intimated to the society at least 4 weeks before the Conference and a typed script of the same should be submitted at least 15 days before. The awardee will have to transfer the copyright of the text of his talk to the Society.

DR. B.N. KHANNA & DR. HARI MOHAN ORATION-2018

Nominations are invited for the above Orations. The nominee should be a voting member of the Delhi Ophthalmological Society.

Selection Procedure
Nomination should be signed by one of the following:
1. Any of the Past Awardees
2. Any of the Past Presidents
3. At least 5 members of the Executive Committee
4. At least 15 Delhi Members of DOS.

The nomination must include an introductory paragraph justifying the nomination, a biodata of the nominee, a statement to the effect that the nominee would accept the award if awarded and would deliver an oration of his choice at the annual conference of the DOS. The topic should be intimated to the society at least 4 weeks before the conference and a typed script of the same should be submitted at least 15 days before. The awardee will have to transfer the copyright of the text of his talk to the Society.

Selection Process for above Awards
The selection will be made by the Award Committee consisting of the President, Secretary and 3 senior, distinguished members from 3 different sub-specialties of Ophthalmology. The Award Committee would take the final decision on the basis of the recommendations of the Award Committee.

The nominations must be received in DOS Secretariat no later than on 15th February, 2018 (5.00 pm).

Advance copy of the nominations may be sent by email at dosrecords@gmail.com. The hard copy must however be received in the DOS Secretariat by the last date for receiving the nominations on 15th February, 2018 (5.00 pm).

Prof. Kamlesh
President, DOS

Prof. Subhash C. Dadeya
Secretary, DOS

Address for all Correspondence:
Prof. Subhash C. Dadeya
Secretary, Delhi Ophthalmological Society,
Room No. 205, 2nd Floor, OPD Block, Guru Nanak Eye Centre,
Maharaja Ranjit Singh Marg, New Delhi – 110002
Ph : +91-11-23210810, 65705229 Email: dosrecords@gmail.com, Website: www.dosoline.org
## DOS TIMES 2017 – 2019 AUTHOR GUIDELINES

Our Author Guidelines is available online at www.dos-times.org

### MANUSCRIPT SUBMISSION

DOS Times is published once in two months (i.e. six issues in a year: July – August, September – October, November – December, January – February, March – April, May – June). Solicited and unsolicited manuscripts of good quality academics are accepted provided that they are not under consideration for publication in any other journal. All submitted manuscripts are subject to editorial review before acceptance.

You may submit your manuscripts along with a covering letter addressed to

**Address for all correspondence**

Dr. (Prof.) Subhash C. Dadeya
Secretary - Delhi Ophthalmological Society
Room No 205, 2nd Floor, OPD Block,
Guru Nanak Eye Centre, Maharaja Ranjit Singh Marg,
New Delhi - 110002

or by email to dostimes10@gmail.com

In case of any queries please contact Mr. Sunil Kumar, DOS Times assistant @ 011-65705229 or by email (dostimes10@gmail.com).

### SCOPE OF THE JOURNAL

DOS Times covers clinical, experimental and basic science research studies related to medical, ethical and social issues in field of ophthalmology. Articles with clinical interest and implications are given preference.

### MANUSCRIPT SUBMISSION AND PROCESSING

A manuscript is reviewed for possible publication with the understanding that it is being submitted to DOS times alone at that point in time and has not been published anywhere, simultaneously submitted, or already accepted for publication elsewhere. Initial screening by the editorial desk assesses the formatting, topicality and importance of the subject, the clarity of presentation, and relevance to the target audience of the journal. Acknowledgement of receipt of all manuscripts will be sent to the corresponding author, once the editorial desk reviews the manuscript for conforming to the requirements of the journal. Manuscripts that are found suitable for publication are sent to two or more expert reviewers for Peer Review through an online reviewer system. The identities of reviewers and authors are kept confidential. Authors and Reviewers are required to disclose potential conflicts of interests/ financial interests. The comments and suggestions (acceptance/ rejection/ amendments in manuscript) received from reviewers are conveyed to the corresponding author. Corresponding authors are requested to submit the revised manuscript along with one highlighted copy with revisions highlighted. The final decision on acceptance of the manuscript for publication lies with the Editor-in-chief. This process is repeated till reviewers and editors are satisfied with the manuscript. Manuscripts accepted for publication are copy edited for grammar, punctuation, print style, and format.

### CONFLICTS OF INTEREST

All authors must disclose all conflicts of interest they may have with publication of the manuscript or an institution or product that is mentioned in the manuscript and/or is important to the outcome of the study presented.

### MANUSCRIPT PREPARATION

Manuscripts under the following subheadings may be submitted:

<table>
<thead>
<tr>
<th>Type</th>
<th>Word limit</th>
<th>Reference limit</th>
<th>Abstract</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original article</td>
<td>2500</td>
<td>40</td>
<td>Structured 150-200 words</td>
</tr>
<tr>
<td>These include randomized clinical trials, prospective and retrospective observational and interventional studies, questionnaire-based studies, qualitative data based studies, quality of life studies etc. excluding references, abstract, figures and tables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Review articles</td>
<td>3000</td>
<td>50</td>
<td>Unstructured 150-200 words</td>
</tr>
<tr>
<td>Includes comprehensive and systematic literature review and meta-analysis. Review articles can be commissioned either by editorial invitation or by submitted proposals</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perspectives</td>
<td>1500</td>
<td>30</td>
<td>Unstructured 100 words</td>
</tr>
<tr>
<td>Authors will be asked to give opinion on a topic of interest. These should be evidence based and relevant and give perspective and practical applications to existing knowledge.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recent advances</td>
<td>1500</td>
<td>30</td>
<td>Unstructured 100 words</td>
</tr>
<tr>
<td>Summary of latest in clinical research, instrumentation and web resources in ophthalmology.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Techniques</td>
<td>1500</td>
<td>30</td>
<td>Unstructured 100 words</td>
</tr>
<tr>
<td>Novel surgical techniques or instrumentation that have the potential to reduce surgical complexity and/or enhance outcomes.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case reports</td>
<td>1000</td>
<td>10</td>
<td>Unstructured 100 words</td>
</tr>
<tr>
<td>Interesting cases with immense clinical significance / rare case reports</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Photo-essay/snap shots</td>
<td>500</td>
<td>10</td>
<td>Unstructured summary in 100 words</td>
</tr>
<tr>
<td>Reports of unusual/uncommon clinical case scenarios with good photographic documentation</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All manuscripts should have the following:

1. Title of the manuscript
2. Type of manuscript
3. Name(s) and surnames of authors with highest academic degree
4. Author affiliations: Department, Institution, and contact details
5. Corresponding author: name, designation and credentials, address, phone, fax, email and digital passport size photograph
6. Information about patient consent and approval for photographs that disclose the identity of the patient.
7. Please submit as word file with embedded figures
8. Figure legend at the bottom of figure
9. Tables with numbering and heading at the top embedded in the text file
10. References as superscripts without brackets numbered consecutively in text. References should be written in standard international format as in PubMed. Authors: Title of citation quoted. Name of journal Year of publication; Volume number, Page numbers.
11. Abbreviations spelled out at the first appearance in the text.
12. Generic drug names are to be used in text, tables, and figures. Suppliers of drugs, equipment, and other brand-name material are to be credited in parentheses (company, name, city, state, country).
# Glaucoma Trials

**Sumit Grover DO, D.N.B, FICO, Ritwika Shankar MBBS**

Dr. Baba Saheb Ambedkar Medical College & Hospital, New-Delhi, India

<table>
<thead>
<tr>
<th>International Trials</th>
<th>Indian Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Manifest Glaucoma Trial (EMGT)</td>
<td>Vellore Eye Study</td>
</tr>
<tr>
<td>Collaborative Initial Glaucoma Trial Study (CIGTS)</td>
<td>Andhra Pradesh Eye Disease Study (APEDS)</td>
</tr>
<tr>
<td>Ocular Hypertension Treatment Study (OHTS)</td>
<td>Advanced Comprehensive Eye Survey (ACES)</td>
</tr>
<tr>
<td>Collaborative Normal Tension Glaucoma Study (CNTGS)</td>
<td>Chennai Glaucoma Study</td>
</tr>
<tr>
<td>Advanced Glaucoma Intervention Study (AGIS)</td>
<td></td>
</tr>
<tr>
<td>Glaucoma Laser Trial Follow up Study (GLTFS)</td>
<td></td>
</tr>
<tr>
<td>Flurouracil Filtering Surgery Study (FFSS)</td>
<td></td>
</tr>
<tr>
<td>Tube Versus Trabeculectomy Study (TVT)</td>
<td></td>
</tr>
<tr>
<td>EAGLE Trial</td>
<td></td>
</tr>
</tbody>
</table>

## International Studies

### 1. Early Manifest Glaucoma Trial (EMGT) 1992
- First randomised control trial with an untreated control arm to evaluate effects of IOP reduction in patients with open angle glaucoma who have Elevated and normal IOP.
- The result was treatment reduced the IOP by 5 mm Hg or 25% and maintained.
- There was a less frequent progression in treatment group (45%) than control (62%).

### 2. Collaborative Initial Glaucoma Treatment Study (CIGTS) 1993
- To compare the long term effect of newly diagnosed open angle glaucoma with standard medical treatment versus filtration surgery.
- Surgery group had more cataract extractions
- Surgical group had more VF and VA loss initially but disappeared in 5 years follow up.
- Surgical group also had more local symptoms initially but not long sustained.
- Surgical group showed 2-3 points lower IOP than medical treatment group though both had substantial decrease in IOP.
- Both groups showed satisfied quality of life post treatment.

### 3. Ocular Hypertension Treatment Study (OHTS) 1994-2009
- To determine whether medical reduction in IOP prevents/delays the onset of glaucomatous visual field loss/disc damage in ocular hypertension.
- To produce history and determine risk factors.
- The probability of developing primary open angle glaucoma was found to be 4.4% in medication group compared to 9.5% in observation group. Decrease in IOP by 23% led to decrease in incidence of POAG by 60%.
- In univariate analysis: risk factors were old age, African American race, male se, high IOP, large C:D ratio (vertical/horizontal), greater Humphrey visual field pattern standard deviation, thinner CCT.
- In multivariate: Risk factors were older age, large C:D ratio (horizontal/vertical), higher IOP, greater pattern standard deviation, thinner CCT.

### 4. Collaborative Normal Tension Glaucoma Study (CNTGS)- 1988
- To ascertain the influence of IOP on course of normal tension glaucoma whether IOP was/was not involved in normal tension glaucoma. Therefore whether aggressive efforts to lower IOP in normal tension glaucoma are warranted.
- One eye of patients with NTG was randomised.
- There was 80% progression free survival in treatment group versus 40% in control arm at 5 years follow up
- Visual field progression was 18% in treatment group and 30% in untreated group.
- Natural history of normal tension glaucoma must be considered before starting treatment.
- Risk factors or prognostic indicators were: migraine, female sex, disc haemorrhage at diagnosis, genetic heritage.

### 5. Advanced Glaucoma Intervention Study (AGIS) 1988-1992
- To assess long range outcomes of sequences of interventions involving trabeculectomy and ALT in eyes those have failed initial medical treatment for glaucoma.
- The study advised: In black patients with advanced glaucoma begin with laser surgery (ATT) and in whites with advanced glaucoma begin with trabeculectomy (TAT).
- Long term visual field outcomes were better for ATT in blacks and TAT sequences in whites.
- Subjects with IOP < 18 mmhg at 100% visits had no VF changes whereas subjects with IOP < 18 mmhg at <50% visits had VF worsening by 0.63 units.

### 6. Glaucoma Laser Trial Follow Up Study (GLTFS) 1984-1987
- To compare safety and long term efficacy of argon laser treatment of trabecular meshwork with standard medical treatment for primary open angle glaucoma.
- Eyes initially treated with ALT had 1.2 mmhg greater IOP reduction and 0.6 db greater VF improvement from entry to GLT.
- Initial treatment with argon laser treatment was at least as efficacious as initial treatment with topical medications.
### 7. Flurouracil Filtering Surgery Study (FFSS) 1985-1988
- To evaluate whether subconjunctival injections of 5-flurouracil increase success rate of filtering surgery in patients with high risk of failure.
- At 5 years success rates were 48% for 5FU group and 21% with standard surgery group.
- Late onset leak in filtering bleb was more in 5FU group (9%) compared to 2% in standard.
- The risk of supra choroidal haemorrhage was not related to 5FU, but to high pre op IOP.
- The study recommends the use of subconjunctival 5-flurouracil after trabeculectomy in eyes that have undergone previous cataract surgery or unsuccessful filtering surgery and cautions against the routine use in patients with good prognosis.

### 8. Tube Versus Trabeculectomy Study (TVT) 1999-2004
- To study the safety and efficacy of nonvalved tube shunt surgery to trabeculectomy with mitomycin c in patients with previous intraocular surgeries.
- Tube shunts had higher success rates compared to trabeculectomy with mitomycin c during 5 year follow up.
- The study supports the expanding use of tube shunts beyond refractory glaucomas.

### 9. Eagle Trial [Jan8,2009 to Dec28,2011]
- To study the Effectiveness of early lens extraction for treatment of PACG.
- Randomization was done from 30 eye hospitals over 5 countries.
- Total of 419 participants, out of which 155 with PAC and 263 with PAG.
- 208 were assigned to clear lens extraction and 211 to standard care.
- Inclusion criteria was: age> 50 years, pressures 30 mmhg or more and non catarctous lens and newly diagnosed PAC and PAG.
- Clear lens extraction showed greater efficacy and was more cost effective than laser peripheral iridotomy and should be considered as an option for first line treatment.

### Indian Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Results: POAG- 0.4%, PACG- 4.32%, OHT- 3.08%</td>
</tr>
<tr>
<td></td>
<td>Hitherto unsuspected high prevalence of PACG.</td>
</tr>
<tr>
<td>1. Andhra Pradesh Eye Disease Study (APEDS) 2000</td>
<td>Purpose: Prevalence and features of open angle glaucoma and angle closure glaucoma in urban south Indian population, cross sectional study.</td>
</tr>
<tr>
<td></td>
<td>Results: Majority of patients with glaucoma were undiagnosed and untreated. Prevalence increased with age.</td>
</tr>
<tr>
<td></td>
<td>Definite POAG-1.62%, suspected POAG-0.79% and OHT -0.32% in &gt; 30 years.</td>
</tr>
<tr>
<td></td>
<td>2.56%, 1.11% and 0.42% in &gt;40 years.</td>
</tr>
<tr>
<td>2. Aravind Comprehensive Eye Study (ACES) 2003</td>
<td>Purpose: Prevalence of glaucoma and risk factors for primary open angle glaucoma in rural south Indian population. It was a cross sectional study.</td>
</tr>
<tr>
<td></td>
<td>Results: Large population was found to be previously undiagnosed. 1/5th of primary open angle glaucoma had blindness in one or both eyes on presentation.</td>
</tr>
<tr>
<td>2. Chennai Glaucoma Study (CGS) 2008</td>
<td>Purpose: To study prevalence and risk factors of POAG, PAG, PAC and PACS in rural and urban south Indian population and their comparison.</td>
</tr>
<tr>
<td></td>
<td>Based on ISGEO classification</td>
</tr>
<tr>
<td></td>
<td>POAG and PAC is more common in urban population(3.51% POAG) and (2.75% PAC)</td>
</tr>
<tr>
<td></td>
<td>PACG and PACS have similar rates.</td>
</tr>
<tr>
<td></td>
<td>Detection rate is low in both groups as 98.5% rural and &gt; 90% were not aware of the disease.</td>
</tr>
</tbody>
</table>

**Correspondence to:**
Dr. Sumit Grover  
Dept. of Ophthalmology  
Dr. Baba Saheb Ambedkar Medical College & Hospital  
New Delhi, India