Botulinum Toxin A and Dermal Fillers in Oculofacial Aesthetics: An Overview

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Abstract: *With the ever-increasing demand for beauty, the importance of facial rejuvenation need not be overemphasized. Correction of facial rhytides and volume loss forms the fundamental principle in aesthetic rejuvenation of the face. Botulinum toxin injections are primarily indicated for correction of dynamic rhytids while dermal fillers are meant for volume augmentation as well as for improvement of static rhytids. The aim of this review article is to briefly discuss the important aspects of botulinum toxin and dermal fillers in the field of ocular and facial aesthetics.*

Key words: *Facial rejuvenation, rhytides, botulinum toxin, fillers.*

The ageing face results from the combined effects of loss of tissue elasticity, collagen loss, soft tissue atrophy, the continued use of facial muscles and the effect of gravity. All these lead to volume loss and the development of facial wrinkles[1]. Photo damage and smoking also contributes to the ageing process[2]. The fundamental principles of facial rejuvenation include improvement of contour, control of movement and volume augmentation[3].

BOTULINUM TOXIN

Botulinum toxin, a powerful neurotoxin causes chemo denervation of the muscles. The word "botulinum" is derived from the Latin word "botulus" which means sausage which came into existence following the many cases of sausage poisoning due to the neurotoxin produced by the bacteria Clostridium botulinum. In 1946, Schantz isolated the crystalline form of the Botulinum Toxin A. The first clinical use of Botulinum toxin injection in ophthalmology dates back to 1981 when Dr. Alan Scott injected botulinum toxin into the extraocular muscles for correction of strabismus following which it has been increasingly used for both cosmetic and therapeutic purposes.

STRUCTURE AND MECHANISM OF ACTION

Botulinum toxin A (BoNTA) is one of the eight exotoxins produced by the anaerobic bacteria Clostridium botulinum and is most commonly used toxin in clinical practice. It consists of two heavy and light chains linked with a disulphide bond. Botulinum toxin acts by inhibiting the release of acetylcholine (Ach) at the neuromuscular junction. Normally, at the junction, SNARE (soluble N-ethylmaleimide-sensitive factor attachment protein receptor) complex, facilitates the release of the Ach. The SNARE proteins are responsible for fusion of vesicle of Ach with nerve cell membrane causing its release into the synaptic cleft and resulting in propagation of the action potential. After injection of the toxin into a target tissue, it is divided into 100kD of the heavy chain and 50kD of the light chain. The heavy chain is responsible for binding with the nerve terminal, which leads to internalization of the molecule into the cytoplasm of the motor nerve terminal. Light chain acts by cleaving and inactivating the SNARE proteins leading to the inhibition of release of the Ach from the junction and paralysis of the muscle. The effects of Botulinum toxin are temporary as new axonal sprouting and turnover of neuromuscular junctions occur[5,6]. They typically last for 3-6 months.

PREPARATION AND TECHNIQUE

The two most common commercially marketed preparations of Botulinum toxin injection are "Botox" and "Dysport" both of which are Botulinum toxin type A. Dysport is thought to have increased diffusion as well as shorter duration of action, which is why Botox is preferred in most centres. These also differ in terms of molecular weight, dosing and units per vial[7]. For most procedures, 1 U of Botox is equivalent to 3-4 U of Dysport[8].

Botox is available in sterile freeze-dried powder containing 50, 100 or 200 units. This has to be reconstituted with preservative free normal saline. Depending on the volume of saline injected and the indication for its use, a solution containing 1.25 to 5 U/0.1 ml is made. This can be stored under refrigeration for up to a week, with some advocating its efficacy up to 6 weeks following reconstitution[9].

Injection is typically given with 30 or 32 G needle to reduce the pain and risk of bruising. Topical lidocaine gel or ice packs are usually given prior to injection which helps in decreasing the pain. However, lidocaine injection should not be given as it can potentiate the effect of BoNTA.

INDICATIONS

BoNTA injection can be used both for aesthetic purpose and therapeutically. The various indications for its use in ophthalmic community are listed in (Table 1). It is FDA approved for the treatment of Blepharospasm, hemi facial spasm, strabismus, glabellar lines and periocular rhytides. Mesobotox is a term used to describe multiple intradermal injection of botulinum toxin in diluted doses. This technique improves skin texture as well as facial contour in the injected area. (Figure 1A,1B,1C) shows the use of BoNTA Inj. for crow's feet (hyperkinetic

Table 1: Ophthalmic indications of Botulinum toxin injection

Aesthetic
- Glabellar lines (Frown lines)
- Orbicularis rhytids (Crows feet)
- Bunny lines
- Smoker lines
- Marionette lines
- Masseter hypertrophy
- Brow lift

Therapeutic
- Essential blepharospasm
- Hemifacial spasm
- Cervical dystonias
- Frey's syndrome
- Strabismus
- Thyroid eye disease
- Temporary chemical tarsorraphy
- Spastic lower lid entropion

Table 2: Contraindications of Botulinum toxin injection

Contraindications
- Allergy to human albumin
- Previous allergic reaction
- Pregnancy / Lactation
- Drugs -Aminoquinolones, calcium channel blockers, cyclosporine and D-penicillamine
- Neuromuscular disorders – Myasthenia, Lambert Eaton syndrome
- Infection at injection site
- Urinary tract infection, urinary retention

orbicularis oculi). Figure 2A to 2D shows the four points injection site for masseter hypertrophy. Figure 3A and 3B shows pre and post injection images for horizontal forehead lines. Figure 4A and 4B shows injection point for forehead frown lines.

CONTRAINDICATIONS

Table 2 lists the contraindications of BoNTA injection. It should not be used in children less than 12 years of age.

ADVERSE REACTIONS

Any treatment is not without its risks and complications. The following adverse reactions can be seen after BoNTA injection
- Pain and eyelid edema
- Diplopia if toxin spreads to the extraocular muscles
- Ptosis if levator palpebrae superioris is affected

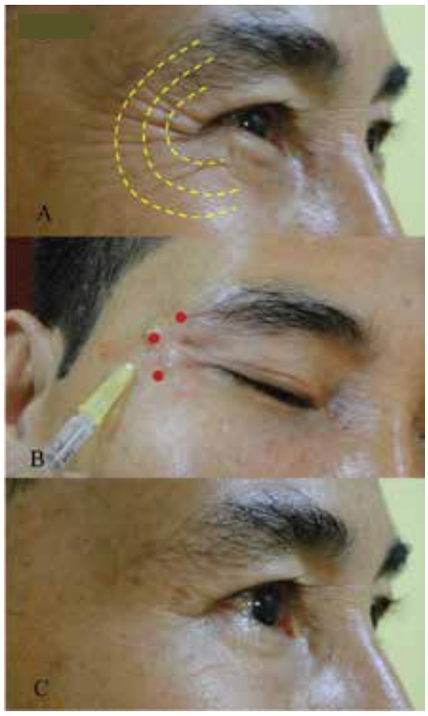

Figure 1A: *Crow's feet (pre-injection BoNTA injection),* ***Figure 1B:*** *Inj. BoNTA sites* ***Figure 1C:*** *Crow's feet (post-injection BoNTA injection).*

- Lagophthalmos causing corneal ulceration
- Ectropion, epiphora
- Mouth droop
- Brow asymmetry, Lid retraction
- Systemic absorption causing - Dysphonia, Dysarthria, Dyspnoea, Dysphagia
- Anaphylactic reactions
- Death

DERMAL FILLERS

Paraffin was the first filler used for the face in 1907[10]. Due to intolerable side-effects its use was abandoned. Subsequently many substances like mineral oil, lanolin, beeswax, vegetable oil, rubber and purified latex were used for cosmetic purpose but were found to have too many undesirable adverse effects[11,12]. Liquid silicone was used off-label for facial augmentation during the 1960s. It was not until 1980s that bovine collagen came to the market under the brand name "Zyderm I" and it became the first FDA approved dermal filler for use in facial rejuvenation[13]. The role of dermal fillers for facial aesthetics has revolutionised with the introduction of Hyaluronic acid (HA) fillers. The first HA filler approved by FDA was Restylane in 2003. Since then, HA fillers have been the cornerstone for volume augmentation of the face.

CLASSIFICATION[14]

Fillers can be classified depending on the duration of effect, material of origin, and reversibility (Table 3). Depending on duration of effect they may be classified as short (less than 3 months), medium (3-12 months), long (12-24 months), or very

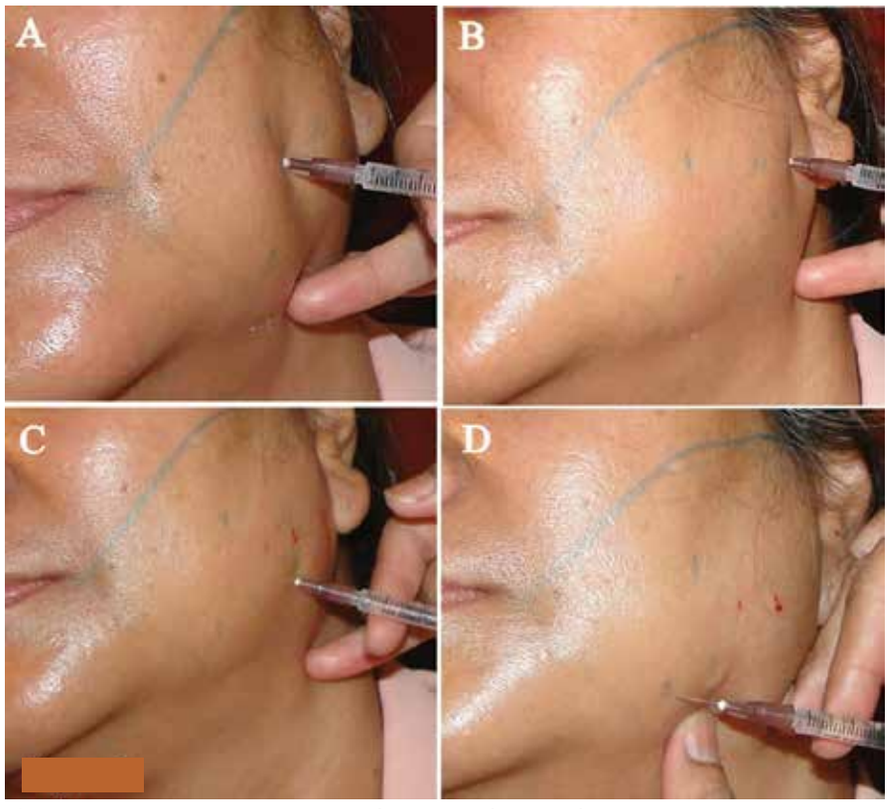

Figure 2A to 2D: *Four point Inj. BoNTA for masseter hypertrophy.*

Table 3: Classification of dermal fillers[14]	
Source	**Example**
Autologous	Fat
Biological	Collagen, Hyaluronic acid
Synthetic	Hydroxyapatite, silicone oil, polymethamethylacrylate microspheres, polyacrylamide hydrogel, hydroxyethyl methylacrylate/ ethyl methacrylate, poly-L-lactic acid
Duration of cosmetic benefit	
Temporary short duration	Saline
Short duration	Bovine collagen
Reversible(medium to long duration)	HA
Nonreversible long duration	Hydroxyapatite, polyacrylamide hydrogel, porcine collagen
Nonreversible very long duration	Silicon oil, PMMA microspheres, hydroxyethylmethacrylate, ethylmethacrylate, poly-L-Lactic acid, Fat
Nonreversible variable duration	Fat
Risk profile	
Low	Saline, HA
Medium	Collagen, hydroxylapatite, PMMA microspheres, poly-L-Lactic acid, fat
High	Hydroxylapatite, polymethylmethacrylate microspheres, poly-L-lactic acid, fat, silicone, polyacrylamide hydrogel, hydroxyethyl methacrylate/ethyl methacrylate
Level Of Physician Skill, Training, Experience, and Judgment	
Low	Saline
Medium	HA, collagen
High	Hydroxylapatite, polymethylmethacrylate microspheres, poly-Llactic acid, fat, silicone, polyacrylamide hydrogel, hydroxyethyl methacrylate/ethyl methacrylate

long acting (more than 24 months). Only Hyaluronic acid fillers will be discussed in brief.

INDICATIONS

Fillers are primarily indicated for volume augmentation and correction of static rhytides. They restore symmetry and are used for mid-face lift. An ideal filler is safe, volumizing, biocompatible, does not migrate, long lasting, easy to inject and cost effective. The following are some common indications for dermal fillers.

1. *Upper face:* Glabellar lines, forehead lines, superior sulcus deformity, temporal fossa hollowing
2. Mid- face: midface lift, tear trough deformity, cheek augmentation, nose augmentation and contouring
3. *Lower face:* Lip augmentation, marionette lines, perioral rhytids, downturned oral commissures, and irregular chin lines, pre-jowl sulcus, chin augmentation

TECHNIQUE

Preoperative consent is a must and like any cosmetic procedure, the patient should be given a mirror and asked to point out the areas where he/she feels needs treatment. Lignocaine topical cream should be applied 30 minutes prior to the filler injection. Ice packs and dental blocks have also been used for anaesthesia[15]. The desired areas are then cleaned with isopropyl alcohol. Different techniques of injection are described. These are serial puncture, linear, crosshatching and fanning techniques. In the serial puncture technique, multiple punctures are made and small boluses

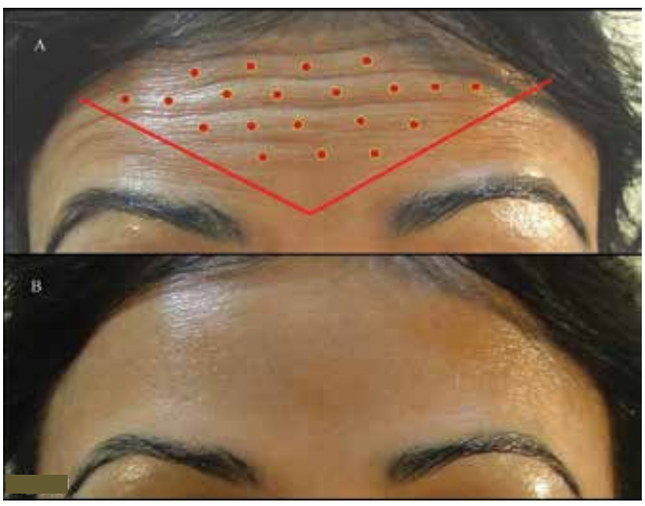

Figure 3A & 3B: *Pre and post injection for horizontal forehead lines.*

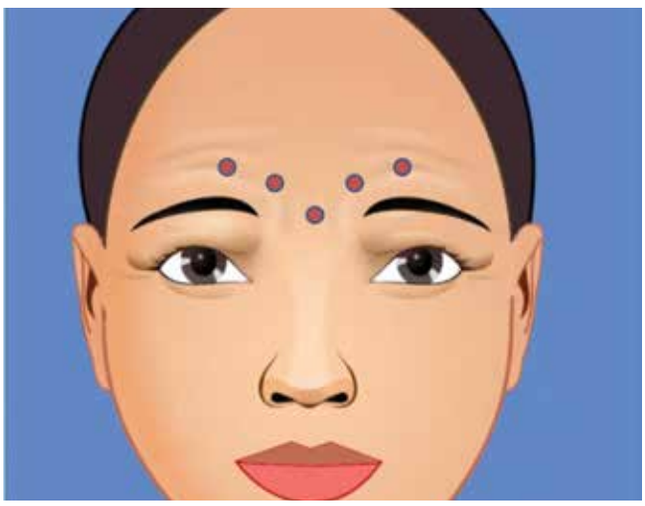

Figure 4A & 4B: *shows injection point for forehead frown lines.*

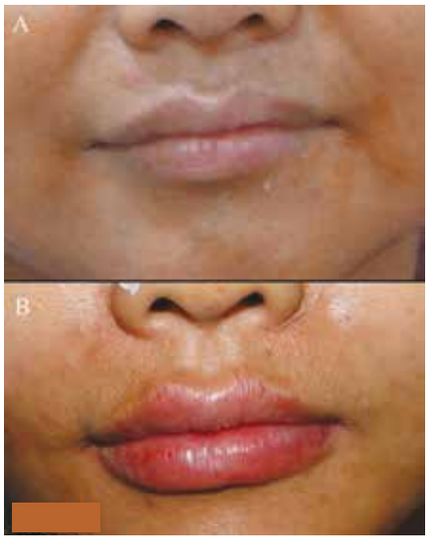

Figure 5A & 5B: *Lip augmentation using HA fillers.*

are injected in close proximity to each other. This is particularly useful for acne scars. The linear technique involves advancing the needle to its full extent into the dermis. Cross hatching again involves two perpendicularly placed injections in a linear fashion. While fanning technique utilises a single injection with multiple linear threads emanating from that point[16].

HYALURONIC ACID FILLERS (HA)

Hyaluronic acid is a naturally occurring compound, which forms a part of the normal extracellular matrix of the dermis and connective tissue[17]. Thus they are highly biocompatible with no immunogenicity. They are hydrophilic and have the ability to imbibe water up to 1000 times its volume. It is rapidly degraded in its natural form and needs to be cross-linked for stabilisation. Various commercial preparations of HA differ on the basis of the following aspects: the source, concentration, particulate size, cross-linking, type of crosslinking agent being used, and whether the HA is monophasic (more cohesive & do not migrate) or biphasic (customized for particular anatomic area), and whether an anaesthetic has been added. The injection technique as well the filler type should be customised to which area is to be treated. For example for treatment of superficial fine wrinkles, less viscous HA should be given while for volume augmentation of the malar area or naso-labial fold, more viscous agents should be preferred. It is always better to undertreat, as HA fillers will expand as they imbibe water overnight. Figure 5A and 5B shows lip

Figure 6A to 6D: *Classic HA fillers injection points for mid face lift.*

Figure 7A & 7B: *Pre and post op images after HA fillers for mid face lift and contouring.*

augmentation using HA fillers. Figure 6A to 6D shows classic HA fillers injection points for mid face lift, and figure 7A and 7B shows pre and post op images after HA fillers for the same.

Some of the commercially available HA fillers are Juvederm XC, Juvederm Ultra XC, Voluma, Vollure.

Advantages of HA fillers are –

- non immunogenicity
- non requirement of skin testing
- reversibility
- long lasting

Adverse effects include pain, bruising, edema, nodule formation, accidental intravascular injection, Tyndall effect (if the injection is given too superficial and the skin is very thin), granuloma, scarring, CRAO (causing blindness)

CONCLUSION

Facial rejuvenation has become an important subject of psychosocial well being in this era of fashion and beauty. BoNTA injections and dermal fillers offer an excellent non surgical method of facial rejuvenation. These procedures should be performed by a skilled facial aesthetics surgeon to meet the patient's expectations. Important knowledge of facial anatomy is a must for the aesthetic surgeon interested in these methods. It is always better to under correct than overcorrect while giving dermal fillers.

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