Botox: Therapy Beyond Beauty

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ABSTRACT

Botulinum toxin originated from the Latin term ‘botulus’ meaning ‘sausage’. Botulinum toxin is a bacterial extract which acts at the synaptic level and inhibits the neuronal uptake of acetylcholine causing inhibition of muscular contraction. This property of botox proves to be useful in various muscle spastic disorders. Commercially accessible under the brand label of Botox and is universally used in cosmetic field in managing wrinkles and crow lines correspondingly it has multitude of use in treating innumerable maxillofacial complex disorders like Temperomandibular disorders, Hypertonicity of lips, gummy smiles, Bruxism, trigeminal neuralgia and other types of facial pain. Botox is regarded as minimally invasive procedure with promising results in muscular disorders as well as cosmetic purpose. Botulinum when used in therapeutic doses proves to be boon to mankind. The effects are dose dependent as it comes with the black box warning. Overcoming this disadvantage of botox, the newly emerged Frotox® based on the (Focussed Cold Therapy) is used nowadays and proves to be more efficacious. This article describes in detail about the origin of the toxin, its commercially available forms. It also describes the clinical technique, its pros and cons with instructions with patient as well as operator point of view.

INTRODUCTION

Botulinum toxin originated from the Latin term ‘botulus’ meaning ‘sausage’. Botulinum toxin is a bacterial extract which acts at the synaptic level and inhibits the neuronal uptake of acetylcholine causing inhibition of muscular contraction. This property of botox proves to be useful in various muscle spastic disorders (Erbguth, 2004; Kerner, 1822).

Mechanism of Action

The Bacterial extract from clostridium toxin acts at the skeletal muscle synaptic level. The toxins can be serologically differentiated into eight types from “A, B, C1, C2, D, E, F, and G”. The neurotoxins A, B possesses antigenic variation but have no dissimilar functions and helps in management of various disorders. It can be used in injectable form via intramuscular, Intra-detrusor also intradermally (Freund et al., 2000; Touche et al., 2010).

As injected into the intramuscularly it leads to proteolysis of Synaptosomal associated protein SNAP-25 in the cytoplasmic region of the neurons, which is essential for discharge of acetylcholine at the synaptic level of neuromuscular junction (Nayyar et al., 2014). Leading to zero action potential and inhibiting the muscular contraction in return leading to paralysis of particular muscle (Figure 1) The effectivity of botox starts deteriorating and completely vanishes off after 3 months and needs re-
Table 1: Evolution of Botox as a Therapeutic Agent

| ERA      | Scientists and Place                          | Observation                                                                 |
|----------|----------------------------------------------|-----------------------------------------------------------------------------|
| 1820     | Justinus Kerner                              | Lethal effect of minute doses and earned himself recognition as pioneer of modern botulinum toxin therapy |
| 1989     | Food and Drug Administration (FDA)           | Therapeutic use in management of ocular muscle spasms                       |
| 1895     | Émile van Ermengem                           | Correctly described the toxin as the bacterial source from Clostridium botulinum |
| 1895-1925| Karl Friedrich Meyer                         | Developed a toxin extraction technique from the organism grew and inactivated the toxin by heating it. |
| 1970’s   |                                               | Botulinum was used in management of strabismus coincidently also noticed that botulinum also reduced wrinkles in the glabella region. |
| Post world war II | In Maryland                                        | Botulinum gained recognition as a weapon at “Fort Detrick in Maryland. |
| 1946     | Carl Lamanna and James Duff                  | Formulated the concentration and crystallization technique given by Edward J. Schantz |
| 1978     | Dr. Allen Scott                              | First clinical test for management of Blepharospasm.                        |
| 2000     | Food and Drug Administration (FDA)           | Neck muscle associated spasticity                                            |
| 2002     | Food and Drug Administration (FDA)           | Cosmetic correction for Glabellar frown lines and in removal of the facial wrinkle lines. |
| 2004     | Food and Drug Administration (FDA)           | Its use in excessive sweating cases                                          |
| 2009     | Food and Drug Administration (FDA)           | Approved for use in Cases of Blepharospasm                                  |

administration of the therapy.

**Commercial Forms of Botox**

Out of the seven types of botulinum toxins have been isolated only toxin A and B types are available commercially. Three forms of Botulinum toxin A (Botox®, Xeomin®, Dysport®) and Only one formulation of toxin B (Myobloc®) are available commercially from various therapeutic and enhancing cosmetic procedures (Kharbanda et al., 2015).

**Each vial contains**

1. 100 units of Botulinum type A neurotoxin complex.
2. 0.5 mg of Human Albumin.
3. 0.9 mg of NaCl in a sterile, vacuum dried form devoid of preservatives.

**Applications**

Botulinum toxin (BT) is known to have multitudes of uses in cosmetic as well as therapeutic effect. Off all the commercially available preparations Botox® is the worldwide commonly used and has maximum approvals (Aurora et al., 2010; Diener et al., 2010; Jackson et al., 2012). BT-B is approved by DA for its use in cases of cervical dystonia, Hemi-facial related spasms (Dharsiyani et al., 2014). The uses of botox are as follows, They can be subdivided grossly into, Cosmetic use and Therapeutic use.

Botulinum toxin finds multitudes of use in head and neck area, it deals with both the cosmetic as well as therapeutic use. It has proved as an adjunct to various treatment modalities. The applications in maxillofacial region are as follows,

1. Gummy smile
2. Chronic headaches/migraines
3. Bruxism
4. Trigeminal neuralgia
5. Temperomandibular disorders (TMD’s)
6. Masseter hypertrophy
7. Black Triangles
8. Dental implantology and surgery

**Excessive Gingival display**

It can be effectively used in patients with gummy smile in which there is display of maxillary gingival tissue while smiling. The gingival complex plays a major role in the overall beauty of a smile (Polo, 2005). It can be due to skeletal defect or hyperactivity of lip muscles. The conventional treatment routinely followed is surgical correction of hyperactive Lip muscle. But this method comes with added disadvantage of scar contraction and relapse of the muscle activity (Hwang et al., 2009; Binder et al., 2000). Hence, dentists generally prefer botulinum injection therapy over the invasive correction.

**Chronic migraine**

Botulinum toxin in case of migraine condition doesn’t weakens muscles rather it inhibits the carrier protein and blocks them. In patients treated for cosmetic purpose it was seen that it also improves chronic headaches. Botulinum toxin A injections when used in patients receiving cosmetic botulinum treatment with associated complain of headache it was observed that there was improvement in chronic headache (Patil et al., 2013).

**Bruxism**

Bruxism is a para-functional activity leading to clenching and grinding of teeth and is usually accompanied with muscular hypertrophy and myofascial pain due to hyper contractibility of muscles. Which often leads to pain in TMJ along with muscle hypertrophy.

**Trigeminal neuralgia**

“Trigeminal neuralgia (TN) is defined as sudden, usually unilateral severe brief stabbing recurrent episodes of pain within the distribution of one or more roots of the trigeminal nerve.” Patients mainly complain of numbness, picking, rubbing, or scratching sensations in the affected areas (Börü et al., 2017). There are case reports and evidence proving the efficacy and its duration on trigeminal neuralgia (Zhang et al., 2019; Lee et al., 2005), (Table 1).

**Temperomandibular disorders**

TMD is a canopy term which houses many pathologies related to the joint and/or the masticatory muscular dysfunctions. The symptoms manifested in Temperomandibular pain are clicking of joint, headaches, joint pain, per auricular pain, neck stiffness and associated pain. Occlusal disharmonies and periodontal problems have a major role in aetiology for TMD’s. In untreated cases of bruxism, there are microfractures in and around restorations the reason being excessive forces along with increases prevalence of tooth decay and these forces may also cause gingival recession. Some studies state that it relieves pain associated with joint and improvizes mouth opening and shows no side effects.
**Dental implants and surgery**

Botulinum has also proved efficaciously in the fields of implantology by allowing unimpeded Osseo integration of implants as any loading stresses on implants can lead to implant failure. However, there is lesser evidence based literature of use in implants and needs further research (Kayikcioğlu et al., 2003). Kayikcioğlu and colleagues conducted a small open label study to examine therapeutic efficacy as an adjunct in fixation in cases of zygomatic fracture the patients were operated 12-48 hrs. An EMG confirmation was done to assure complete muscle denervation post injection. The temporary effect of paralysis of masseter allowed fewer mini-plate fixation and complications (Choi et al., 2014).

**Massetric hypertrophy**

Patients with history of bruxism are commonly found with massetric hypertrophy. The facial appearance of the patients changes due to increase in the size of muscle. The jaw seems swollen and misshaped. Conventional treatment modality to be followed is surgical correction but nowadays minimally invasive technique of injection (Kharbanda et al., 2015), (Table 1).

**Other uses**

**Sialorrhea**

Botulinum acts as anticholinergic reduces the salivary secretions and can be effectively used in cases of sialorrhea (Kharbanda et al., 2015). Cosmetic uses for marinette line, crow lines, and nasolabial fold drop (Table 1).

**Aesthetics & Black triangle**

The war lies in harmonizing between the white and pink. Botox acts as dermal fillers and provides volume to the tissues and enhances the aesthetics. Botox are injected into the interdental spaces and it replaces the lost interdental soft tissue which is of prime importance while replacing missing anterior. Botox replaces the lost and enhances aesthetic to prosthesis. There are lack of case reports pertaining to the botox used as fillers for the lost interdental papilla. The treatment effect lies approximately for 8 months (Kharbanda et al., 2015).

**Contraindications**

1. Patients should not be advised management with botox who are:
2. Psychologically unstable with unrealistic expectations
3. Are on Anti-Cholinergics
4. Allergic to any of the composition of botulinum preparation
5. Pregnant or lactating females
6. Suffering from neuromuscular disorders.

**Clinical Technique**

Botulinum for the treatment has to be freshly prepared before use and has to be injected intradermal and the preparation has to be refrigerated at 2-4°C the preparation has to be diluted with sterile saline, and is advised to be used within 4 hours after preparation and to be injected using tuberculin syringe. The site to be injected is to be made aseptic using alcohol with sterile sponge gauze pieces. Aspiration during injecting is to be assessed to avoid involuntary deposition at the undesired site such as facial arteries. The effects of botulinum are short term and is effective for only 4-6 months

After care post treatment, the patient should not lie down for the first 4 hours. Exposure to sun must be taken care and avoided also strenuous exercises for a minimum period of 24 hours. Skin manipulation activities to be avoided that shall cause flushing like effect namely acupressure facial massage, heat or cold pack, any topical applications, and consumption of alcohol (Kayikcioğlu et al., 2003).

**Maintenance**

The effects are reversible and hence the maintenance has to be taken care off and needs to be administered 2-3 times a year depending on the declining effect. Injections are given with a sparing time for a minimum of three months approximately to avoid the immune response which would prevent Botox from working the next time (Kayikcioğlu et al., 2003). Safety margin of botox that is lethal dose in humans can reach up to 40 U/kg BW).

**Frotox as an Alternative**

Cold therapy or cryotherapy is a procedure in which the cold energy is focussed and delivered at the targeted area of the nerve fibre. Which is also known as cryoneuromodulation which temporarily interrupts the neuronal connection and immediately freezes the targeted muscle. A close-ended needle that is filled with highly pressurized liquid nitrous oxide which is not released into the skin. Frotox has immediate effect as compared to botox. Frotox works on the specific target which gives the most natural look. Frotox lasts up to 4 months.

**RESULTS AND DISCUSSION**

The fundamental aspects in facial aesthetics are mouth and teeth. Botox is non-invasive procedure
| Disorders or Problems          | Dose               | Muscle marks                          | Landmarks                  | Treatment Reports                                                                 | Effect With Evidence Reports                                                                 | Duration       |
|-------------------------------|--------------------|---------------------------------------|----------------------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|----------------|
| Gummy smile                   | 3-5U each Bilaterally | 'Yonsei' point                         | Lip Hyperactivity reduces. | Hwang et al. (2009); Binder et al. (2000)                                           |                                                                                               | 3-4 months    |
| Drooping corners of lips      | 2-5U each Bilaterally | Trajectory of nasolabial fold to the jaw line. Masseter belly | Improvement of the facial features. Zandijcke and Marchau (1990) |                                                                                   | Muscle relaxation                                                                                 | 3-4 months    |
| Bruxism                       | 25-50U each Bilaterally | -Masseter and temporalis. | Freund et al 1999 stated relief in pain, tenderness and also improvement in mouth opening. Zhang et al. (2019) | Lee et al in (2005) conducted a small open label trial study reported no side effects during management of TMD cases 5-12 month follow up period. Polo (2005) |                                                                                                                                               | -3 months 27 |
| TMD                           | 2.5-7.5U each Bilaterally 150 U | -Masseter and temporalis. Börü et al (2017) | Freiberg et al 1999 stated relief in pain, tenderness and also improvement in mouth opening. Zhang et al. (2019) | Lee et al in (2005) conducted a small open label trial study reported no side effects during management of TMD cases 5-12 month follow up period. Polo (2005) | Efficacy was maintained until 19 weeks. Patil et al. (2013)                                                                                   | 3 months      |
| Chronic Migraine              | Total of 155U (divided into 7 muscles bilaterally) | Frontalis(20U) Corrugator(10U) | -Relief in pain also associated chronic headaches are relieved. Shah et al. (2014); Brin et al. (1987) | In Randomized controlled trials concluded botulinum beneficial for chronic daily headaches and chronic migraines Verma et al. (2015) |                                                                                               | 3 months      |
| Trigeminal neuralgia          | 25-75U39 | Peri-cranial muscles. Kharbanda et al. (2015) | -88.9% patients had relief (6 month follow up.13 | Males exhibited better treatment outcomes comparatively. -concluded long-term effectivity of the treatment Polo (2005) |                                                                                               | 1-10 months   |
| Masseter hypertrophy          | 30U each bilaterally | Masseter belly                         | Injection into the masseter muscles resulted reduction in masseter muscle hyperactivity. Pisulkar et al. (2019) |                                                                                   |                                                                                               |                |
| Oro-mandibular dystonia       | 30U                | Masseter and/or Sub-mental complex     | 67.9% improvement inspeaking, swallowing, and eating. (10yr follow up study) Yiannakopoulou (2015) |                                                                                   |                                                                                               |                |
which has reversible effects, conservative, non-surgical, treatment modality to achieve optimum aesthetics. It becomes easy for the dentists to learn the injecting techniques as they are already aware about the anatomical landmarks to be considered while managing the cases during administration of local anaesthesia thus patients are at ease and comfort. The preparation has to be freshly made before every use. The dilution is prepared by following user guidelines and to be used within 4 hours. The calibrated tuberculin syringe is used. Botulinum is known as the neurotoxin it acts at the synaptic level to inhibit release of the neurotransmitter Acetyl choline and aborts muscular contractions leading to a chemo-denervation process. As the use, knowledge and awareness of botulinum is in increasing day by day in leaps and bounds. Caution has to be taken about the adverse deadly reaction occurring due to its poisonous nature. Dose has to be calibrated and administered. Neither literature nor clinical randomized controlled trials shows any reports with such adverse reactions to botulinum. Some animal studies report that Botulinum after being injected spreads up to 30-45mm away from the target site and causes it to diffuse into adjacent muscles, the consequence of generalized diffusion of toxin is not well known. Systemic toxin spread can lead to consequences suggesting botulism leading to weakening of muscles or paresis, dysphagia and respiratory arrest. These when left untreated can prove to be fatal to mankind (Choi et al., 2014).

CONCLUSIONS

Botulinum toxin therapy is one of the trending and unique adjunctive treatment modality in the field of dentistry and acts as arsenal in managing the cosmetic as well as the therapeutic fields of Oro-facial complexes as the botulinum comes with the black box warning label onto the vial the doses should be carefully monitored and wisely delivered at the targeted sites for the desired result.as the effects are reversible over a period of time it needs to be revised. There are no such adverse reactions note in the literature evidences and the effect being quick and aesthetic. Though botox has its limitation in being used widely ethically as it is yet to be FDA approved for many of its application and is obvious that BT offers a range of valued results for dentist and will take dental profession to one step ahead in the field of progress.

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Conflict of Interest

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