BOTOX– An innovative treatment modality in dentistry: A review

Anubha Agarwal[1], Himanshu Aeran[2,*], Amrinder S.Tuli[3], Nitin Bhatnagar[4]

[1]Deputy Medical Superintendent, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, [2]Director Principal and HOD, Dept. of Prosthodontics, [3]Professor, [4]Post-graduate, Dept. of Periodontics and Implantology, Seema Dental College and Hospital, Rishikesh, Uttarakhand, India

***Corresponding Author:**
Email: drhimanu4@gmail.com

Abstract
Botox i.e botulinum toxin (BTX), is a neurotoxin protein which is produced by the bacteria clostridium botulium and the other bacteria's of same species. It has been used in various treatment modalities in medical science. Botox has been approved by FDA for its use in medical industry. Apart from medical application it has also been found useful in various dental treatments, which includes treatment for temporo-mandibula disorders, its use in patients with habit of bruxism and clenching. Botox has also been found useful in enhancing facial aesthetic by removing wrinkle line, treating gummy smiles and also in treating black triangles. Botox is becoming a popular noninvasive treatment modality for various aesthetic and functional problems with minimum trauma and discomfort to the patient.

Keywords: Black triangles, Botulinum toxin A, Bruxism, Gummy smile.

Introduction
Botox being lethal, naturally occurring substance possess a significant and elaborated history of medically therapeutic usage in various conditions like cervical dystonia, hyperhidrosis, strabismus, blepharospasm. It can also be used as an effective and powerfull medication when administered in approved dosage (FDA).[1] Botulinum toxin (BT) is a neurotoxin produced by anaerobic Bacteria clostridium botulinum, it is highly toxic neurotoxin which causes a serious disease called botulism characterised by paralysis of the musculature in the body leading to death which was first noticed by Emile van ermengem in 1897.[2]

The first therapeutic use of botulinum toxin was conceived by Kerner and coined the name botulism (from latin botulus meaning sausage").[3] Botox has been approved by the food and drug administration (FDA) for therapeutic treatments of eye muscle problems (in 1989), neck problems (in 2000), and excessive sweating (in 2004). In 2002, the FDA approved Allergan's botox cosmetic for the purpose of temporarily erasing facial lines.3 Botulinum toxin can be differentiated serologically into eight kinds of toxins named from A to G (A, B, C1, C2, D, E, F, and G).[4,5] Neurotoxin strains A and B are antigenically different, but have similar functions and are commercially available for medical treatments.[6,7]

Dentist who is trained and experienced with the use of botox, is allowed to use botulinum toxin for various aesthetic and functional needs of the patient. This is in accordance with the statement given by The Dental Quality assurance of Washington. Use of Botox as a dermal filler for various aesthetic treatment is also been practiced now a days. There are various serotypes which are produce by the clostridium botlinum i.e. type A, type B, type C1, type D, type E, type F and type G. botulinum toxin is a naturally occurring substance apart from being natural it lethal when used in inappropriate dose and when used by unskilled operator.

Botulinum toxin type A (Botox-Cosmetic®) is available in Indian market for use in various aesthetic and functional needs. Each bile of botulinum toxin type A contains,

1. 100 IU of botulium toxin (purified neurotoxin complex)
2. 0.5 mf of Albumin protein.
3. 0.9 mg of NACL

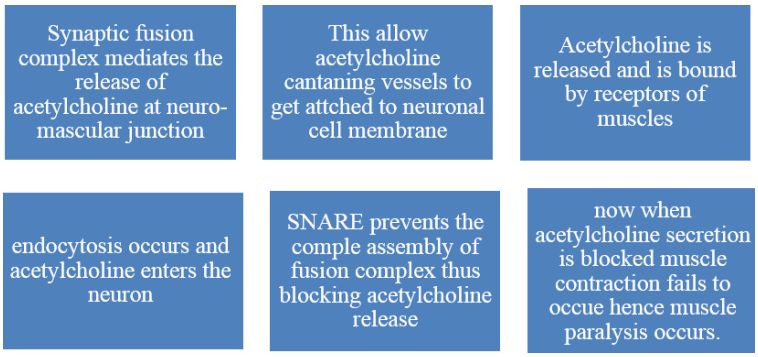
History
1. A German poet, doctor and scientist, Dr. Justinus Kerner of Wurttemberg, first explained the disease called botulism (1817 to 1822) caused by 'sausage poison'.
2. Already imagined that the toxin that caused such a serious disease, could be used to treat diseases like muscular spasms.
3. Dr Emile Pierre van Ermengem (Belgium) in 1895 successfully isolated this bacterium, named it Bacillus botulinus.
4. Botulinum toxin was first used to treat human disease (1980) by Dr Alan Scott (ophthalmologist) and Edward Schantz, in treating strabismus.
5. In 1987, ophthalmologist Jean Carruthers observed that frown lines disappeared after the use of botulinum toxin A for blepharospasm.
6. In 1996, they published the first paper on the use of Botox for cosmetic purposes.
7. In 2002, the FDA announced the approval of BOTOX® Cosmetic to temporarily improve the appearance of moderate-to-severe frown lines between the eyebrows (glabellar lines).
8. In July 2004, the FDA approved BOTOX® to treat severe underarm sweating, known as primary

axillary hyperhidrosis that cannot be managed by topical agents.[8]

Mechanism of Action

Botulinum toxin inhibits the secretion of acetylcholine at neuromuscular junction which causes paralysis of the target muscle.

Flow Chart 1: Mechanism of action of botulinum toxin



Preperation and Storage

Botox® is available in a freeze-dried powder that clumps at the bottom of the vial. During reconstitution, the rubber seal on the vial should be wiped with an alcohol swab before using a 5 ml, 25-guage needle syringe to inject the desired volume of normal preservative-free saline. Rotating the vial during injection also assists a gentle reconstitution. Botox® should be reconstituted after the journey. Agitation during transport may denature the toxin and greatly reduces its duration of action. Almost all of the injections are intramuscular and not subcutaneous. One ml tuberculin or insulin syringes can be used as it gauges the dose accurately in minute quantities also.[9,10] A safe and reproducible injection point for Botulinum toxin A around the converging area of the three muscles has been proposed and proved effective in clinical applications. Intramuscular injection for correction of excessive gingival display is given at ―Yonsei poing. Botulinum toxin-A is diluted by adding 4.0 ml of 0.9% normal saline solution without preservatives to 100 U of vacuum-dried C botulinum type A neurotoxin complex, according to the manufacturer‘s dilution technique. This results in a 2.5 U/0.1 ml dose.[11]

Theraputic application of BOTOX

Periodontal Application

Prominent Gums\Gummy smile: Gummy smile is excessive display of the gingival tissues on smiling with a prevelance of 7% in young males and 14% in young females. Excessive display can be related to muscle functioning, muscles like levator labii Superioris alaeque nasi are most commonly involved with gummy smile. Apart from various surgical techniques which have been used for treatment of gummy smile, use of Botulinum toxin has shown promising results for gummy smile correction. Toxin is in small, carefully titrated doses to limit any over activity of the musculature, thus it reduces the exposure of excessive gingival tissues on smiling.

A study by Hwang et al. which took place at Yonsei University College of dentistry, Seoul, Korea in it they have proposed a technique of injection point for botulinum toxin at the centre of triangle formed by levator labii superioris, levator labii superioris alaeque nasi and zygomaticus minor with a dose of 3U at each injection site and they named this as Yonsei point.[12]

Black Triangle: Black triangle are one of the most challenging esthetic concern following placement of crowns, bridgesand especially implants or after periodontal surgery. Botox is injected into the areas where papillas are blunt and space is present, botox pumps up the papilla and is minimally invasive way to create proper and more pleasing gingival contours.[13]

Dental implants and maxillofacial fractures: Excessive functional forces, especially in patients with parafunctional habits can hamper the process of osseointegration. Thus, the overloading of implant results in its failure. Forces from hyperactive masticatory muscles can also prevent or impede fracture callus formation after maxillofacial fracture fixation. Hence in both conditions muscular relaxation can be achieved with BT injections into the masticatory muscles allowing a more stable environment for implant integration and fracture healing. In a open-label study to prospectively examine the use of BT as an adjunct to zygomatic fracture fixation, prophylactic injections of 100 units of BT into the masseter muscle of patients with zygomatic bone fractures at the fractured site before the surgical procedure resulted in temporary paralysis of the masseter muscles which allowed for fewer miniplate and/or microplate insertions in all patients, and also resulted in no complications related to either the botulinum toxin injections or surgical procedures.[14]

Other Theraputic Application

Mandibular Spasm: This category of muscle spasm includes muscles of mastication and other related muscles of mandible. Mandibular spasm leads to

restricted mouth opening i.e. 'trismus'. There are various problems which are associated with mandibular spasm which includes hindrance in maintaining proper oral hygiene, hindrance in performing dental procedures, difficulty in performing functional movements like eating and talking. Injecting botulinum toxin in the targeted muscle will lead to paralysis and will finally reduce the hyper activity or spasms of the muscle.[15]

Enhancing Facial Esthetics: Botulinum toxin is becoming very popular and effective in enhancing upper face aesthetics now days. Problems like facial wrinkles which can be a cause of un-aesthetic appearance can be treated with Botox. pathogenesis of wrinkles should be known first. Treatment option for lower face can be use of dermal fillers whereas for upper botox can be miracle treatment option. Wrinkles are mainly caused due to hyperactivity of muscle which ultimately deforms the covering skin, exact pathology should be known to the doctor before treating the wrinkle with botox therapy.[16]

Bruxism: Bruxism being para functional habit, includes excessive grinding of the teeth. Bruxism is unrelated to normal function such as eating and talking. Aching of jaw muscles is one the symptom associated with bruxism. Use of botulinum toxin has shown positive results in decreasing the symptoms of bruxism. A study conducted by Ivanhoe *et al*[17] in which he has injected botulinum toxin into the masseter muscle and observed the changes in overall symptoms of bruxism, 200 IU was the dose of botulinum which was injected and it took time duration of 19 weeks to show the therapeutic response.[18]

Trigeminal Neuralgia: Chronic pain disorder affecting the trigeminal nerve, it can be typical or a-typical. It is a neurological disorder with episodes of severe, sudden, shock-like pain or constant burning pain with less severity; it usually affects one side of the face. A study by Boru et al. conducted a study to check the efficacy of Botox in treating patients with trigeminal neuralgia, he has observed that injecting botulinum toxin in roots of maxilla and mandible has successfully decreased the pain severity and attack frequency. Botox can be used as an adjunctive treatment modality in these patients which acts on nerve endings, thereby reducing the severity of the pain.[19]

Temporomandibular Disorders: Temporomandibular disorder (TMD) often causes severe pain and discomfort. It can be temporary or last many years. It might affect one or both sides of your face. More women than men have it, and it's most common among people between the ages of 20 and 40. Temporomandibular disorder usually affects masticatory function, that can be due to TMJ pathology or can be due to dysfunction of muscles of mastication. TMD can happen due to number of causes these include bruxism, external stressors, oromandibular dystonia, and psychomotor behaviors.

Treating patients with excessive occlusal forces by conventional techniques includes intraoral appliances, occlusal adjustments, and dental restoration.

Technique of injecting botulinum toxin has been used successfully to treat various pain syndromes that also includes TMDs. Using botulinum toxin requires special skill as correct injection technique and appropriate dosing guidelines are very important for successful results. Botulinum toxin it paralyse the muscles of mastication thus reduceds the amount of occlusal force that results in reduced clenching and bruxism.[20,21].

Massetric Hypertrophy: Chronic habit of clenching can result in hypertrophy of masseter muscle. This habit leads to increased size of masseter muscle which can be easily appreciated in one's facial profile and intraoral swollen gums can be seen. Surgical correction was the only treatment option before botulinum toxin was introduced. Surgical resection was the only surgical method of correcting hypertrophy. After introduction of botox it has become easier to correct such problems. Injecting botulinum toxin into the masseter muscle decreases its hyper-activity and with course of time size has found to be decreased.[22]

Oromandibular Dystonia: Oromandibular dystonia (OMD) is basically a form of focal dystonia, it can be characterized by involuntary repetitive movements of the jaw and forceful contractions of the face. The muscles of mastication are mostly involved in this case however; lower facial and tongue muscles may also be involved. It causes difficulty in performing functional movements like speech, swallowing and chewing and often leads to severe psychosocial discomfort. Most often it is idiopathic. Botulinum toxin injection of the affected muscles is the treatment of choice for oromandibular dystonia. A study conducted by Tan and Jankovic in which they have enrolled 162 individuals with OMD, Botulinum toxin type A was injected into the masseters and/or into the submental complex. Improved functional movements were observed within 16-21 week of time.[23]

Sialorrhea: Sialorrhea or ptyalis or drooling is a debilitating system which can be seen when there is excessive saliva in the mouth. Children with cerebral palsy and adults with neurological disorder can be seen dealing with such problems. Botox therapy can be of great help in such cases as it blocks the release of acetylcholine at the cholinergic thus this toxin can block cholinergic parasympathetic secretomotor fibers of the salivary gland this can decrease the amount of saliva.[24]

Adverse Effect[25]:

I. Adverse effects of limited duration that are common, localized and not of a serious nature:

Common with any percutaneous injection

a. Mild stinging, burning or pain with injection
b. Edema around injection site

c. Erythema around injection site
d. Mild headache, localized and transient

Technique dependent
a. Ecchymosis lasting 3 to 10 days
b. Asymmetry
c. Oral incompetence and asymmetric smile
d. Lack of intended cosmetic effect

Rare and idiosyncratic
a. Numbness and paresthesias(localized and transient)
b. Focal tonic movements (twitching)
c. Mild nausea and occasional vomiting
d. Mild malaise and myalgias (localized and generalized)

II. Rare adverse effects of longer duration that can be serious and are not technique dependent :
a. Immediate hypersensitivity reactions
b. Urticaria
c. Dyspnea
d. Soft tissue edema
e. Anaphylaxis

CONTRAINDICATIONS[26]:

Patients with following features should not be treated with BOTOX:

1. Psychologically unstable patients
2. Patient who belongs to entertainment industry i.e. uses their facial movements and expressions for their livelihood.
3. Patient with neuromuscular disorder.
4. Patient who are allergic to botox or any of their component.
5. Patient under any kind of medication which can interfere with botulinum toxin.
6. Pregnant or lactating females.

Conclusion

BOTOX therapy is becoming a treatment of choice for patients with temporo mandibular joint (TMJ) and bruxism problems, and for patients with chronic TMJ and facial pain. Role of BOTOX in aesthetic dentistry is also becoming popular these days. This therapy is minimally invasive method to treat various problems such as gummy smile, black triangles, high lip-line etc. use of BOTOX post orthodontics has become a treatment of choice to relax the facial muscles for proper functioning. Furthermore studies and research need to be carried out for use of this toxin in regular dental practice. Approval from FDA for many more procedures are still awaited or required. Botulinum toxin has come out as a noninvasive approach and it has also broadened the horizon of dentistry.

References

1. Barbano, Richard. Risks of erasing wrinkles: Buyer beware! Neurology. 2006;67:E17–18.
2. Erbguth FJ. Historical notes on botulism, Clostridiumbotulinum, botulinum toxin, and the idea of the therapeutic use of the toxin. MovDisord. 2004;19:S2-6.
3. Clostridium Botulinum- Public health agency of Canada. Phac-aspc. gc.ca 2011;04:19.
4. Freund B, Schwartz M, Symington JM. Botulinum toxin: New treatment for temporomandibular disorders. Br J Oral Maxillofac Surg. 2000;38:466–71.
5. MartosDíaz P, Bances del Castillo R, Mancha de la Plata M, Naval Gías L, Martínez Nieto C, Lee GY, et al. Clinical results in the management of Frey's Syndrome with injections of Botulinum Toxin. Med Oral Patol Oral Cir Bucal. 2008;13:E248–52.
6. MG Berry, Jan J. Stanek: Botulinum neurotoxin A: A review. Journal of Plastic, Reconstructive & Aesthetic Surgery 2012;20:1-9.
7. Hatheway CL. Clostridium botulinum and other clostridia that produce botulinum neurotoxins. In: Hauschild AHW, Dodds KL, eds: Clostridium botulinum Ecology and Control in Foods. New York, NY: Marcel Dekker, Inc 1992:3–10.
8. Dastoor SF, Misch CE, Wang HL. Botulinum toxin (Botox) to enhance facial macroesthetics: A literature review. J Oral Implantol 2007;33:164-71.
9. Woo-Sang Hwang: Surface anatomy of the lip elevator muscle for the treatment of gummy smile using botolium toxin. Angle orthodont.2009;79:70-7.
10. Kate coleman moriarty: botolium toxin in facial rejuvenation; revised; 2006
11. Mario polo. Botolium toxin type A (botox) for the neuromascular correction of excessive gingival display on smiling (gummy smile) Am J Orthod Dentofacial Orthop 2008;133:195-203.
12. Hwang, et al. Surface anatomy of the lip elevator muscles for the treatment of gummy smile using botulinum toxin. Angle Orthod. 2009;79:70-77.
13. Chandra S, Devi MP, Ravindra SV, Singh D, Kumar S. Botoxonomics: A palliative prick. Int J Sci Stud 2014;2:108-111.
14. Kayikvioglu A, Erk Y, Mavilli E, Vargel I, Ozgur F. Botulinium toxin in the treatment of zygomatic fracture. PlastReconstr Surg. 2003;111:341–6.
15. Cersósimo MG, Bertoti A, Roca CU, Micheli F. Botulinum toxin in a case of hemimasticatory spasm with severe worsening during pregnancy. Clin Neuropharmacol 2004;27:6-8.
16. Suman T. Enhancing facial esthetics by other modalities. Int J Dent 2011;2011:513957.
17. Ivanhoe CB, Lai JM, Francisco GE. Bruxism after brain injury: Successful treatment with botulinum toxin-A. Arch Phys Med Rehabil 1997;78:1272-3.
18. Tan EK, Jankovic J. Treating severe bruxism with botulinum toxin. J Am Dent Assoc 2000;131:211-6.
19. Sinha A, Hurakadli M, Yadav P. Botox and derma fillers: The twin face of cosmetic dentistry. Int J Contemp Dent Med Rev 2015.
20. Freund B, Schwartz M, Symington JM. Botulinum toxin: New treatment for temporomandibular disorders. Br J Oral Maxillofac Surg 2000;38:466-71
21. Gobel H, Heinze A, Heinze-Kuhn K. Botulinum Toxin A is effective in cases of oromandibular dysfunction even if previous bite splint therapy has proved unsuccessful. Cephalalgia. 2001:514-15.
22. Rijsdijk BA, Van Es RJJ, Zonneveld FW, et al. Botulinum toxin type A treatment of cosmetically disturbing masseteric hypertrophy. Ned Tijdschr Geneeskd. 1998;142:529-32.
23. Lim YC, Choi EC. Treatment of an acute salivary fistula after parotid surgery: botulinum toxin type A injection as

primary treatment. Eur Arch Otorhinolaryngol. 2008;265:243-45.
24. Rao LB, Sangur R, Pradeep S. Application of Botulinum toxin Type A: An arsenal in dentistry. Indian J Dent Res. 2011;22:440-45.
25. Kromminga, A. & Schellekens, H. (2005). Antibodies against erythropoietin and other protein-based therapeutics: an overview. Ann N Y Acad Sci, 1050:57–65.
26. Patel D,Mehta F, Trivedi R,Thakkar S, Suthar J.Botulinum Toxin and Gummy smile-A Review.IOSR Journal of Dental and Medical Sciences. 2013;4:1-5.