

Botox: An Advancement In Dentistry: An Overview

Pragathi R. Bhat^{1*}, Palak Janiani¹ and Vijay A. Trasad²

¹Department of Periodontics, S.D.M.College of Dental Sciences & Hospital, Sattur, Dharwad(India)

²Department of Pedodontics& Preventive Dentistry, S.D.M.College of Dental Sciences & Hospital, Sattur, Dharwad(India)

ABSTRACT

Botox has been used in the medical field since 1987 principally for its cosmetic treatment of wrinkles on the face and for its therapeutic uses in the management of strabismus, cervical dystonia, blepharospasm and juvenile cerebral palsy amongst other disorders. The toxin used is botulinum toxin A (BTX-A), which is a neurotoxin, extracted from the anaerobic bacteria -Clostridium botulinum. These BTX-A molecules act by inhibiting the release of acetylcholine from presynaptic vesicles at the nerve terminals leading to an inhibition of muscle contraction. A growing number of dental surgeons have now been using this toxin as a part of their armamentarium for the management of various muscle-related dental disorders like bruxism, masseteric hypertrophy, myofascial pain, trismus, TMJ disorders and for retraining muscles during orthodontic treatment. This procedure has also been found to be a minimally invasive, safe and reproducible alternative to surgery for perioral esthetic enhancement, which includes treating high lip-line cases, gummy smiles and lip augmentation. Pleasing and promising results have been obtained with this technique showing none or mild and transient side effects.

Keywords: Botulinum Toxin A, Minimally Invasive, Muscle Related Disorder, Esthetics

Introduction

The art of Dentistry for more than a century involves enhancing esthetics and restoring beautiful smile of an individual. A beautiful smile is the blending of full complement of teeth along with a pleasing perioral facial esthetics.¹ Although it is rightly said that “beauty lies in the eyes of the beholder”, apart from the facial esthetics, a beautiful smile adds to the personality of an individual, which in turn produces an increase in the self-esteem.^[2] With these expectations of improving one’s self esteem, more and more patients today focus on the minute perfections with respect to the teeth and gums along with the facial esthetics. Garber and Salama’s² observations reveal that the relationships between the teeth, lips and gingiva determine the esthetic appearance of an individual.

Enhancing a dynamic facial esthetics has been improved by leaps and bounds ever since the concept of the cosmetic use of botulinum toxin was discovered. In the facial esthetic front, it is the first choice to treat wrinkles, forehead creases, frown lines and crow’s feet at the corner of the eyes.^{2,3} With the promising results obtained since the past two decades in the facial esthetics, Botox is recognized by the dentists and introduced into clinical dentistry.³

History

Botulinum is derived from the Latin word botulus, meaning sausage. The use of Botulinum toxin as a therapeutic agent was first developed by a German physician – Justinus

Kerner (1786-1862). He called this toxin as a “sausage poison” as it was observed that the illness followed after consuming spoiled sausage. According to him, they did act by interrupting the signal transmission within the peripheral sympathetic nervous system.^[4]

In 1949, Burgen discovered that the toxin did block the neuromuscular transmission.

In 1989, Scott et al isolated 7 antigenically distinct toxins of the gram positive bacteria called Clostridium Botulinum which were lettered A through G.^[6,7] However, the toxin A was most extensively studied under two strains Type A and Type B. It was observed in monkeys that when the Type A strain was ingested, the toxin spreads to peripheral cholinergic nerve endings and blocks the release of acetylcholine. This strain was approved by the US Food and Drug Administration (FDA) in 1989 under the trade name – Botox (Allergan, Inc, Irvine, Calif) which was used for treating hemi facial spasm, strabismus and blepharospasm in young adults.^[4] In the year 2000, Botox was approved to treat cervical dystonia (wry neck) and in 2002 it obtained a green signal to treat severe frown lines between the eyebrows (glabellar lines). Type B by FDA is approved to treat cervical dystonia.^[1,3,4,5]

Since then, its benefits are recognized by the dentists and used in Dentistry. In 2005, Mario Polo used botox to treat the gummy smile which was caused by the hyper functional upper lip elevator muscles.^[3,4] According to

the Dental Quality Assurance Commission (DQAC) of Washington in 2013, Botox and dermal fillers can be used to treat functional or aesthetic dental conditions. In 2014, Michigan board of dentistry and New Jersey state board also approved the use of Botox and dermal fillers by general dentists.^[3]

Drug Pharmacology and Mechanism of Action

Botulinum toxin is synthesized by anaerobic spore forming bacilli – *Clostridium Botulinum*. The spores are heat resistant and germinate to produce toxin in an anaerobic condition, liquid medium, low acidity as found in some foods. The toxin is ingested and absorbed through the gastrointestinal tract into the systemic circulation.^[3]

At the neuromuscular junction, the Botox interrupts with the nerve transmission and inhibits the exocytosis of acetylcholine on cholinergic nerve endings of motor nerves.⁸ It thus prevents the vesicle where the acetylcholine is stored from binding to the membrane where the neurotransmitter can be released.^[9] Botulinum toxin achieves this effect by its endopeptidase activity against SNARE proteins which are required for the docking of the ACH vesicles to the presynaptic membrane and thus blocks the release of acetylcholine by the neuron. This effectively weakens the muscle for a period of 3 -4 months.^[9,10]

Commercially Available Products & Dosage:³ There are three forms of botulinum toxin type A (Botox, Dysport and Xeomin) and one form of botulinum toxin type B (MyoBloc) which are commercially available. Each vial of BOTOX contains:

1. 100 Units (U) of *Clostridium botulinum* type A neurotoxin complex.
2. 0.5mg of Albumin Human,
3. And 0.9 mg of sodium chloride in a sterile, vacuum-dried form without a preservative.

Is Botox injection safe???

The therapeutic margin (LD_{50}/ED_{50}) is in the order of 15:1 which means that the systemic toxicity of Botox does not occur until doses reach 15 times the effective therapeutic dose.^[11] Most of the side effects with Botox occurs due to the drifting of the drug into the adjacent sites, thus resulting in unwanted muscle weakness such as symmetrical smile or dry mouth and inability to swallow. The local injection sequelae include bruising, erythema and infection.^[11,12]

Botox Applications in Dentistry:

1. **Gummy Smile:** An excessive display of the maxillary gingiva while smiling can cause the “Gummy Smile” which is actually an esthetic concern for most of the patients. It is due to the hyperfunctional upper lip and

on smiling or over-contraction of the muscles of the upper lip and the condition can be embarrassing to the patient.¹ The appearance of the lip framework is determined by the activity of various facial muscles such as the levator labii superioris (LLS), levator labii superioris alaeque nasi (LLSAN), Zygomaticus major (ZMj) and minor muscles (ZMi), of which LLS, LLSAN and ZMi determine the amount of lip elevation during smiling.^[2]

Although correction of the upper lip morphology can be done surgically by LeFort I maxillary osteotomies, Rubinstein and Kostianovsky, Miskinyar, Rees and LaTrenta techniques, gingivectomy techniques, the use of Botox to correct the over-contraction of the upper lip^[3] is also implemented in dental practice to correct the problems associated with excessive gingival display.^[1,2,3]

Botox is injected in small, carefully titrated doses to limit the over-contraction of the upper lip. Hwang et al at the Yonsei University college of dentistry, Seoul, Korea proposed an injection point for botox and named it as the Yonsei point which is located at the centre of the triangle formed by LLS, LLSAN and ZMi.^[13]

Polo M. (2005)^[14] injected 0.25U of Botox injection in five patients with excessive gingival display due to hyperfunctional upper-lip elevator muscle. 0.25U of botox was injected per muscle bilaterally into LLS, LLSAN and at the overlap areas of LLS and ZMi muscles. The results were effective in all the patients with an increase in the length of the upper-lip on smiling averaging upto 124.2%. The effect did last upto 3-6 months with no reported adverse effects.^[14]

However, it should be noted that the effect is temporary and the injection should be repeated every 6 -12 months.^[2,3]

Freund B. (2014) ^[11] used dermal fillers along with botox injection in patients with gummy smile and observed esthetic and functional improvements. He also used this combination to manage smoker's lines which were obliterated by relaxing the orbicularis oris muscle.

2. **Dermal Fillers** - These are the filler products classified as permanent (PMMA, calcium hydroxyl appetite and e-PTFE) or non-permanent (collagen or hyaluronic acid) which are known to increase the volume of subcutaneous tissues. The hyaluronic acid incorporated products include Juvederm (Allergan) and Restylane (Medicis) which are viscous, easy to use, antigenically safe and can be dissolved after inadvertent injection with hyaluronidase.^[11]

3. **Facial Aesthetics:** Botox injection along with dermal fillers are also used to enhance facial aesthetics by increasing the volume around the mouth such as the nasolabial folds, marionette lines, creating smile lines and lip-line.^[11]
4. **Correction of lip deformity:** Botox along with dermal fillers are also used to correct lip deformities where there is sagging of the lip on one side. This is the most challenging esthetic problem for the dentist.^[3,11]
5. **Treatment of Black Triangles:** Dermal fillers are injected into the interdental papilla between the teeth or dental implants to increase the tissue volume by puffing up the tissue and close the black triangles.^[11] Daines SM and Williams EF. (2013)^[11,15] observed that the interdental soft tissue fillers along with Botox injection did fill up the black triangles and the effect did last for 3-4 months.^[15]
6. **Dental Implants:** Nishimura K. (1997)^[16] and Kayikvioglu A. (2003)^[17] observed that an increased pressure or loading on the muscles of mastication, did interfere with the osseointegration around the dental implants. According to the authors, injecting Botox Type A to the masticatory muscles can be therapeutically beneficial by allowing the dental implants to osseointegrate better.
7. **Oral Surgery:** Kayikvioglu group (2003)^[17] injected 100 U of botulinum toxin Type A as an adjunct to zygomatic fracture fixation surgery. He injected this Botox into the masseter muscle of the fractured site after which the patients were operated on 12 to 48 hour. EMG confirmed the muscle denervation. It was observed that the temporary paralysis of the masseter muscle did allow for fewer miniplate and microplate insertions in patients. They also noticed the benefits of adjunct botulinum toxin treatment for surgical reduction of mandibular and condylar bone fractures.
8. **Bruxism:** Van Zandijcke and Marchau (1990)^[18] injected 100 U of a botulinum toxin Type A injection into the masseter and temporalis muscle after which severe bruxism symptoms were reduced. Ivanhoe et al (1997)^[19] injected 200 U of botox injection into the masseter muscle and appreciated a therapeutic response after 19 weeks.
9. **Temporomandibular joint disorders;** Temporomandibular joint disorder (TMD) includes diseases affecting masticatory function which may be pathologic or due to masticatory muscle dysfunction, further manifesting in headache, facial pain, neck and peri-auricular pain, headache, TMJ sounds or decreased jaw excursion.³ However, majority

of TMD cases include a muscle spasm secondary to stress, bruxism or oromandibular dystonia.^[20] Although TMDs can be corrected with occlusal adjustments, restorations or intraoral appliances or surgeries, muscular relaxation with botox A injection could be a viable alternative as it produces the relaxation of the muscles of mastication thus reducing or eliminating the clenching reflex and thus provide relief to the muscle-centered TMDs.^[3] Freund and Schwartz (2000)^[21] injected Botox A injection into masseter and temporalis in pilots who had headache associated with muscle-centered TMDs and observed that there was a relief in symptoms for 2-4 months. According to the authors, the pain reduction was attributed to the Botox A injection which blocked the neurotransmitters (CGRP, NGF₁ and NP-Y) along with acetylcholine.^[21] This not only relieved the pain but also relaxed the temporalis muscle and reduced the headache induced by hyperactivity of temporalis muscle secondary to clenching.

10. **Oromandibular Dystonia:** This disease is characterized by involuntary muscle spasm and contractions that results in difficulty in swallowing, eating and speaking.^[3] Studies by Brin (1987)^[22], Hermanowicz (1991)^[23], Jankovic (1987)^[24] Tan (1999)^[25] and Laskawi (2001)^[26] have reported improvement of OMD, chewing and swallowing function on injecting Botox A into the masseter and submental complex.
11. **Mandibular Spasm:** This is a condition where there is semi-contraction of the mandibular muscle or spasm leading to restricted mouth opening further leading to restrictions on the dental and periodontal treatment procedures, and difficulty in eating.^[3] Studies by Erdal J. (1996)^[27] and Cersosimo MG. (2004)^[28] have noticed that Botulinum Toxin A injection into the masticatory musculature diminishes the effects of hyperfunctional or spastic muscles.
12. **Orthodontic considerations of Botox:** Orthodontic patients who are clencher, have excessive forces generated on the periodontium which leads to gingival recession and bone loss, along with TMDs. Freund B. and Schwartz M. (1999)^[29] used Botox Type A injection in orthodontic patients who had the habit of clenching, after which it was observed that there was a reduction in the orthodontic treatment time and patients were more comfortable while swallowing, eating and chewing. Botox can also prevent relapse of orthodontic treatment in patients with stronger mentalis muscle activity. It also reduces the intensity of the muscle post treatment and facilitating the muscle training to a more physiologic movement.^[30]

13. **Prosthetic considerations of Botox:** Botox is also used in patients with a new denture specially in cases of long history of edentulousness and a decreased vertical dimension.^[31]
14. **Toothache:** Botox toxin Type A can be used to rule out if the toothache is from the pulpal or muscular origin. Rao LB. (2011)^[32] explained that muscle pain from anterior temporalis is referred to the teeth. Thus use of Botox is both diagnostic as well as prophylactic.
15. **Sialorrhea:** Botox Type A blocks the release of acetylcholine at the cholinergic synapses at the autonomic nervous system and thus blocks the cholinergic parasympathetic secretomotor fibres of the salivary gland. Lim and Choi (2008)^[33] reported that Botox Type A injection is effective in the treatment of acute postparotidectomy salivary fistula, Gustatory sweating (Frey syndrome) and achalasia, mucocoeles and Ranula.
16. **Trigeminal Neuralgia:** Botox 25-75 U injected into the pericranial muscles blocks the nerve impulses that trigger contractions and relax the overactive muscles further relieving the pain.^[11] Elcio (2005)^[34] observed that the excruciating pain associated with inflammation of the trigeminal nerve of head and face was relieved by Botox injections.

Side Effects Of Botox Therapy:^[12]

1. Temporary side effects like fever, palpitations, tingling sensations and nausea which usually subside within 1-2 days.
2. Temporary partial weakness of the injected muscle
3. Muscle soreness for few days after injection
4. If Botox is injected for a long time, it may cause atrophy of the muscle injected which can be reversible if the Botox therapy is discontinued.
5. Edema around the injection site
6. Mild, localized and transient headache
7. Ecchymosis lasting 3 – 10 days
8. Numbness and parasthesia
9. Mild malaise and myalgias
10. Occasional vomiting

Contraindications:^[35]

1. Psychologically unpredictable patients who are unstable and have unrealistic expectations
2. Patients dependent on intact facial movements and expressions for their livelihood (Eg: actors, singers, musicians and media personalities)

3. Patients with neuromuscular disorder (Myasthenia gravis, Eaton-Lambert syndrome)
4. Patients allergic to any components of Botox Type A or Type B
5. Patients taking medications that interfere with neuromuscular impulse transmission and potentiate the effects of Botox like aminoglycosides, penicillamine, quinine and calcium blockers.
6. Pregnant or lactating mothers

Botox is a safe, non-surgical, reversible, minimally invasive treatment modality to achieve cosmetic results. In the recent past it is introduced into dentistry. Although Botulinum toxin A is used in the injectable form, it is used similarly as the administration of local anesthesia although training is absolutely necessary for dentists to administer the injection.^[1,4,11] At present, the Indian Academy of Facial Aesthetics (IAOFE) in conjunction with the American Academy of Facial Aesthetics (AAFE) is offering Botox and dermal fillers training course for dentists and physicians.^[3]

Botulinum toxin A is kept frozen at 2-4 degrees in a vial until it is ready to use. The drug is put into solution by adding 0.9% saline solution and used within four hours. Usually 26 and 30 gauge needle with a preferred syringe calibrated at 1.0mL tuberculin syringe is used. Before injecting, the needle is aspirated so as to avoid involuntary deposition of toxin into the facial arteries.^[3]

Botulinum toxin injection shows immediate results after a single appointment although the results last only upto 6-8 months (Grover S. 2014).^[36] The injection needs to be administered 2-3 times a year depending upon the declination of its effect. The therapeutic effects of Botox injection appear within 1st 3 days and reaches a peak within 1 – 4 weeks and later declines after 3 -4 months.^[1,11] This could be attributed to a study conducted by Patel D. et al (2013)^[1] in which it was observed that there was sprouting of new processes along the nerve axon and formation of multiple muscle synapses along with up-regulation of the muscle nicotinic receptors after 3 -4 weeks after a single injection of Botulinum toxin A in a mice model. The neuronal sprouts would further undergo regression and the original synaptic connection was restored with the restoration of the original neuromuscular junction. Therefore, Botulinum toxin injections need to be administered 2-3 times a year.^[1,36]

The injections are given in a span of every 3 months so as to minimize the risk of antibody formation to the protein, which would prevent Botox from working the subsequent time (Rao LB 2013).^[32]

However the major disadvantage of Botox Injection is the cost factor to a slightly higher level.

Conclusion

With the clinical uses of BOTOX as an adjunct therapy in the cases of bruxism, TMDs, facial pain, aesthetic dentistry cases as a minimally invasive alternative to surgically treating high lip-line cases, lip augmentataion, gummy smiles, periodontal cases and also for orthodontic cases to retrain the facial muscles, BOTOX is indeed an advancement in dentistry.^[2,3,4] Although it is still in its teething stages in India, it is persuading most of the practicing dentists to bring it into their clinical practice.

References

- 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):1-5.
- Vaghamsi M, Mahadevia S, Daruwala N and Krishnamurthy. “Botox”- A new vista, in the envelope of esthetic dentistry. The Journal of Ahmedabad Dental College and Hospital 2010; 1(1): 29-34.
- Nayyar P, Kumar P, Nayyar PV and Singh A. “Botox: Broadening the Horizon of Dentistry”. Journal of Clinical and Diagnostic Research 2014; 8(12): 25-29.
- Azam A, Manchanda S, Thotapalli S and Kotha SB. “Botox Therapy in Dentistry: A Review”. Journal of International Oral Health 2015; 7:103-105.
- Frank J. Erbguth. “From poison to remedy: the chequered history of botulinum toxin”. Journal of neural transmission 2008; 115: 559-65.
- Fenicia L, Franciosa G, Pourshaban M, Aureli P. “Intestinal toxemia botulism in two young people, caused by Clostridium butyricum type F”. Clin Infect Dis. 1999; 29: 1381-7.
- Harvey SM, Sturgeon J, Dassey DE. “Botulism due to Clostridium baratii type F toxin. J Clin. Microbiol. 2002; 40: 2260-2.
- Meunier FA, Schiavo G, Molgo J. “Botulinum neurotoxins: from paralysis to recovery of functional neuromuscular transmission”. J Physiol (Paris). 2002; 96 (1-2): 105-13.
- Aoki KR. “Evidence for antinociceptive activity of botulinum toxin type A in pain management”. Headache. 2003; 43: S9-15.
- Edwards, Michael (2006). “Anal fissure”. Dumas Ltd. Retrieved August 21, 2010.
- Freund B, Finkelstein I and Ko G. “Review of the applications of Botulinum Toxin and Tissue Fillers in Dental Practice”. 2015; 3: 1-16.
- Sinha A, Hurakadli M, Yadav P. Botox and derma fillers: The twin face of cosmetic dentistry. Int J Contemp Dent Med Rev 2015; 2015: Article ID: 131214. DOI:10.15713/ins.ijcdmr.27.
- Hwang et al. “Surface Anatomy of the lip elevator muscles for the treatment of gummy smile using botulinum toxin”. Angle Orthod. 2009; 79(1): 70-77.
- Polo M. “Botulinum toxin Type A in the treatment of excessive gingival display”. Am J Orthod Dentofacial Orthop. 2005; 127 (2): 214-18.
- Daines SM, Williams EF. “Complications associated with injectable soft-tissue fillers: a 5-year retrospective review”. JAMA Facial Plast Surg. 2013; 15: 226-31.
- Nishimura K, Itoh T, Takaki K. et al. “Periodontal parameters of osseointegrated dental implants: A four-year controlled follow-up study. Clin Oral Implants Res. 1997; 8: 272-78.
- Kayikvioglu A, Erk Y, Mavif E. et al. “Botulinum toxin in the treatment of zygomatic fractures”. Plast Reconstr Surg. 2003; 111: 341-46.
- Van Zandijcke M, Marchau MM. “Treatment of bruxism with botulinum toxin injections”. J Neurol Neurosurg Psychiatry. 1990; 53: 530.
- Ivanhoe CB, Lai JM, Francisco GE. “Bruxism after brain injury: Successful treatment with botulinum toxin-A”. Arch Phys Med Rehabil 1997; 78: 1272-3.
- Castenada R. Occlusion. In: Kaplan A, Assael L (eds): Temporomandibular Disorders. Philadelphia, Pa: Saunders, 1992.
- Freund B, Schwartz M, Symington JM. et al. “The use of botulinum toxin for the treatment of temporomandibular disorders: Preliminary findings”. J Oral Maxillofac Surg. 1999; 57: 916-21.
- Brin MF, Fahn S, Moskowitz C. et al. “Localized injections of botulinum toxin for the treatment of focal dystonia and hemifacial spasm”. Mov Disord. 1987; 2: 237-54.
- Hermanowicz N, Truong DD. “Treatment of oromandibular dystonia with botulinum toxin”. Laryngoscope. 1991; 101: 1216-18.
- Jankovic J, Orman J. “Botulinum toxin for cranial-cervical dystonia: a double-blind, placebo-controlled study”. Neurology. 1987; 27: 616-23.
- Tan EK, Jankovic J. “Botulinum toxin A in patients with oromandibular dystonia: Long-term follow-up”. Neurology. 1999; 53: 2102-07.
- Laskawi R, Rohrbach S. “Oromandibular Dystonia: Clinical forms, diagnosis and examples of therapy with botulinum toxin”. Laryngorhinootologie. 2001; 80: 708-13.
- Erdal J, Werdelin L, Prytz S. et al. “Experience with long-term botulinum toxin treatment of oromandibular dystonia, guided by quantitative EMG”. Acta Neurologica Scandinavica. 1996; 94: 210.
- Cersosimo MG, Bertoti A, Roca CU, et al. “Botulinum toxin in a case of hemimasticatory spasm with severe worsening during pregnancy”. Clin Neuropharmacol. 2004; 27: 6-8.
- Freund B, Schwartz M, Symington JM. “Botulinum Toxin: New treatment for temporomandibular disorders”. Br J Oral Maxillofac Surg 2000; 38: 466-71.

30. Glaros A, Tabacchi K, Glass EG. "Effect of parafunctional clenching on TMD pain and hearing loss". J Orofacial Pain. 1998;12:145-52.
31. Farias A, Sushma R and Varma M. "Botulinum Toxin: A Peek at a Wonder Drug for Dentistry". Sch. J. Dent. Sci. 2015; 2: 163-69.
32. Rao LB, Sangur R, Pradeep S. "Application of Botulinum toxin Type A: An arsenal in dentistry". Indian J Dent Res. 2011;22:440-45.
33. 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.
34. Elcio JP. "BOTOX injections relieve severe facial pain". Available from: <http://www.news-medical.net/news/2005/10/25/14010.aspx>. [last cited on 2009].
35. BOTOX. (Onabotulinum toxin A) Medication Guide: Initial U.S Approval, 1989.
36. Grover S, Malik V, Kaushik A, Diwakar R, Yadav P. "A future perspective of Botox in Dentofacial Region". J Pharm Biomed Sci. 2014; 04:525-31.

***Corresponding author:**

Pragathi R. Bhat, Department of Periodontics & Pedodontics, S.D.M. College of Dental Sciences & Hospital, Sattur, Dharwad-580009, Karnataka, India.

Phone: +91 836-2468142

Email: bhat.pragathi3@gmail.com

Financial or other Competing Interests: None.