Biomodelation of Gummy Smile with Botulinum Toxin: An overview

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Abstract: Gingival smile is a constant complaint and its treatment modalities vary from simple methods like use of botulinum toxin, to even complex ones as orthognathic surgery. In this era of passion to look beautiful, various new technologies are emerging to enhance and improve the physical appearance. Use of this toxin is emerging as a popular, cost-effective, and least invasive treatment option to improve facial anomalies. Botulinum toxin is a protein produced by the bacterium Clostridium botulinum, and is considered one of the most powerful neurotoxins ever discovered and is now marketed under the trade name of Botox. The use of Botox is now common and is provided by many dental practitioners as an adjunct to the range of cosmetic treatments they offer to the patients. In spite of few pit falls, weighing the amount of psychological benefit to the patient, it is quite a breakthrough in the field of cosmetic surgery in the treatment of gingival smiles. This article elaborates on the treatment of gummy smile through orofacial biomodelation with Botulinum toxin, which creates a shield in the canine fossa area, avoiding the exaggerated gingival display on smiling due to a wide action of the levator muscle of angle of mouth. (201 words)

Keywords: Botox, Botulinum toxin, gummy smile

Background: Botulinum toxin (BTX), also called a “miracle poison,” is a neurotoxin produced by the bacterium Clostridium botulinum. Justinus Kerner, a German physician and poet, first identified botulinum toxin between the years of 1817 and 1822. He described it as a “sausage poison” (sausage in Latin is botulus) and “fatty poison,” as this bacterium often caused poisoning by growing in improperly handled or prepared meat products. The toxin was first isolated in 1946 and a medical application for the substance was discovered in the 1950s. There are seven main serotypes of the neurotoxin that have been identified: A, B, C (1 and 2), D, E, F, and G. All seven serotypes are structurally similar but immunologically distinct in their potency, duration of action, and cellular target sites. They possess similar molecular weights and subunit structure, but have different amino acid sequences.

Humans can be affected by the toxins of five strains (A, B, E, F, and G) and are not affected by the toxins of strains C and D. When injected, the various preparations of BTX produce local, temporary, and reversible cholinergic chemonervation of muscles and glands. The property of the toxin that interferes with neural transmission and blocks the release of acetylcholine, causing muscle paralysis, plays an important role in the management of many cosmetic, medical, and dental conditions. Depending on the target tissue, BTX can block cholinergic neuromuscular innervations of intra- and extrafusal muscle fibers and cholinergic autonomic innervations of sweat, lacrimal and salivary glands, and smooth muscles. Thus, it acts as a versatile clinical tool for a growing list of conditions resulting from muscular hyperfunction. It gains its appeal as a cosmetic drug because it does not require general anesthesia or surgery. BTX is widely used in cosmetic applications for the treatment of facial wrinkles after local injection, but conditions such as cerebral palsy, muscular spasms, urinary incontinence, headaches, tinnitus, excessive sweating, cricopharyngeal achalasia, post-stroke spasticity, hemifacial spasms, temporomandibular joint disorders, bruxism, sialorrhea, neuropathic facial pain, muscle movement disorders (dystonias), masticatory myalgias, and facial nerve palsy could be treated with this drug.

In pedodontics and orthodontics, it can be used to treat developing gummy smiles, lip augmentation, and also for cases where retraining of the facial muscles is required. Many other indications are under investigation, and further applications for BTX are likely to be developed. Botulinum toxin in the dental office offers a reversible alternative to more aggressive procedures such as fullmouth reconstruction, orthodontics, and orthognathic surgery. Recently, BTX is reported to be clinically used in dental implantology for the prophylactic reduction of masseter and temporalis muscle strength after implantation in immediate load protocols.

In December 1989, BTX-A was approved by the U.S. Food and Drug Administration (FDA) under the trade name Botox (Allergan, Irvine, CA, USA) for the treatment of strabismus, blepharospasm, and hemifacial spasm in patients younger than 12 years old. In 2000, Botox was approved for treating cervical dystonia (wry neck) and two years later, on April 15, 2002, the FDA announced the approval of botulinum toxin type A to treat...
moderate-to-severe frown lines between the eyebrows (glabellar lines). Since then, BTX has been evaluated off-label for the treatment of spasticity and muscle pain disorders. Botulinum toxin type B (BTX-B) received FDA approval for treatment of cervical dystonia on December 21, 2000. Trade names for BTX-B are Myobloc in the United States and Neurobloc in the European Union. Serotype F is also under investigation in patients who are resistant to serotypes A and B.

At present, there are six different BTX preparations available commercially, out of which five contain BTX-A (Botox, Dysport, Xeomin, Prosigne, and PurTox) and the sixth contains BTX-B (Myobloc/Neurobloc). Botulinum toxin A is usually preferred because of its long duration of action and ease of production. Approval procedures are complex and vary between preparations and countries, but in general Botox has garnered the most approvals worldwide, followed by Dysport. Active research is underway on the possible uses of this toxin in several fields of medicine and dentistry. Though more extensive confirmation of its use in the dental profession is needed, it is evident that the potential of BTX in the dental profession can be of great value. Judicious use of BTX will ensure that it continues to be an important therapeutic option and improves the quality of life of patients.

What is Botox®?

Botox® is the trade name for the neurotoxin protein BTX type A produced by fermentation of anaerobic bacterium Clostridium botulinum. Type A is one of the seven distinct botulinum toxins produced by different strains of the bacterium. It is a stable, sterile, vacuum-dried powder sold in vials that is diluted with saline solution without preservatives for it to be injected.

BTX in dentistry

BTX is nowadays commonly used to treat:
1. Gummy smiles
2. Temporomandibular disorder (TMD),
3. Dental implants and surgery,
4. Masseteric hypertrophy,
5. Mandibular spasm,
6. Headache,
7. Migraine, and trigeminal neuralgia,
8. Myofacial pain and neck pain,
9. Bruxism and clenching cases,
10. Angular cheilitis,
11. Orthodontic relapse and depressed orthodontic appearance,
12. For reducing muscle hyperactivity for retention of removable prosthodontics

What is Gummy Smile?

When an excess of gingiva superior to the maxillary anterior teeth is displayed upon full smile, it is termed a gingival smile. The gingival smile is known by a variety of terms including — gummy smile, high lip line, short upper lip, and full denture smile. Perhaps this variety in terms is indicative of the many different causes of a gummy smile. The smile itself and the aesthetics of the smile are influenced by 3 components: teeth, gums, and lips. An attractive smile depends on the proper proportion and arrangement of these 3 elements. The upper lip should symmetrically expose up to 3 mm of the gum and the gum line must follow the contour of the upper lip. The exposure of more than 3 mm of the gum during the smile is known as gingival or gummy smile. For some patients, gummy smile represents an aesthetic disorder. Hulsey noted that the most attractive smiles were those in which the upper lip rested at the height of the gingival margin of the maxillary incisor.11

Tjan et al reported gender differences in the smile line. The low smile line is predominant (2.5:1) in men, whereas high smile lines are predominant in women (2:1). Gummy smiles range from mild, moderate, and advanced, to severe. Rosemarie Mazzuco et al., classified gummy smile into anterior, posterior, mixed, or asymmetric, based on the excessive contraction of muscles involved. Goldstein classified the smile line (consisting of the lower edge of the upper lip during the smile) according to the degree of exposure of the teeth and gums into 3 types: high, medium, or low.13

Etiology of gummy smile

Some people with excessive gingival display are self-conscious or embarrassed about it, and some are psychologically affected. Etiological factors involved in the formation of gummy smile can be:
1. Skeletal (vertical maxillary excess),
2. Gingival (passive eruption) or
3. Muscular (hyper functional upper lip)

Possible Causes of Gummy Smile development during Orthodontic Treatment:
1. Unexpressed Vertical Growth
2. Extrusive Forces
3. Anterior-Posterior Position of the Maxilla

Treatment options range from Le fort I osteotomy, crown lengthening, intrusion, myectomy to muscle resection etc.

BTX and Gummy smile:
BTX is indicated when the gummy smile is due to hyper function of upper lip elevator group of muscles (Fig 1):
1. Levatorlabiisuperioris (LLS)
2. Levatorlabiisuperiorisalaequenasii (LLSAN)
3. Zygomaticus major
4. Zygomaticus minor
5. Depressor septii

Storage and Preparation of commercially available BTX,

Botox is kept frozen (2–4 degree celsius) in a vial until it is ready to use. The drug is put into solution, following manufacturer’s guidelines, by adding normal saline (preservative-free 0.9% saline solution). During reconstitution, the rubber seal on the vial should be wiped with an alcohol swab before pricking. Rotating the vial during injection also assists a gentle reconstitution. Botox® should be reconstituted after any transport/journey. Agitation during transport may denature the toxin and greatly reduces its duration of action. Each vial of Botox® contains 100 unit of BTX-A toxin. According to manufacturer’s recommendations, a dose of 2.5 U/0.1 ml is prepared by adding 4.0 ml normal saline solution to 100 units of vacuum-dried Clostridium botulinum toxin type-A. Once prepared it should be used within 4 hours. Reconstituted Botox® should be clear, colorless and free of particulate matter. The preferred syringe is a calibrated 1.0-ml tuberculin syringe, and the needle selected for injection usually is between 26 and 30 gauge. Skin preparation involves alcohol wipes and dry sterile gauze sponges. Aspiration before injection is recommended. Usually, dosing is established by the diagnosis and reason for use of the toxin, size of the muscle, and medical conditions or medications. Until studies narrow down all specifics, the final dilution and dosage used is left to the clinical experience and discretion of the practitioner. The number of injection sites usually is determined by the size of the muscle.

Theoretically, it may be appropriate to inject more sites with smaller doses, and using more injection sites should facilitate a wider distribution of BTX to nerve terminals; however, too many injection sites may cause local injection site pain. The proper targeting of muscles is an crucial factor in achieving efficacy and reducing adverse effects from BTX-A injections. Its therapeutic effects first appear in 1 to 3 days, peak in 1 to 4 weeks, and decline after 3 to 6 months.

### Titratin:

<table>
<thead>
<tr>
<th>Diluents added (0.9% NaCl)</th>
<th>Resulting dose: Units per 0.1ml</th>
</tr>
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<tbody>
<tr>
<td>1 ml</td>
<td>10 Units</td>
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<tr>
<td>2 ml</td>
<td>5 Units</td>
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<tr>
<td>4ml</td>
<td>2.5 Units</td>
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<td>8ml</td>
<td>1.25 Units</td>
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### Injection technique:
1. **Conventional Technique:**
   Mario Polo has advocated 2.5 units of BTX-A is injected under sterile conditions at 4 sites, 2 one each side of the face. The needles are inserted at the overlapping points of (Fig. 2 & Fig. 3):
   I. Levator labii superior islaeque nasi and levator labii superioris muscles;
   II. Levator labii superiors and zygomaticus minor muscles
- On each side of the face. The injection sites were determined by muscleanimation (smiling) and palpation on contraction to ensure precise muscle location before injection. A skin marker was used to mark the injection points to reduce the risk of asymmetry.

**Reference points used for measurements:**

A. Lowest margin of upper lip perpendicular and superior to the midportion of maxillary central gingival margin.
B. The maxillary central incisors gingival margin at its midpoint.
C. The midpoint of the incisal edge of the maxillary central incisor.

**Fig2.** Overlapping area of levatorLabiisuperiorisalaequenasi and levatorlabiisuperioris

**Fig3.** Overlapping area of levatorLabiisuperioris and Zygomaticus minor

2. **Yonsei point**[17]:

Hwang et al at Yonsei university college ofdentistry, Seoul, Korea have proposed a single injection point for BTX-A and named it as Yonsei point. A dose of 3U is recommended at each injection site. It is basically a point located at the centre oftriangle (**Fig.4**) formed by levatorlabiisuperioris,levatorlabiisuperiorisalaequenasi andzygomaticus minor. If applied in small, carefully titrated doses, these muscles can be proportionately weakened with BTX, which will reduce exposure of the upper gums when smiling.

**Fig4.** Photograph indicating Yonsei point for the single injection technique

**Followup:**

Effect of BTX is seen within 5-10 days and lasts about 6 months, with a range of 4 to 8 months, at which time the patient can return to repeat the process. It is important not to give injections prematurely (before the effects of the treatment have worn off), as this can result in a buildup of antibodies to BTX that would dilute the effect of further treatments.

**Mechanism of Action**[18]

BTX decreases muscle activity by blocking overactive nerve impulses that trigger excessive muscle contractions or glandular activity:

1. **Phase I.**

   **Nerve-Muscle Communication is blocked:**

   BTX blocks the transmission of overactive nerve impulses to the targeted muscle by selectively preventing the release of the neurotransmitter acetylcholine (ACh) at the neuromuscular junction, temporarily preventing muscle contraction. This is primarily a local effect. BTX may also prevent the release of pain-stimulating neuropeptides in peripheral nerves.

   **A) Binding:**

   The heavy chain portion of the active ingredient in BTX binds to the cell membrane of the motor nerve via an unidentified high-affinity “acceptor” molecule. This high-affinity binding action allows for efficient uptake of BTX by the motor nerve and facilitates selective, targeted treatment at the injection site.

   **B) Internalizing:**

   After binding, the BTX protein molecule passes through the cell membrane of the motor nerve and into its cytoplasm via a process called endocytosis. It is here that the enzymatic component (light chain) of the BTX protein molecule is activated.

   **C) Blocking:**

   Inside the motor nerve, the light chain of the BTX protein molecule cleaves apart a protein (called SNAP25) that enables vesicles which store the neurotransmitter acetylcholine to attach to the cell membrane. Cleaving SNAP25 prevents these vesicles from fusing with the membrane and prevents the release of acetylcholine into the neuromuscular junction (the space between the motor nerve and the muscle). Thus, nerve impulses that control muscle contractions are blocked, decreasing muscle activity. Cleaving SNAP25 also blocks release of neuropeptides involved in the transmission of painful sensations (including substance P, glutamate and calcitonin gene-related peptide, or CGRP), theoretically reducing pain sensitization of peripheral nerves. This may be how BTX reduces the neck pain associated with cervical dystonia, although the exact mechanism of action is unknown.
2. Phase II.

Nerve-Muscle Communication is restored
The effect of BTX is generally temporary. Previous nerve impulse activity and associated muscle contractions resume over the course of a few to several months, depending on the individual patient and the indication for which they are being treated.

A) Nerve Sprouting:
New nerve endings sprout and connect to the muscle after the original nerve ending is blocked, renewing the ability of the nerve to cause muscle contractions.

B) Original Nerve Connection Reestablished:
Eventually, the new nerve sprouts retract and the original nerve ending regains its function, suggesting that treatment with BTX does not permanently alter the neuromuscular junction.

Advantages of BTX
1. Psychological benefit to the patient
2. Minimally invasive

Disadvantages of BTX
1. Short term effect
2. Asymmetrical/unnatural appearance of smile sometimes due to improper injection technique
3. Cost factor

Complications of BTX therapy:
As previously noted, there are a number of complications associated with the use of BTX. These complications may include the following:
1. Mild pain with injection.
2. Local edema.
3. Erythema.
4. Transient numbness.
5. Mild nausea.
6. Transient headache.
7. Production of neutralizing (IgG) antibodies against Btx-A (in injections over 200U given at once or repeated injections within one month of treatment session).
10. Local spread, causing unwanted paralysis of nearby muscles.
11. Flu-like symptoms.
12. Development of tolerance.

Contraindications of BTX therapy:
1. During pregnancy or while breast feeding
2. Presence of inflammation or infection at the site of proposed injection
3. Anyone with known hypersensitivity or allergies to human albumin, BTX, or saline solution.
4. Anyone with known motor neuropathy, neuromuscular disorders such as myasthenia gravis, Lambert-Eaton Syndrome, muscular dystrophy, multiple sclerosis etc.
5. Anyone taking Aminoglycoside antibiotics because aminoglycosides may interfere with neuromuscular transmission and potentiate the effect of BTX therapy.
6. Anyone taking Calcium Channel Blockers.
7. It will be important for the patient to avoid taking aspirin or related products, such as ibuprofen (e.g., Advil) or naproxen if possible after the procedure to keep bruising to a minimum.

If there is an accidental overdose, an antitoxin is available that will neutralize the toxin, if given within a few hours of the overdose. Also, BTX is contraindicated for people with diseases that affect neuromuscular transmission, such as myasthenia gravis and women who are pregnant or nursing.
Administration of BTX by dentists: The Indian Scenario:

We performed a pubmed/medline search and reviewed 20 Indian case reports and review articles. We found that still there is no published guideline/protocol by any dental authority/association on administering BTX by a dentist in India till date. But certain Indian case reports [20, 21] have reported administration of BTX in a dental setup, but all the administrations were done by dermatologists who were licensed in administration of BTX.

3. Conclusion

BTX is no doubt is emerging as an attractivetreatment option in comparison to surgicalalternatives. However is much more is stillto be discovered to allow its routine use in dentalclinics for various problems. There are still many dental conditions which require FDA approval to be treated by BTX. The use of BTX is minimal invasive and will surely take dental profession to one step ahead in the field of progress.

References:


Fig 1: upper lip elevator group of muscles

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Fig 2. Overlapping area of levator labiisuperioris alaeque nasali and levator labiisuperioris

Fig 3. Overlapping area of levator labiisuperioris and Zygomaticus minor

Fig 4. Photograph indicating Yonsei point for the single injection technique