Review Article

# Botox: In Orthodontics

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## Abstract

Botulinum toxin type A (BTX-A) (Botox, Allergan, Irvine, CA, USA) has been studied since the late 1970s for the treatment of several conditions associated with excessive muscle contraction. Smile esthetics has become a major concern among patients and orthodontists. This article describes the efficient, nonsurgical, and less invasive use of BTX-A injection for the correction of a gummy smile in orthodontics.

**Key words:** Botulinum toxin, gummy smile, orthodontics

## Introduction

As society becomes more esthetically conscious orthodontists are more challenged to produce not only outstanding occlusions but also outstanding esthetics. Every minute, detail is becoming more important in separating the good from the great orthodontist. Recent studies have indicated that the amount of gingival display on smiling is very important to smile attractiveness.[1] In fact, Van der Geld *et al*. found that the amount of gingival display was an important characteristic in a person's own satisfaction with their smile.[2]

The display of excessive gingival tissue in the maxilla upon smiling, or "gummy smile," is both an oral hygiene and cosmetic issue with no simple remedy. Excessive gum exposure is frequently attributable to over-contraction of the upper lip muscles, particularly the levator labii superioris alaeque nasi. Although several surgical techniques have been reported in the literature for the correction of hyperfunctional upper lip elevator muscles, such as the Rubenstein and Kostianovsky,[3] Miskinyar,[4] and Rees and LaTrenta[5] techniques, they are not routinely used to treat a gummy smile.[6] In general, the most common surgical corrections currently used are the LeFort I maxillary osteotomies with impaction for skeletal vertical maxillary excess, and gingivectomies for delayed passive dental eruption with excessive gingival display.[6,7]

Some patients do not wish to go through the long presurgical orthodontic treatment in preparation for a LeFort I osteotomy. Others wish to avoid the possible complications surrounding surgery such as postoperative pain, swelling and infection, permanent or temporary nerve damage, root damage during osteotomy, surgical or orthodontic relapse, possible need for blood transfusion, and finally a less than optimal occlusal outcome.

A nonsurgical alternative for reducing excessive gingival display caused by muscle hyperfunction would be advantageous. Botulinum toxin (BTX) has been under the clinical investigation since the late 1970s for the treatment of several conditions associated with excessive muscle contraction or pain.[8] Furthermore, it is the first-choice treatment for wrinkles located on the upper third of the face, BTX is also widely used in the prevention and correction of changes caused by muscle contraction in the middle and lower thirds of the face and neck, including a gummy smile.

## Botulinum Toxin

BTX, a natural protein, is one of the most potent biological substances known. The toxin inhibits the release of acetylcholine (ACH), a neurotransmitter responsible for the activation of

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muscle contraction and glandular secretion. Administration of the toxin results in a reduction of tone in the injected muscle. Some nerve terminals are not affected by the toxin, allowing the injected dystonic muscle to contract, but with less force. This weakness allows for improved posture and function of the hypertonic muscle. The degree of weakening depends on the dose, and the duration of weakness is further dependent on the serotype of BTX employed.

The seven distinct serotypes, A, B, C, D, E, F, and G, differ in their potency, duration of action, and cellular target sites.[9,10] BTX-A is marketed worldwide under the name Botox® (Allergan Inc., Irvine, CA, USA) and in Europe as Dysport® (Speywood Pharmaceuticals Ltd., Maidenhead, UK). Botox® has been approved by the US Food and Drug Administration (FDA) for the treatment of strabismus, blepharospasm,[11] focal spasms, including hemifacial spasm,[12] cosmetically for the facial glabellar lines,[13] and more recently for the treatment of cervical dystonia[14] and axillary hyperhydrosis. BTX-B has been approved by the FDA for the treatment of cervical dystonia and will be marketed under the name Myobloc® in the US and Neurobloc® in Europe (Solstice Neurosciences Inc., South San Francisco, CA, USA).

## Structure

BTX is synthesized as a large single-chain peptide. Activation requires a two-step modification in the tertiary structure of the protein. This process converts the single-chain neurotoxin to a di-chain neurotoxin comprising a 100,000-Da heavy chain (HC) linked by a disulfide bond to a 50,000-Da light chain (LC). BTX acts at the neuromuscular junction where it exerts its effect by inhibiting the release of ACH from the presynaptic nerve terminal. ACH is contained in vesicles, and several proteins (vesicle-associated membrane protein [VAMP], synaptosomal-associated protein 25 kDA [SNAP-25], and syntaxin) are required to release these vesicles through the axon terminal membrane. BTX binds to the presynaptic terminal via the HC. The toxin is then internalized, and the HC and LC are separated. The LC from BTX-A cleaves SNAP-25, the LCs from serotypes B and F cleave VAMP, and from serotype C cleaves syntaxin.[15] This disrupts ACH release and subsequent neuromuscular transmission resulting in weakness of the injected muscle.

## Potency

The potency of BTX is expressed as mouse units, with 1 mouse unit equivalent to the median lethal dose (LD 50) for mice. Botox® is dispensed in small vials containing 100 U, while a vial of Dysport® contains 500 U. The relative potency of Botox® units to Dysport® units is approximately 1:4.

The lethal dose of Botox® in humans is not known, although it has been estimated to be about 3000 U. The usual maximum total recommended dose at an injection session in the dental office is about 80-100 U. This means that the injector will have to inject 30 vials before a potentially lethal outcome. There is such a huge disproportion between the clinical dose and the lethal dose that a fatal overdose is almost impossible.

## Preparation

The toxin is produced by the gram-negative anaerobic bacterium *Clostridium botulinum*. It is harvested from a culture medium after fermentation of a toxin-producing strain of *C. botulinum*, which lyses and liberates the toxin into the culture. The toxin is then extracted, precipitated, purified, and finally crystallized with ammonium sulfate. In this form, BTX-A should be stored in a refrigerator but not frozen. BTX-A should be diluted with preservative-free saline and the preparation used within 4 h of reconstitution. Conditions for the stability of the toxin in solution include pH 4.2-6.8 and temperature <20°C. The large molecule is very fragile and is inactivated easily in solution by shaking.

## Injection Site for Gummy Smile: Yonsei Point

BTX should be injected in small, carefully titrated doses to limit muscular over-contraction of the upper lip, thus reducing exposure of the upper gums when smiling. Hwang *et al*., at Yonsei University College of Dentistry, Seoul, Korea have proposed an injection point for BTX and named it as Yonsei point.[16] It is basically a point located at the center of the triangle formed by levator labii superioris, levator labii superioris alaeque nasi, and zygomaticus minor. A dose of 3 U is recommended at each injection site. If applied in small, carefully titrated doses, these muscles can be proportionately weakened with Botox, which will reduce exposure of the upper gums when smiling.

## Contraindication

Patients should not be treated or treated with extreme caution who are:

1. Psychologically unstable or who have questionable motives and unrealistic expectations.
2. Dependent on intact facial movements and expressions for their livelihood (e.g. actors, singers, musicians, and other media personalities).
3. Afflicted with a neuromuscular disorder (e.g. myasthenia gravis and Eaton-Lambert syndrome).
4. Allergic to any of the components of BTX-A or BTX-B (i.e., BTX, human albumin, saline, lactose, and sodium succinate).
5. Taking certain medications that can interfere with neuromuscular impulse transmission and potentiate the effects of BTX (e.g. aminoglycosides, penicillamine, quinine, and calcium blockers).
6. Pregnant or lactating (BTXs are classified as pregnancy category C drugs).[17]

## Complications

Local effects of BTX are generally transient. Hypersensitivity reactions have not been described. At present, no long-term

complications of Botox therapy have been identified.[18] Some short-term, unwanted side effects are a pain, bruising, weakness of adjacent muscles, ptosis, delayed eyelid closure, decreased blink response, excessive tearing, asymmetry of the face, headache, antibody development, and necrotizing fasciitis.[19]

## Discussion

According to Sarver, a slight amount of gingival exposure is acceptable and that contrary to posed smile, an unposed smile is natural in that it expresses authentic human emotion.[20] The best orthodontically treated subjects may not be satisfied by the treatment if soft tissue problem is not corrected. Botox is indicated when the gummy smile is due to hyperfunctional upper lip elevator muscles (muscular capacity to raise the upper lip is higher than average), and Botox is an excellent nonsurgical alternative. Botox is a conservative, safe, minimally invasive treatment modality to achieve enhancing esthetic results. The procedure is to be performed by a dermatologist who is also a Botox certified physician. BTX-A was diluted according to the manufacturer's recommendations to provide 2.5 units per 0.1 ml by adding 4.0 ml normal saline solution to 100 units of vacuum-dried clostridium BTX-A.[21]

Training is absolutely necessary for dentists to administer injections, but the learning curve is very short because dentists can already achieve profound anesthesia in the orofacial region, thus making patient more comfortable and at ease.

Polo[6] conducted a study on 30 patients received BTX-A injections to reduce excessive gingival display. Patients were followed at 2, 4, 8, 12, 16, 20, and 24 weeks postinjection, with changes documented by photographs and videos. At week 2, the patients rated and evaluated with the effects of BTX-A. The result stated that BTX-A injections for the neuromuscular correction of gummy smiles caused by hyperfunctional upper lip elevator muscles were effective and statistically superior to baseline smiles, although the effect is transitory.

Sandler *et al*.[22] treated a female patient of age 35 with a gummy smile, and the result showed that the BTX-A injections for the neuromuscular correction of gummy smiles caused by hyperfunctional upper lip elevator muscles were effective minimally invasive and temporary treatment outcome.

Patel *et al*.[23] conducted a study on 60 subjects age from 18 to 23 years with excessive gingival display due to hyperfunctional upper lip elevator muscles were treated with BTX-A injections, and the patients were evaluated clinically evaluated after 3 days, 7 days, 14 days, 1.5 months, 2.5 months, 4.5 months, and 6 months. The study concluded that the treatment modality was effective, producing esthetically acceptable smiles in these patients, and the improvements lasted 3-6 months.

Amin *et al*.[7] reported a case in which the patient with excessive gingival display was treated with BTX-A injection, and it was concluded that the use of Botox is conservative treatment in a patient with short upper lip and gummy smile. However, the improvement is temporary and must be repeated every 6 months to 1 year.

Hyperfunction of the upper lip elevators muscles (levator labii superioris, alaeque nasi, levator anguli oris, and the zygomaticus muscle) can all play a major etiological role in a gummy smile. Thus, concise evaluation of etiology, diagnosis, and implementation of treatment plan had an important role in treatment outcome. The ability of BTX-A to produce muscle paralysis by chemodenervation has been utilized to treat the patient with hyperactive upper lips. The only disadvantage is that treatment with Botox is not a permanent option, unlike other surgical alternatives. The effect of this treatment is for short-term usually for 6 months, and the patient has to get it redone after that. It is important to note that injection of Botox should not be given prematurely before the effect of earlier treatment has worn off completely as this can result in buildup of antibodies to Botox that will dilute the effect of further treatments. Moreover, the treatment might sometimes produce asymmetrical results due to injection at wrong site or by an inexperienced clinician, and the cost is also high for such a treatment.[24]

## Conclusion

Injection with BTX-A provides effective, minimally invasive, temporary improvement of gummy smiles for patients with hyperfunctional upper lip elevator muscles.

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### Conflicts of interest

There are no conflicts of interest.

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