Botox: Buy Me Beauty!

Jyothi Kiran Hurkadle, Archana Jatania, Ravi Shanthraj, Bhagya Lakshmi, Pradeep Subbiah, Shiva Linga

ABSTRACT

‘Beauty lies in the eyes of the beholder’. Beauty has been admired since time immemorial not only by the medical personals but also by the general masses. Beauty undoubtedly has a strong influence on human life. Orthodontists have a special interest in facial beauty. One of the most socially significant of human behaviors is expression of emotions on the face with smile being the most important of those emotions. The display of excessive gingival tissue in the maxilla upon smiling has been called a ‘gummy smile’, a condition some consider esthetically displeasing. Some people with excessive gingival display are self-conscious or embarrassed about it, and some are psychologically affected. There are a number of different treatment methods described in the literature for the treatment of gummy smile. These includes both surgical and nonsurgical options, including Le Fort I osteotomy, crown lengthening procedure, maxillary incisor intrusion, self-curing silicone implant injected at the anterior nasal spine and finally myectomy and partial resection of the levator labii superioris or muscle repositioning. Some patients do not wish to go through the long presurgical orthodontic treatment in preparation for a Le Fort I osteotomy while others wish to avoid the possible complications surrounding surgery, such as post-operative pain, swelling and infection, permanent or temporary nerve damage and root damage during osteotomy. A nonsurgical alternative for reducing excessive gingival display caused by muscle hyperfunction would be advantageous. Botulinum toxin has been under clinical investigation since the late 1970s for the treatment of several conditions associated with excessive muscle contraction or pain. The aim of this article is to give an overview about the science of Botox and its various uses.

Keywords: Beauty, Gummy smile, Botulinum toxin.


Source of support: Nil

Conflict of Interest: None

INTRODUCTION

The writer Margaret Wolfe Hungerford (1878) famously said ‘Beauty lies in the eyes of the beholder’.

Beauty has been admired since time immemorial not only by the medical personals but also by the general masses, but the quantification of beauty is always subjective because beauty is interpreted not just on esthetic values but also on the taste the quantification of beauty is always subjective because beauty is interpreted not just on esthetic values but also on the taste the quantification of beauty is always subjective because beauty is interpreted not just on esthetic values but also on the taste of an individual.1 Perceptions of facial beauty are multifactorial, with genetic, environmental and cultural foundations.2 Beauty can be defined as a combination of qualities that give pleasure to the senses or to the mind. Esthetics is the study of beauty and, to a lesser extent, its opposite, the ugly.

The term esthetics, derives from the German ästhetisch or the French esthétique, both derived from the Greek aesthetikos ‘esthetic-sensitive-sentient’. Esthetics as perceived generally is not just the ability to discriminate at a sensory level. It goes beyond the sensory level. As delicacy of taste is not merely ‘the ability to detect all the ingredients in a composition’, the judgment of beauty is based on sensory, emotional and intellectual all at once.

Beauty undoubtedly has a strong influence on human life. According to Shakespeare, ‘Beauty itself doth of itself persuade the eyes of men without an orator.’ The philosopher Pascal commented, ‘Had Cleopatra’s nose been shorter, the whole face of the world would have changed!’ From Homer’s Helen of Troy, whom the poet Christopher Marlowe described as having a ‘face that launched a thousand ships’, to Queen Nefertiti, whose name literally means the ‘Perfect One’, to modern models and actors, facial beauty has always been the most valued aspect of human beauty.

Orthodontists have a special interest in facial beauty as Wahl3 wrote, ‘Now it appears that facial esthetics is again in the forefront as we realize why patients come to us in the first place’. One of the most socially significant of human behaviors is expression of emotions on the face with smile being the most important of those emotions. ‘The smile is the most recognizable signal in the world. Smiles are such an important part of communication that we see them far more clearly than any other expression. We can pick up a smile at 300 feet – the length of a football field’.4 Just as a nice smile can act as a powerful communication tool, an unpleasing smile can have the equally powerful negative impact and this is often one of the reasons why patients seek orthodontic treatment. The display of excessive gingival tissue in the maxilla upon smiling has been called a ‘gummy smile’, a condition some consider esthetically displeasing. Some people with excessive gingival display are self-conscious or embarrassed about it, and some are psychologically affected. Etiologic factors can be skeletal, gingival, muscular, iatrogenic or some combination of these. The literature contains many reports that address the skeletal problem of vertical maxillary excess5-8 and gingival problems related to delayed passive eruption.9,10 The muscular capacity to raise the upper lip higher than average (hyperfunctional muscle) can cause excessive gingival display.11 Upper lip elevator muscles include the levator labii superioris, levator labii superioris alaque nasi, levator anguli oris, zygomaticus major, zygomaticus minor and the depressor septi nasi. There
are a number of different treatment methods described in the literature for the treatment of gummy smile. These includes both surgical and nonsurgical options including; Le Fort I osteotomy, crown lengthening procedure, maxillary incisor intrusion, self-curing silicone implant injected at the anterior nasal spine and finally myectomy and partial resection of the levator labii superioris or muscle repositioning. Some patients do not wish to go through the long presurgical orthodontic treatment in preparation for a Le Fort 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 and/or orthodontic relapse, possible need for blood transfusion and finally a less than optimal occlusal outcome.12,13

A nonsurgical alternative for reducing excessive gingival display caused by muscle hyperfunction would be advantageous. Botulinum toxin has been under clinical investigation since the late 1970s for the treatment of several conditions associated with excessive muscle contraction or pain.14

The aim of this article is to give an overview about the science of Botox and its various uses.

**A Brief History of Turning Back Time with Botulinum Toxins**

Botulinum toxins have formed the foundation of minimally invasive esthetic facial treatments, beginning with their use to smooth glabellar frown lines and expanding to include other facial areas as well as combination use with other minimally invasive agents and procedures.

The observation that botulinum toxin smoothed facial lines when used therapeutically led researchers to study the toxin’s effect on glabellar frown lines. In 1992, the first published esthetic study on botulinum toxin established that botulinum toxin type A safely and effectively diminished the appearance of glabellar lines.15 Additionally, large scale, randomized, controlled trials documented safety and efficacy, leading to the approval by the United States Food and Drug Administration (FDA) of the first botulinum toxin for cosmetic use in 2002.16 It was used in 2005 on patients with hyperfunctional upper lip elevator musculature to correct a gummy smile and to establish the optimal minimal dose of BTX-A needed to obtain cosmetically pleasing results.17

**The Science of Botulinum Toxins: Composition and Pharmacology**

Botulinum toxins occur in seven known serotypes labeled A-G produced by different strains of *Clostridium botulinum*.18 Clinically important biologic activity, particularly in the cosmetic arena, is limited primarily to the type A serotype, although a type B formulation is approved in several countries for treating cervical dystonia. Although botulinum toxin type B has been studied for cosmetic use, it generally elicits more pain upon injection and has been found to have a faster onset but shorter duration of action than the type A serotype.19,20 Therefore, this review will be restricted to products containing botulinum toxin type A. Botox (Allergan, Irvine, Calif) is a purified BTX-A isolated from the fermentation of *C. botulinum*. It is a stable, sterile, vacuum-dried powder that is diluted with saline solution without preservatives. BTX-A weakens skeletal muscles by cleaving the synaptosome-associated protein SNAP-25, thus blocking the release of acetylcholine from the motoneuron and enabling the repolarization of the postsynaptic terminal. As a result, the muscular contraction is blocked. The production of acetylcholine is not affected by this blockade of the neuromuscular transmission. The effects last 3 to 6 months, although some investigators have reported a longer duration in patients exposed over a prolonged period of time.

**Pharmacokinetics**

Botulinum toxin type A is not expected to be present in the peripheral blood at measurable levels following intramuscular injection at the recommended doses. The recommended quantities of neurotoxin administered at each treatment session are not expected to result in systemic, overt distant clinical effects, i.e. muscle weakness, in patients without other neuromuscular dysfunction. However, subclinical systemic effects have been shown by single-fiber electromyography after intramuscular doses of botulinum toxins appropriate to produce clinically observable local muscle weakness.

**Uses**

BTX-A has been used to treat strabismus,21 (visual problem in which the eyes are not aligned properly and points in different directions. Botox is thought to affect muscle pairs inducing an atropic lengthening of the injected muscle and a corresponding shortening of the muscle antagonist) cervical dystonia,22 blepharospasm and hemifacial spasm,23 hyperfunctional larynx,24 juvenile cerebral palsy,25 spasticity,26 pain and headache,27 occupational dystonia and writer’s cramp,28 temporomandibular disorders,29 myofacial pain,30 and oromandibular dystonia and bruxism,31 and gummy smile.

**Contraindications**

Botox is contraindicated in the presence of infection at the proposed injection site(s) and in individuals with known hypersensitivity to any ingredient in the formulation.
Precautions

The safe and effective use of Botox depends upon proper storage of the product, selection of the correct dose, and proper reconstitution and administration techniques. An understanding of standard electromyographic techniques is also required for treatment of strabismus and may be useful for the treatment of cervical dystonia.

Caution should be used when botox treatment is used in the presence of inflammation at the proposed injection site(s) or when excessive weakness or atrophy is present in the target muscle(s).

Drug Interactions

Coadministration of Botox and aminoglycosides or other agents interfering with neuromuscular transmission (e.g., curare-like compounds) should only be performed with caution as the effect of the toxin may be potentiated.

The effect of administering different botulinum neurotoxin serotypes at the same time or within several months of each other is unknown.

Excessive neuromuscular weakness may be exacerbated by administration of another botulinum toxin prior to the resolution of the effects of a previously administered botulinum toxin.

Pregnancy: Pregnancy Category C

When pregnant mice and rats were injected intramuscularly during the period of organogenesis, the developmental NOEL (No-observed-effect-level) of botox was 4 U/kg. Higher doses (8 or 16 U/kg) were associated with reductions in fetal body weights and/or delayed ossification which may be reversible.

In a range finding study in rabbits, daily injection of 0.125 U/kg/day (days 6 to 18 of gestation) and 2 U/kg (days 6 and 13 of gestation) produced severe maternal toxicity, abortions and/or fetal malformations. Higher doses resulted in death of the dams. The rabbit appears to be a very sensitive species to Botox.

There are no adequate and well-controlled studies of Botox in pregnant women. Because animal reproductive studies are not always predictive of human response, Botox should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential risks, including abortion or fetal malformations which have been observed in rabbits.

Carcinogenesis, mutagenesis, impairment of fertility: Long-term studies in animals have not been performed to evaluate carcinogenic potential of Botox.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when botox is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in children below the age of 12 have not been established.

Geriatric Use

Clinical studies of botox did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function and of concomitant disease or other drug therapy.

Adverse Reactions

Skin rash (including erythema multiforme, urticaria and psoriasiform eruption), pruritus and allergic reaction. In general, adverse events occur within the first week following injection of Botox while generally transient may have a duration of several months. Localized pain, tenderness and/or bruising may be associated with the injection. Local weakness of the injected muscle(s) represents the expected pharmacological action of botulinum toxin. However, weakness of adjacent muscles may also occur due to spread of toxin.

Immunogenicity

Formation of neutralizing antibodies to botulinum toxin type A may reduce the effectiveness of Botox treatment by inactivating the biological activity of the toxin. The rate of formation of neutralizing antibodies in patients receiving Botox has not been well studied.

Dosage and Administration

Botox is supplied in a single use vial. Because the product and diluent do not contain a preservative, once opened and reconstituted, store in a refrigerator and use within 4 hours. Any remaining solution has to be discarded. Do not freeze reconstituted Botox.

Botox is to be reconstituted with sterile, nonpreserved saline prior to intramuscular injection.
Vial Size

There are two sizes of vials available in India, 100 and 50 units. The former contains 100 units (U) of Clostridium botulinum toxin type A, 0.9 mg of sodium chloride in a sterile, 0.5 mg of human serum albumin, in vacuum-dried form without a preservative.

Reconstitution

To reconstitute vacuum-dried Botox® (Botulinum toxin type A), use sterile normal saline without a preservative; 0.9% sodium chloride Injection is the recommended diluent. For a 100 unit pack, use 2.5 ml of saline so that each 0.1 ml contains 1 unit of Botox®. Draw up the proper amount of diluent in the appropriate size syringe. Since, Botox® is denatured by bubbling or similar violent agitation, inject the diluent into the vial gently. Discard the vial if a vacuum does not pull the diluent into the vial. Record the date and time of reconstitution on the space provided on the label. Once, a bottle of Botox® is reconstituted, it should be used within 4 hours. During this time period, reconstituted Botox® should be stored in a refrigerator (2-8°C). However, recent studies have shown that once refrigerated, it can be used till 6 weeks.

Dosage

The dosage of Botox® varies for each injection site, the extent of the facial lines and the mass of the muscle.

- Frown lines : 20 to 25 units.
- Crow's feet : 12 units per eye, i.e. 24 units in total
- Forehead lines : 16 to 20 units
- Bunny lines : 4 to 8 units
- Masseter hypertrophy : 25 units on each side of the jaw, i.e. in total 50 units
- Hyperhidrosis : 25 units in each palm, i.e. 50 units in total.

Botox® offers sustained relief, dose after dose. The effect of the first treatment lasts up to 4 months. The treatment can be continued as long as the treatment symptoms respond to Botox® therapy. Usually, Botox® treatment is required approximately 3 times a year. Since symptoms can change overtime, the amount and duration of relief can vary. Also the dosage may change based on the severity of the condition and the indication for which it has to be administered.

For the treatment of gummy smile a dose of 1.25 U per muscle site per side was selected as a baseline.17 Under sterile conditions, 1.25 U per side should be injected in both the right and left levator labii superioris and levator labii superioris alaeque nasi muscles (LLS), and an additional 1.25 U per side at the overlap areas of the levator labii superioris and zygomaticus minor muscles (LLS/ZM).

CONCLUSION

Although surgical techniques have been reported in the literature, they are not routinely used to treat hyperfunctional upper lip elevator muscles resulting in a short upper lip and a concomitant gummy smile. Most of the surgical correction currently used seems to be Le Fort I maxillary osteotomies with impaction for skeletal vertical maxillary excess and gingivectomies for delayed passive dental eruption with excessive gingival display. Because BTX-A is used frequently for the temporary correction of perioral rhytides, care should be taken when injecting these anatomical areas in patients with hypotonic, flaccid lips to avoid further muscle weakening and an esthetically unacceptable smile because of excessive soft tissue covering the smile line.

REFERENCES


ABOUT THE AUTHORS

Jyothi Kiran Hurkadle (Corresponding Author)
Associate Professor, Department of Orthodontics and Dentofacial Orthopedics, JSS Dental College and Hospital, Mysore, Karnataka, India
Phone: +91-9448163485, e-mail: drjyothikiran8874@gmail.com

Archana Jatania
Former Postgraduate Student, Department of Orthodontics and Dentofacial Orthopedics, JSS Dental College and Hospital, Mysore, Karnataka, India

Ravi Shanthraj
Associate Professor, Department of Orthodontics and Dentofacial Orthopedics, JSS Dental College and Hospital, Mysore, Karnataka, India

Bhagya Lakshmi
Reader, Department of Orthodontics and Dentofacial Orthopedics, JSS Dental College and Hospital, Mysore, Karnataka, India

Pradeep Subbiah
Lecturer, Department of Orthodontics and Dentofacial Orthopedics, JSS Dental College and Hospital, Mysore, Karnataka, India

Shiva Linga
Professor and PG Incharge, Department of Orthodontics and Dentofacial Orthopedics, JSS Dental College and Hospital, Mysore, Karnataka, India