

## **BOTOX-A COMPREHENSIVE REVIEW AND ITS USES IN DENTISTRY**

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### **ABSTRACT**

The use of botox as a part of cosmetic rehabilitation and minimally invasive facial rejuvenation procedures is ever-growing. Botulinum toxin is a neurotoxin derived from the bacterium *Clostridium botulinum*, which acts by temporarily paralyzing the muscles by blocking the release of acetylcholine at the neuromuscular junction. Traditionally approved for the treatment of strabismus, the use of botox has become more versatile over the years. From minimising the appearance of facial wrinkles, neckbands, correction of masseter hypertrophy to the treatment of cervical dystonia, overactive bladder, TMJ disorders etc., its use is ever expanding in cosmetic and non-cosmetic branches of medicine. Though the use of botulinum toxin is overall safe, at times minor side effects such as hematoma formation, droopy eyelid, crooked smile etc. may arise. The effects of botox show optimal results after 10-15 days of application and last about 3-6 months.

This article aims to highlight the basic mechanism of action of botulinum toxin, injection techniques, its various uses including its vast application in the field of dentistry and possible side effects.

**KEYWORDS** - Botox, Botulinum toxin, Wrinkles, Facial Rejuvenation, Mechanism of action, Side Effects, Uses in Dentistry

## **Introduction**

Facial rejuvenation procedures have gained immense popularity over the years. The use of “Botox”, a form of botulinum toxin derived from the bacterium *Clostridium botulinum*, is one of the most sought after treatment options as a form of minimally invasive facial rejuvenation procedures [1]. Botulinum toxin is a neurotoxin that has eight antigenically distinguishable exotoxins (A, B, C1, C2, D, E, F and G) [2]. All the botulinum serotypes block the release of acetylcholine at the neuromuscular junction causing an interference in the impulse transmission that results in temporary muscle paralysis [2],[3]. The clinical use of botox is ever-expanding in both cosmetic and non-cosmetic branches of medicine. Initially, botulinum was used for the treatment of strabismus, but at present it is considered to be a popular choice for the treatment of cervical dystonias, blepharospasm, torticollis, laryngeal dystonia, and oromandibular dystonia, as well as hemifacial spasms, and some forms of limb spasticity [4],[5],[6]. The use of Botox as a part of facial rejuvenation procedures targeting glabellar frown lines, wrinkles around the lips and marionette lines, platysmal bands in the neck, facial wrinkles, etc., is gaining popularity not only among females but also among males [7],[8]. The effects of botox become visible in the first 3-4 days of its use peaking after approximately 15 days, which last for 3-6 months.

## **Historical Perspective**

A Belgian scientist, Emile Pierre discovered *Clostridium Botulinum* after the outbreak of botulism in Belgium [9]. During World War II, Carl Lamanna and Dr.Edward Schantz successfully isolated the toxin into a crystalline form. Dr.Schantz continued his research at the University Of Wisconsin with Eric Johnson and his co-workers [10]. In 1965, Drachman demonstrated paralysis and atrophy of chick’s muscles after Botulinum toxin injection [11]. This encouraged Dr.Allan Scott to further research the treatment of strabismus using monkeys [12]. It was the first biological toxin licensed for the treatment of human diseases. In the late 1980s, it was approved for the treatment of strabismus [13]. In 2002 it was approved by the FDA in the USA for the treatment of facial wrinkles [13]. As years passed, the use of botulinum toxin was extended for the treatment conditions such as cervical dystonia, hyperhidrosis, migraine, hyperactive bladder, etc.

## **Indications**

### **Facial wrinkles**

Botulinum toxin is a key member of the branch of cosmetology and is gaining more and more popularity with each passing day. The appearance of wrinkles is a part of the natural ageing process as a result of repetitive contraction of facial muscles. Injecting a small amount of botulinum toxin causes temporary paralysis of the facial muscles at the site, thereby relaxing the muscles. As a result the appearance of facial wrinkles is minimised giving a smoother and tighter finish to the face [14].

Facial wrinkles may be static or dynamic. Dynamic wrinkles such as glabellar lines, crow's feet lines, marionette lines and smoker's lines are treated using botox [8],[15]. Glabellar lines, also known as forehead furrows, are present in the forehead region between the eyebrows and above the nose. Crow's feet lines are the lines that are present around the lateral canthus of the eye and appear mostly while smiling. Marionette lines are a common phenomenon of ageing that appear in the form of vertical lines extending between the mouth and chin giving a sagging, pulled down appearance to the lower half of the face [14]. Lip wrinkles, also known as smoker's lines, are vertical lines that appear around the lips [14]. The use of botox minimises the appearance of these wrinkles to a great extent, giving not only a younger looking appearance but also boosts self-confidence.

Static wrinkles on the other hand are those that are visible even when the muscles are at rest. Such wrinkles are treated using a combination of dermal fillers and botulinum toxin to achieve optimal results [14].

Apart from cosmetic uses, botox has also been used to treat many medical conditions such as -

- a. Treatment of blisters and redness associated with Hailey Hailey disease [8],[16]
- b. Overactive bladder syndrome[17]
- c. Cervical dystonia or spasmodic torticollis [15],[18],[19].
- d. Hyperhidrosis i.e. excessive sweating of the palms, axilla, feet etc[20],[21]
- e. Excessive sebum production[22],[23]
- f. Blepharospasm and strabismus [22],[23]
- g. Chronic migraine[24]

### APPLICATION IN DENTISTRY

The use of botox in the branch of dentistry for treating TMJ disorders such as bruxism, facial pain and neuralgias etc., is ever-evolving. **TMJ disorders** are broadly distributed into two types - myofascial (related to the muscles) and atherogenic (related to the bone), characterised by headache, periauricular pain, neck pain, decreased jaw movements, jaw locking, which may be unilateral or bilateral [25].

Ø **MPDS**, is related to hyperactivity of the masseter and temporalis muscle, that elicits unilateral pain. The use of botox provides relief by temporarily paralyzing the muscles [26].

Ø **Bruxism**, which is a condition involving clenching /grinding of teeth, also results in hyperactivity of the masseter muscle. Various studies conducted have shown Botox to be a useful measure in the treatment of the condition [27],[28].

Ø **Masseteric hypertrophy** adds an increased bulk in the cheek area giving a bulky and fuller appearance to the face. The use of botulinum toxin reduces the volume of the muscle providing a more well-defined jawline and slimmer look to the face [29].

Ø **Condylar Fracture Stabilization-** An unconventional method for the stabilization of condylar fractures involves using a higher dose of botox. The paralyzed muscle serves as a temporary splint for stabilization of the fractured segment [30],[31].

Ø **Post herpetic neuralgia-** Reactivation of the Varicella Zoster Virus causes a painful, itchy unilateral rash. The use of botulinum toxin has shown reduced frequency and intensity of painful attacks [32],[33],[34].

Ø **Orthodontic correction-** Facial muscles have a tendency to regain their original position and function causing a relapse of orthodontic treatments, the use of botulinum toxin can prevent such a relapse [35].

### CONTRAINDICATIONS

Overall the use of botulinum toxin has no major contraindications, but like every drug there are a few exceptional cases where its use is not recommended.

These include –

- a. Respiratory problems such as asthma [36],[37]
- b. Bleeding disorders [36],[37]
- c. Allergy to any component of botulinum toxin A or B [36],[37]
- d. Skin infections at the site of injection [36],[37]
- e. Pregnant or lactating women[37]
- f. Keloids and hypertrophic scars from wounds[37]
- g. Uncontrolled systemic disease[37]
- i. Patients with neuromuscular disorders such as Myasthenia gravis, ALS, Eaton Lambert syndrome, etc.[37]
- j. Additionally patients who work as actors, singers, classical dancers or public speakers are usually advised against the use of botulinum toxin.

### SIDE EFFECTS

Like every treatment the use of Botox is associated with some potential side effects. However, these side effects are usually mild and transient. Light bruising or hematoma formation is one of the most commonly encountered side effects lasting 2-3 days. Other minor side effects include pain and swelling at the site of injection [14]. Certain side effects may arise due to improper administration techniques such as drooping eyelids, uneven eyebrows, crooked smile, torticollis etc [2],[14],[38]. Headache, nausea, dry mouth, dry eyes have also been reported in some cases.

In severe cases, difficulty in speaking, dysphagia, visionary disturbances and anaphylaxis may occur [14].

### MECHANISM OF ACTION

Botulinum toxin is a potent neurotoxin derived from the bacterium *Clostridium botulinum*. All the botulinum serotypes block the release of acetylcholine at the neuromuscular junctions, thus interfering in impulse transmission resulting in temporary muscle paralysis [3],[4]. At a cellular

level it acts by cleaving a protein called synaptosomal-associated protein of 25 kDA (SNAP-25) on the nerve membrane. This inhibits the release of acetylcholine at the neuromuscular junction [39]. Out of the two chains in which the botulinum neurotoxins are cleaved, the heavy chain binds to target receptors and the light chain binds to the SNARE protein complex [39]. However, it is accepted to be a transient process. The inhibition of acetylcholine release by botulinum toxin is terminated by restoration of the SNARE protein complex turnover [39]. With time SNAP-25 is regenerated and the neuromuscular signalling is restored [14]. Muscle paresis in striated muscle usually occurs after 2–5 days lasting for 2–3 months before it gradually starts to wear off [39]. Repeated treatments are usually required every three to six months depending on the area treated, the dose used, and how one responds to the botox injected.

## TREATMENT USING BOTOX

### Patient selection

To achieve desirable results with botulinum toxin, the right patient selection is very important. Type of wrinkles, area to be injected, age of the patient, gender, and the profession of the patient are important factors to be considered while planning the treatment. It is essential to understand the patient's needs and provide a realistic idea of the possible treatment outcome. Treatment of dynamic wrinkles with botox is sufficient while the treatment of static wrinkles usually requires a combination of botox and dermal fillers.

### Vial preparation and dose calculation

The human lethal dose for botulinum toxin is calculated to be 3000 U. For cosmetic purposes such as treatment of wrinkles the dosages are usually less than 100 U. Each vial is prepared with a mixture of botulinum toxin, 0.5 mg of human albumin, 0.9 mg of sodium chloride in a sterilised vacuum-dried form without any preservative.

### Dilutions:

Theoretically dilutions with saline are to be done from 100 U/ml to 10 U/ml. Most physicians dilute botox with 1-4 ml saline (100 units/4 ml) for the face. Each vial is a vacuum dried vial.

**Table 1:**

Diluents added to 100 unit vial	Resulting dose units per 0.1 ml	Diluent added to 50 unit vial	Resulting dose units per 0.1 ml
4 ml	2.5 units	2 ml	2.5 units
2.5 ml	4 units	1.25 ml	4 units

2 ml	5 units	1 ml	5 units
1 ml	10 units	0.5 ml	10 units

Source[40]

**·Determining the facial anatomy:**

Before starting the treatment the muscular anatomy, nerve supply and blood supply should be thoroughly identified with respect to the area to be treated to prevent any side effects. For facial wrinkles, various expressions like frowning, squinting, raising the eyebrows, moving eyes up and down, and smiling are used as an aid to get a better understanding of the muscular anatomy.

**·Handling and injecting botulinum toxin:**

Botox vials should be stored at 2- 8°C and must be used within 4 -6 hours of preparation. The prepared solution is then injected in required areas with a 30 gauge hollow teflon-coated short needle. The quantity can be altered depending on the patient, areas to be injected and type of muscle. Larger muscles require high doses and females in comparison to males require lower doses [3].

Some botulinum toxin formulations which are approved by the US Food and Drug Administration include -

**Table 2 :**

Toxin	Brand name	Manufacturer	Storage temp.
Onabotulinum toxin A	Botox®/Vistabel®	Allergan Inc.	Below 8°
Abobotulinum toxin A	Dysport®/Azzalure®	Ipsen, pharma	Below 8°
Incobotulinum toxin A	Xeomin®/Bocouture®	Merz Pharmaceuticals	Below 25°

source[41]

**Table 3:**

<b>Expression lines</b>	<b>Muscle</b>	<b>Actions</b>
Frown lines	Corrugator supercillii Procerus and depressor supercillii	Eyebrows are drawn medially  Eyebrow depressor
Marionette lines	Depressor anguli oris	Corner of mouth depressor
Crow's feet	Lateral orbicularis oris	Lateral eyebrow depressor
Horizontal forehead lines	Frontalis	Eyebrow levator
Eyebrow lift	superior lateral orbicularis oris	Superior lateral eyebrow depressor
Bunny lines	Nasalis	The nose is drawn up and medially
Radial lip lines	Orbicularis Oris	Lip puckering
Gummy smile and nasolabial fold	Levator labii Superioris alaeque nasi	Central lip levator

source [41]

**·Injection technique/doses:**

Botulinum toxin is injected intramuscularly. Depending on the site of injection and the type of muscle the needle may be inserted perpendicularly or may be angulated. The injection techniques for some of the facial wrinkles are as follows:-

**1. Frown lines**

The procerus muscle lies in the midline of the face near the upper nasal bridge. The muscle can be held between the finger and thumb of one hand while injecting the solution with the other hand. The needle is placed above the orbital rim to protect the levator palpebrae superioris muscle to prevent blepharoptosis [42]. Eyebrows are never considered as a landmark as they may itself be ptotic, plucked, shaped or modified in other ways [42].

## **2. Forehead rhytids**

For forehead wrinkles, the forehead is divided into three parts vertically and horizontally. Horizontally – upper forehead, middle forehead and lower forehead. Vertically – Right, left and the middle region. The needle should be placed above the orbital rim to prevent eyebrow ptosis and the appearance of a frozen forehead [42].

## **3. Eyebrow Lift**

Techniques used are

- Injecting the glabella alone.

- Injecting the lateral orbicularis oculi lateral to the mid-pupillary line.

The purpose for injecting only the glabella is when the depressor muscles of brows are weak, they prevent the opposing action of the frontalis muscle which results in brow upliftment [42].

## **4. Bunny lines**

The target area is the lateral side of the nasal wall just above the nasofacial groove. Massaging the area should be avoided to prevent diffusion into the lip muscles to prevent lip ptosis [42].

## **5. Elevation of the corner of the mouth**

To locate depressor anguli oris the patient is asked to make a ‘sad face ‘expression while showing their lower teeth to locate the muscle. The site of injection is the meeting point of the jawline and nasolabial fold on each side [42]. The site of the injection must be carefully visualised and assessed to prevent altered sphincter function of the orbicularis oris [42].

## **6. Elevation of the tip of the nose**

The injection is placed at the base of the columella at the junction of the nose and face.

## **7. Dimple chin**

The needle is placed at a deeper level due to the presence of fat present at the chin area. Three injections are given one at the midline and two on each side of the midpoint point of the chin area [42].

## **8. Crow’s feet**



The area at the lateral canthus of eyes is where the formation of crow's feet wrinkles is seen. The needle is placed superficial and lateral to the orbital rim into the orbicularis muscle. The needle is directed outwards, to prevent diffusion associated strabismus or lid ptosis [42].

### **9. Infraorbital folds**

The needle is directed towards the pretarsal portion of the face, lateral to the orbital rim in a horizontal and tangential direction towards the lower eyelid. Two sites are injected, one is 3 mm below the ciliary margin of the mid-pupillary line and the second is injected halfway behind the mid-pupillary line and lateral canthus of the eye. The injection must be placed superficially to avoid diffusion into the inferior oblique muscle which can in turn cause diplopia [42].

### **10. Excessive gingival show ('Gummy' smile)**

The botulinum toxin solution is injected bilaterally into both the nasofacial grooves, targeting the levator labii superioris alaeque nasi muscle [42].

### **11. Platysmal bands**

The patient is asked to forcefully contract the neck area by clenching to locate the platysmal bands. Each band is held between the index finger and the thumb and then injected [42].

## **AFTERCARE**

Patients are usually advised to take rest and refrain from performing any physical activity for a few days post treatment. In the case of facial wrinkles, especially when the forehead region is injected, patients are advised not to lie down for a few hours post treatment. This is to prevent diffusion of the toxin into the adjacent muscles which may cause complications like drooping brows. Additionally, it must be ensured that the treated area is not massaged or rubbed. In the event of bruising, cold packs may be applied to the area for 2-3 days [39].

## **FOLLOWUP**

The effects of botox start appearing within 2-3 days and peak approximately 15 days after the procedure. Static wrinkles show relatively slower results. The procedure may be repeated in two weeks if the desired results are not achieved [39]. The effect of botox usually last for 3-6 months.

### **Common errors due to improper administration of botulinum toxin**

- A. Injecting high doses
- B. Accidentally injecting wrong or adjacent muscle
- C. Injecting too high or too low in the target area
- D. Omitting some area on the face thus giving less effective results
- E. Handling male and female patients in the same way thus giving feminine appearance in males and vice versa

F. Lack of familiarity with muscle anatomy, resulting in overcorrection of stiles causing an unnatural appearance [43].

## **CONCLUSION**

The use of botulinum toxin has revolutionized the field of medicine with its versatile application in the field of cosmetic and non-cosmetic medicine, which is now advancing to the field of dentistry. Traditionally approved for the treatment of strabismus, the use of botulinum toxin has expanded for treating cervical dystonia, overactive bladder syndromes, etc. With the growing demand for aesthetic procedures in dentistry ranging from smile designing, to gingivoplasty, gingival depigmentation, orthodontic treatment, bleaching etc., the integration of the use of “Botox” as a minimally invasive facial rejuvenation procedure, provides a wholesome treatment approach. The use of botox is overall safe and free of any major side effects if used with proper knowledge and safety. This article provides a wholesome review of the use of Botox and its integration into the branch of dentistry.

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