

# Botulinum toxin-An Innovative Treatment Approach in Dental Practice

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## ABSTRACT:

**Objective:** Dental diseases are a result of two main factors, the microbial colonization in the oral cavity and the overactive orofacial musculature. The hyperactive orofacial musculature exerts excessive biting forces and dental trauma which results in various forms of damage to the teeth and periodontium such as bruxism, TMJ disorders asymmetrical smiles, oromandibular disorders and excessive gingival display and many others. These muscle generated damages can be managed both by non surgical and surgical methods, but are invasive, irreversible and expensive for most of the patients. Hence, there is clearly a pronounced need to improve the options available for preventive treatment of muscle generated dental diseases which requires effective and safe agents that have minimal side effects which are well tolerated for long term use and will eliminate or reduce the need to use other irreversible treatment modalities. Recently, injections of Botulinum toxin or botox have shown promising results in managing the hyperactive orofacial musculature. Thus the purpose of this article is to review the nature, mechanism of action and applications of botulinum toxin in dentistry.

**Key-words:** Hyperactive orofacial musculature, Botulinum toxin, Applications, Dentistry.

**Key-Messages:** Botulinum toxin or popularly known as Botox worldwide, is a neurotoxin which when used in therapeutic doses can produce wonders in cosmetic problems of orofacial regions. Its applications are not just restricted to cosmetic therapy but also has got wide array of uses in the treatment of painful dental conditions. This article reviews the various applications of Botox in dentistry and its current status in India.

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## INTRODUCTION

Botulinum toxin (BT) is a neurotoxin produced by anaerobic *Bacteria clostridium botulinum*, it is highly toxic neurotoxin which causes a serious disease called botulism characterised by paralysis of the musculature in the body leading to death which was first noticed by Emile van ermenhem in 1897.<sup>1</sup>

The first therapeutic use of botulinum toxin was conceived by Kerner and coined the name botulism (from latin *botulus* meaning sausage).<sup>2</sup> Botox has been approved by the food and drug administration (FDA) for therapeutic treatments of eye muscle problems (in 1989), neck problems (in 2000), and excessive sweating (in 2004). In 2002, the FDA approved Allergan's botox cosmetic for the purpose of temporarily erasing facial lines.<sup>3</sup>

Botulinum toxin can be differentiated serologically into eight kinds of toxins named from A to G (A, B, C1, C2, D, E, F, and G).<sup>4,5</sup> Neurotoxin strains A and B are antigenically different, but have similar functions and are commercially available for medical treatments.<sup>6,7</sup>

"Botox" is the USA trade name for botulinum neurotoxin type A.<sup>8</sup> BT is a high-molecular weight protein complex made of 3 different proteins: First, a 150-kDa toxin which itself is composed of a 100-kDa heavy chain and a 50-kDa light chain that are binded together with disulfide non-covalent bonds. This bond disrupts during toxin activation. Second, a non-toxin hemagglutinin protein, which protects the toxin from being destroyed by acids. Third, a non-toxin non-hemagglutinin protein.<sup>9</sup> Although botulinum toxin is a lethal, naturally occurring substance, it can be used as an effective and powerful medication in the treatment of overactive oro-facial musculature.<sup>10</sup>

## Mechanism of Action

BT mainly inhibits the release of acetyl choline at the neuromuscular junction resulting in paralysis of muscles. At therapeutic doses BT

causes localised paralysis of target muscles. When it is injected to the muscle it causes proteolysis of proteins Synaptosomal associated protein SNAP-25 in the neuronal cytoplasm, which is very essential for the release of acetyl choline at the neuromuscular junction. Thus, there is loss of neuronal activity and ultimately localised paralysis of the isolated muscle.<sup>11</sup> This therapeutic effect is reversible, which first appear in 1 to 3 days, peak in 1 to 4 weeks, and decline after 3 to 4 months.<sup>12</sup>

## PREPARATIONS

There are several BT preparations in different countries. The most common available BT-A preparations are Botox, Dysport, Xeomin, Prosigne and PurTox. Myobloc is a BoNT-B preparation. The treatment dose varies for each brand of toxin and for different parts of the body.

## Dosage

Each vial of Botulinum toxin (BT) contains-

1. 100 Units (U) of Clostridium botulinum type A neurotoxin complex,
2. 0.5 milligrams of Human albumin and 0.9 milligrams of sodium chloride in a sterile, vacuum-dried form without a preservative. Adding 4 ml of 0.9% preservative-free normal saline solution makes injections and the preparation should be used within 4 hours.<sup>17</sup>

The potency of BT is expressed as mouse units. A unit of BOTOX is defined as the LD<sub>50</sub> for a colony of 20 gm Swiss-Webster mice,<sup>18</sup> the usual maximum dose recommended for dental applications at an injection session is about 80–100 U.<sup>19</sup>

**Table 1: Different available Botulinum toxin preparations<sup>13-16</sup>**

Sl no	Brand name	Company	Dose
1.	Botox <sup>13</sup>	Allergan Inc, USA	5ng BONT-A, 500µg albumin and 900µg sodium chloride
2.	Dysport <sup>13</sup>	Ipsen Limited, UK	12.5ng BONT- A, 125 µg albumin, 2.5µg lactose
3.	Xeomin <sup>14,15</sup>	MerzPharma, Germany	No accessory proteins
4.	Prosigne <sup>16</sup>	Lanzhou Biological products, China	BoNT- A
5.	PurTox <sup>15</sup>	Mentor Corp, USA	Purified BoNT-A
6.	Myobloc <sup>13</sup>	Solstice Pharma, USA	25ng BoNT-B, 0.05% albumin

**Applications**

The BT-A was initially approved for use in focal dystonia, primary axillary hyperhidrosis, blepharospasm, and strabismus. One of the most popular and successful applications of BT has been in the treatment of hyperkinetic facial lines. In 2000, FDA approved BoNT/B for the treatment of cervical dystonia in patients who developed BoNT/A resistance.<sup>20</sup>

**Applications of Botulinum toxin (BT) in dentistry-**

Botulinum toxin (BT) can be used in the following general dental disorders:

**Periodontal Applications**

**Prominent gums**

The excessive maxillary gingival tissue which is displayed upon smiling is often aesthetically displeasing with no simple remedy, which could be due to skeletal, gingival and hyperactive lip elevator muscles.

Results of surgical correction of the hyper functional lip elevator muscles are not promising as they may end up with scar contraction and relapses. Hence, minimally invasive treatment modality like BT would be advantageous when the gummy smile is due to hyper functional upper lip eleva-

tor muscles. BT limits muscular over contraction when applied in small, carefully titrated doses. These muscles can be proportionately weakened with BT, which will reduce exposure of the upper gums when smiling.<sup>29,30</sup>

**Black triangle**

Black triangles are one of the most challenging esthetic concern following placement of crowns, bridges and especially implants or after periodontal surgery. By injecting BT into these areas, it literally plump up papilla and is a minimally invasive way to create proper and more pleasing gingival contours.<sup>31</sup>

**Dental implants and maxillofacial fractures**

Excessive functional forces, especially in patients with parafunctional habits can hamper the process of osseointegration. Thus, the overloading of implant results in its failure. Forces from hyperactive masticatory muscles can also prevent or impede fracture callus formation after maxillofacial fracture fixation. Hence in both conditions muscular relaxation can be achieved with BT injections into the masticatory muscles allowing a more stable environment for implant integration and fracture healing. In an open-label study to prospectively examine the use of BT as

Conditions	Signs and symptoms	Clinical studies
Bruxism	Tooth wear, Periodontal disease, headaches and TMJ disorders	BT injection in the masseter muscles is an effective and safe means of intervention in cases of severe post-traumatic bruxism. <sup>21</sup> A marked reduction in bruxism after injection of botulinum toxin-A into the masseter and temporalis muscles in a patient recovering from a coma <sup>22</sup>
Temporomandibular disorder (TMD)	Headaches, ear-related symptoms and cervical spine disorders	Injections of 150 units of BT to the temporalis and masseter muscles significantly decreased pain and tenderness and improved function and mouth opening in TMD patients. <sup>23</sup> Lee et al, during the 5-12 months follow-up study on the effect of BT injections on pain in six patients with limited mouth opening due to TMD found clinical remission of symptoms without any adverse effects <sup>24</sup>
Temporomandibular dislocation	Condyle protrudes too far forward into the articular eminence and causes the jaw to lock in an open position.	Mandibular dislocation has been treated with BT injection into lateral pterygoid muscles and results lasted for a minimum of three months. <sup>25</sup>
Masseteric hypertrophy	Increased size of masseter muscles is evident in the patient's facial appearance, which is often altered, e.g., the jaw can appear swollen and misshapen.	Injection of small aliquots of botox into the masseter muscles resulted in a sustained reduction of masseter hyperactivity. <sup>26</sup>
Mandibular spasm	Mandibular closing musculature remains semi- contracted or in spasm, resulting in restricted mouth opening.	Treatment of mandibular spasms treated with BT injections responded positively to botox injections. <sup>27</sup>
Sialorrhea	Sialorrhea, or drooling, is the result of excess saliva production or the inability to hold saliva within the mouth or swallow.	BT was injected into parotid, sub-mandibular gland or both and doses of toxin varied from 10-100 units, which resulted in reduction in saliva production and effect lasted for 1.5 to 6 months. <sup>28</sup>

an adjunct to zygomatic fracture fixation, prophylactic injections of 100 units of BT into the masseter muscle of patients with zygomatic bone fractures at the fractured site before the surgical procedure resulted in temporary paralysis of the masseter muscles which allowed for fewer miniplate and/or microplate insertions in all patients, and also resulted in no complications related to either the botulinum toxin injections or surgical procedures.<sup>4,32</sup>

### Contraindications, limitations and adverse events

As such there are no absolute contraindications but a few relative contraindications like pregnancy, lactation, neuromuscular diseases (myasthenia gravis, Eaton-Lambert syndrome), motor-neuron diseases, concurrent usage of amino glycosides and sensitivity to toxin.

The potential adverse effects of Botulinum toxin in oromandibular disorders include facial nerve palsy, pain at the injection site, flu-like symptoms, non-targeted muscle weakness, dysphagia, and hematoma. These effects of BT therapy are generally transient and resolve within a couple of weeks.<sup>33,34</sup>

### Status of Botox application in India

Botox may have been around for a decade but Indians have started seeking it only recently. The Indian Academy of Facial Esthetics (IAOFE) in association with the American Academy of Facial Esthetics (AAFE) is a professional and multidisciplinary organization, whose primary mission is teaching the best non-surgical and non-invasive facial esthetic techniques such as dermal filler training courses and Botulinum Toxin (Botox) Training Courses for dentists

and physicians. The Indian Academy of Facial Esthetics continues to develop successful proven techniques and trains dentists to integrate these procedures into dental esthetic and dental therapeutic treatment plans.<sup>35</sup>

Dr Madhuri Behari, who heads neurology at the All India Institute of Medical Sciences (AIIMS) in Delhi and is a pioneer in botox therapy in India. It was Behari's work that led the Ethics Committee of AIIMS to approve botox as a treatment for blepharospasm.<sup>36</sup> In India a botox injection costs anywhere up to Rs. 5000 per injection and a chin treatment using botox would perhaps cost anywhere between Rs. 50,000 to Rs. Lakhs.<sup>37</sup>

## CONCLUSION

Botulinum toxin therapy is one of the most promising and exciting novel additions to the dentist's arsenal for the treatment of various orofacial and cosmetic corrections. BT provides a treatment that is reversible, conservative, quick and painless in comparison to other surgical alternatives. There are still many dental conditions which require FDA approval to be treated by botulinum toxin. Hence more extensive confirmation of its use in multiple dental applications is needed. It is evident that BT offers an array of valuable solutions for dentist and will surely take dental profession to one step ahead in the field of progress.

## SUMMARY

- Botulinum toxin though a highly toxic neurotoxin produced by anaerobic Bacteria *Clostridium botulinum*, causes a fatal disease called botulism, presently it is finding its place in the therapeutic needs of medical and dental fields. Botulinum toxin can be differentiated serologically into eight kinds of toxins named from A to G (A, B, C1, C2, D, E, F, and G). Neurotoxin strains A and B are antigenically different, but have similar functions and are commercially available for medical treatments. BT basically causes loss of neuronal activity and ultimately localized paralysis of the isolated target muscle.
- There are several BT preparations in different countries. The most common available BT-A preparations are Botox, Dysport, Xeomin, Prosigne and PurTox. Myobloc is a BoNT-B preparation.
- The potency of BT is expressed as mouse units. A unit of BOTOX is defined as the LD50 for a colony of 20 gm Swiss-Webster mice, 18 the usual maximum dose recommended for dental applications at an injection session is about 80–100 U.
- The BT-A was initially approved for use in focal dystonia, primary axillary hyperhidrosis, blepharospasm, and strabismus. One of the most popular and successful applications of BT has been in the treatment of hyperkinetic facial lines. In 2000, FDA approved BoNT/B for the treatment of cervical dystonia in patients who developed BoNT/A resistance. BT is used for many dental conditions and disorders such as bruxism, masseteric hypertrophy, TMJ disorders and in maxillofacial fractures and implants. There are no absolute contradictions, complications or adverse effects. The effects of BT therapy are generally transient and resolve within a couple of weeks. The Indian Academy of Facial Esthetics continues to develop successful proven techniques and trains dentists to integrate these procedures into dental esthetic and dental therapeutic treatment plans in India. BT provides a treatment that is reversible, conservative, quick and painless in comparison to other surgical alternatives in the field of orofacial and esthetic dentistry.

## ABBREVIATIONS USED

Botulinum toxin (BT) ; Synaptosomal Associated Protein (SNAP) ; Botulinum Neurotoxin A (BoNT/A) ; Botulinum Neurotoxin B (BoNT/B) ; Food and Drug Administration (FDA) ; Temporomandibular disorder (TMD) ; The Indian Academy of Facial Esthetics (IAOFE) ; American Academy of Facial Esthetics (AAFE).

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