# Botulinum Toxin – The New Paradigm A Review Article

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**Abstract:** Application of Botulinum toxin-A (Botox) in the field of dentistry is a new and upcoming. It acts by preventing the release of Acetylcholine at neuromuscular junction, which inhibits the contraction of muscles. This blockade is temporary, inhibiting the masticatory efficiency and function. It will return to its original levels once the effect of Botox has subsided, varying from three to four months. Botox is a viable treatment for many facial, TMD and oral dysfunctions when they are musculature based. Using Botox requires minimal training for a general dentist. It is most appropriate in patients who are refractory to other treatments.[Shah S NJIRM 2014; 5(3):126-132]

**Key Words:**Botulinum toxin - A, Botulinum toxin – B, neurotransmitter release

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**Introduction:**Commercially available botulinum toxin is the purified exotoxin of the anaerobic bacteria, Clostridium botulinum. This same neurotoxin is the cause of the rare but serious paralytic illness, botulism. Seven types of botulinum toxin have been isolated type A, B, C, D, E, F, and G but only two, types A and B, have been made commercially available.The toxin acts by preventing the release of acetylcholine from presynaptic vesicles at the neuromuscular junction resulting in an inhibition of muscular contraction. This blockade is temporary, varying from three to four months, after which sprouting of new axon terminals result in a return of neuromuscular function. Therefore, treatment with botulinum toxin cannot be considered curative but a palliative and symptomatic approach to the management of a problem. The toxin has also been shown to block acetylcholine release at parasympathetic nerve terminals.[1,2,3,4,5]

**Mechanism Of Action:** BOTOX blocks neuromuscular transmission by binding to acceptor sites on motor or sympathetic nerve terminals, entering the nerve terminals, and inhibiting the release of acetylcholine. This inhibition occurs as the neurotoxin cleaves SNAP-25(synaptosomal protein of 25 kDa), a protein integral to the successful docking and release of acetylcholine from vesicles situated within nerve endings.[6]

When injected intramuscularly at therapeutic doses, BOTOX produces partial chemical denervation of the muscle resulting in a localized reduction in muscle activity. In addition, the

**Figure 1: Mechanism Of Action Of Normal Neurotransmitter Release**
**SNARE – Soluble-N-Ethylmaleilide-Sensitive Attachment Factor Receptor**
**SNAP-25 –Synaptosomal Protein Of 25 Kda**

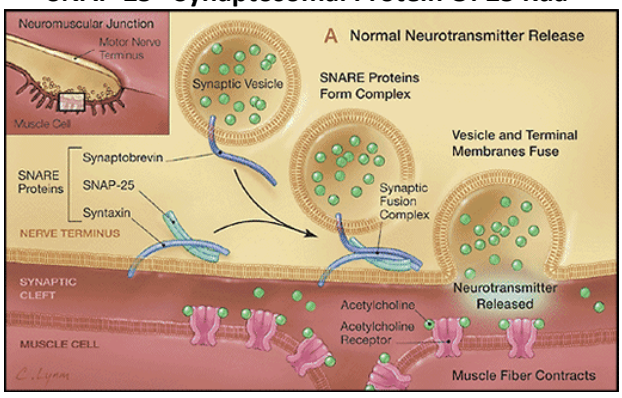
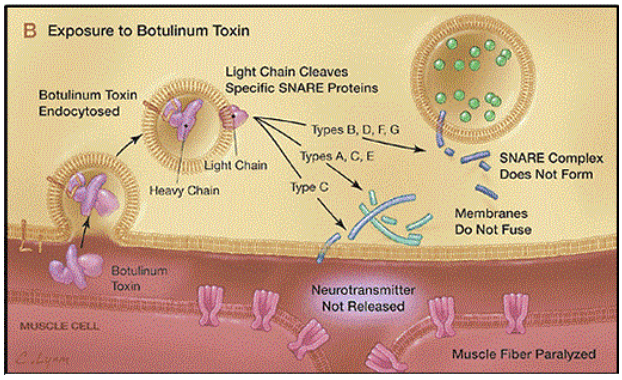



**Figure 2: Mechanism Of Action On Exposure To Botulinum Toxin**




muscle may atrophy, axonal sprouting may occur, and extrajunctional acetylcholine receptors may develop. There is evidence that reinnervation of the muscle may occur, thus slowly reversing muscle denervation produced by BOTOX. When

injected intradermally, BOTOX produces temporary chemical denervation of the sweat gland resulting in local reduction in sweating. [6]

**Applications:** Botox is used in various disorders as a treatment modality. Along with general applications it also has some specific dentofacial applications.

**General Applications[5,6,8]:**

- Treatment of overactive bladder
- Treatment of urinary incontinence due to detrusor over activity associated with a neurologic conditions.
- Prophylaxis of headaches in adult patients with chronic migraine
- Treatment of upper limb spasticity in adult patients Treatment of cervical dystonia in adult patients
- Treatment of severe axillary hyperhidrosis that is inadequately managed by topical agents in adult patients
- Treatment of blepharospasm
- Treatment of strabismus

**Dentofacial Applications[5,7]:**

- Extracapsular myogenic pain by masticatory muscle hypertonicity
- Trigeminal neuralgia, migraine, mandibular spasm, neck pain
- Limits clenching after periodontal therapy
- Sialorrhea
- Gummy smile
- Elimination of bruxism
- Masseter hypertrophy
- Mandibular spasm
- Limits muscle hypertonicity after orthopaedic and orthognathic surgery, post-operative muscle pull on the periosteum in responsible for pain
- Secondary dental pain
- Patients with para-functional habits and oromandibular dystonia
- Limits muscle forces during orthodontic treatment
- After trauma to oral tissues
- Trismus
- Adaptation to rapid change in vertical dimension associated with oral prosthesis

**Contraindications[6]:**

- Known hypersensitivity to Botulinum Toxin
- Infection at the injection site(s)
- Urinary Tract Infection or Urinary retention

**Precautions[6]:**

- Lack of interchangeability between Botulinum Toxin products
- Spread of toxin effect
- Injections In or Near Vulnerable Anatomic Structures
- Hypersensitivity reactions
- Pre-existing Neuromuscular Disorders
- Dysphagia and breathing difficulties in treatment of Cervical Dystonia
- Pulmonary effects of BOTOX in patients with compromised respiratory status treated for spasticity or for detrusor over activity associated with a neurologic condition
- Corneal exposure and ulceration in patients treated with BOTOX for blepharospasm
- Retrobulbar haemorrhages in Patients Treated with BOTOX for strabismus
- Bronchitis and Upper respiratory tract infections in patients treated for spasticity
- Autonomic Dysreflexia in patients treated for detrusor over activity associated with a neurologic condition
- Urinary tract infections in patients with overactive bladder
- Urinary retention in patients treated for Bladder Dysfunction
- Human albumin and transmission of viral diseases

**Dentofacial Applications:** Botox is the generic name for the neurotoxin protein botulinum toxin Type A produced by fermentation of anaerobic bacterium Clostridium botulinum, which is a secure, sterilized and vacuum‐dried powder diluted with saline solution.[9] Botox decreases the muscle activity by blocking overactive nerve impulses that trigger excessive muscular contractions by selectively preventing the release of the neurotransmitter acetylcholine (ACh) at the neuromuscular junction. [10]

**Temporomandibular joint Disorder (TMD):**In a temporomandibular joint disorder (TMD), there might be one or multiple trigger points in muscles to which a patient points. Palpating these areas

immediately sends a cascading pain along the muscle or neuronal tracks that radiate from the trigger point outwards. Many agents have been used and injected directly into these trigger points to treat these areas, including sterile saline and local anaesthetic. The theory of trigger point injections is that the disruption of the trigger point might be enough to bring short-term or even long-term relief. The success of these treatments have been limited, primarily because the effect of sterile saline or local anaesthetic lasts for a few hours. Other treatments have been used for TMD, include psychological therapy, maxillary or mandibular repositioning, orthodontic devices, neuromuscular therapy, drug treatments such as anti-inflammatory agents, non-narcotic and narcotic pain medications, muscle relaxants, chiropractic therapy, massage, acupuncture and even antidepressants.[11,12]

The use of Botox therapy for TMD symptoms has been in use for many years.[13,14] For trigger point injections, it makes much more sense to use Botox products because the effects will last for three months and it helps relieving the intensity of the contraction of the muscle, which is usually in spasm.[15]Botox injections produced significant improvement in pain, function, mouth opening, and tenderness.[16] Botox neurotoxins can be generally applied to a number of muscles of facial expressions and mastication, including the masseter, temporalis, pterygoids, frontalis, procerus, corrugator, orbicularis oculi, orbicularis oris, mentalis, and depressor anguli oris.[17] The use of Botox products in TMD therapy can give us a totally new insight for helping these patients who have had a lot of trouble getting relief before.

**Headache, Migraine, Trimeginal Neuralgia and Myofacial pain:** Standard medications used in the treatment of headache and migraine causes a number of side effects, such as stomach upset, drowsiness, and weight gain. Such side effects for BOTOX treatment are relatively rare. BOTOX 25−75U injected into pericranial muscles relieves headache by relaxing the over active muscles by blocking nerve impulses that trigger contractions. For migraines, there is no muscle component involved. It is believed that BOTOX works by blocking the protein (SNAP-25) that carries the message of pain to the brain and relief typically takes effect in two to three weeks after injection. The longer the treatment duration, the better the pain relief.[7,18] According to Elcio, excruciating pain associated with inflammation of the trigeminal nerve of the head and face can be substantially relieved by injections of BOTOX.[19] According to Lawrence Robbins, BOTOX actually is an anti-inflammatory substance, decreasing, or antagonizing the inflammatory (neuronal/brain) effects of Calcitonin gene-related peptide.[20]

The aetiology of myofacial pain syndrome is incompletely understood. Some clinicians believe that it characteristically results from either an acute episode of muscle overload or from chronic and/or repetitive muscle overload. Active myofacial trigger points, which cause pain, exhibit marked localized tenderness and often refer pain to distant sites and disturb motor function. Injection of muscles with BOTOX has been reported to be effective for myofacial pain caused by trigger points.[7]

**Bruxism:** Bruxism is a diurnal or nocturnal parafunctional activity that includes clenching, grinding, bracing, and gnashing.[21]There have been numerous theories as to why this occurs and certainly most bruxism cases will manifest itself nocturnally. Certainly, there are components of psychological stress that might cause it. However, there is no question that bruxism leads to the destruction of otherwise healthy dentition, exacerbates periodontal disease, causes TMD and is the cause of headaches and facial pains. Traditionally, intraoral appliances have been the treatment of choice for bruxism with good success as to relieving some or all of the symptoms. Bruxism and TMD patients are treated with bilateral injections of Botox into the masseter and temporalis muscles. A practicing clinician must have a good feel as to what the proper dosage is because too much of the Botox will paralyze the muscles of mastication and interfere with the patient's ability and confidence in chewing and talking. Too small of a dosage will not have any effect at all. Using the right amount of Botox will reduce the intensity of contractions of these muscles of mastication as well as give the patient full competence for chewing, eating properly and

speaking. The relief afforded to patients by Botox neurotoxins can help eliminate facial pain, grossly reduce their TMD symptoms and can significantly help the other associated treatments of periodontal disease by removing the bruxism elements.[12]Botox injections can be a safe and effective treatment for severe tooth grinding. It is, however, an expensive treatment and should be considered as a therapeutic option only for those who have complicated or disability bruxism and are refractory to other medical and dental therapy.[22]

**Masseter Hypertrophy:**Masseteric hypertrophy literally means enlargement of the masseter muscles. Most often, this is associated with clenching and bruxism, even when it is mild to moderate. One of the treatment for masseteric hypertrophy is Botox being injected into the belly of the masseter muscle. This will cause a slenderizing of the face in addition to reducing the intensity of contractions of the masseter muscles, and like all other Botox treatments, repeat injections are required every few months.[12] In several small but well-documented clinical trials by(1) Al-Ahmad, Al-Qudah (2) Mandel and Tharakan[23] and (3) Rijsdijk and Vanes[24] injection of small amounts of Botox into the masseter muscles resulted in a sustained reduction of masseter hyperactivity.[7]

**Mandibular Spasm:**It is a condition when the mandibular closing musculature remains semi-contracted or in spasm, resulting in restricted mouth opening. This type of muscular spasm limits completing the basic oral hygiene necessary to prevent oral disease and places restrictions on dental treatment.[12]The study by Kim et al[25]described theeffectiveness of BOTOX in patients with hemi- masticatory spasm. Botox application effects the spastic muscle. It significantly improves the functions and increases mouth opening, reduces pain and tenderness on palpation.

**Gummy Smile:**The display of excessive gingival tissue in the maxilla upon smiling or the ‘‘gummy smile’’ is both an oral hygiene and aesthetic issue with no simple remedy. 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.

Excessive gum exposure is frequently attributable to over contraction of the upper lip muscles, particularly the levatorlabiisuperiorisalaequenasi. When this is the case, a less invasive approach is to limit muscular over-contraction. 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.[7] Polo conducted a study in which five patients with excessive gingival display due to hyper-functional upper lip elevator muscles were treated with BOTOX under electromyographic guidance. Patients received one 0.25 U injection per muscle bilaterally into the levatorlabiisuperioris, superiorislabiialaequenasi, and at the overlap areas of the levatorlabiisuperioris and zygomaticus minor muscles. The effective increase in upper lip length upon smiling averaged 124.2% and the duration of effect ranged from 3 to 6 months with no adverse effects reported or observed.[26]

**Sialorrhea:**Sialorrhea or excessive salivation, and drooling, are common and disabling manifestations in different neurological disorders. A review is made of the literature, based on a PubMed search, selecting those articles describing clinical trials involving the injection of botulinum toxin A in the salivary glands of patients with different diseases characterized by sialorrhea.

The most frequently treated diseases were infant cerebral palsy (30%), Parkinson’s disease (20%) and amyotrophic lateral sclerosis (15%). Over half of the authors injected the product into the parotid glands, 9.5% into the submaxillary glands, and 38% into both. The total doses of toxin injected varied from 10-100 units of Botox® or 30-450 units of Dysport®. A reduction was observed in the production of saliva following these injections, and the duration of the therapeutic effect was one and a half to six months. The presence of adverse effects such as dysphagia, xerostomia and chewing difficulties were seen. [27, 28]

**Orthodontic Treatment:**Relapse has been a continuous problem for many general and orthodontic dental practitioners and there are a

number of theories as to why this happens. There are so many patients who have a hyperactive mentalis muscle that might be disrupting the alignment of the teeth. Other muscles in spasm can usually be observed as well, with proper training. Botox can reduce muscle contraction intensity, and over time, muscles can be trained to work normally. This idea could revolutionize how we deal with orthodontic relapse as dental practitioners.[12]

**Orthognathic Surgery and Trauma:** Maxillofacial fracture repair often requires multiple fixation sites and hardware to overcome the strong forces of masticatory musculature. Excessive forces created by para-functional clenching impede healing and reattachment of gums and bone in the mouth following trauma.[7] Pre-surgical Botox therapy also plays a key role in attaining muscular relaxation during surgical repair of multiple maxillofacial fractures associated with road traffic accident. Inappropriately attended hypertonic peri-traumatic musculature may lead to impedance of formation of callus.[12]

**Patients with Para-Functional Habits and Oromandibular Dystonia:**Excessive forces created by para-functional clenching impede healing and reattachment of gums and bone in the mouth following trauma. Low doses of BOTOX can potentially limit the para-functional clenching and its intensity and thus allow traumatized tissues to heal. High doses can be used as a ''pharmaceutical splint,'' limiting muscle contraction before resetting and during rehabilitation after fracture of the facial bone, e.g. fractured mandibular condyle.[5] Because para-functional clenching contributes to periodontal trauma, limiting clenching before and after periodontal surgery can benefit in healing. The use of a splint is often contraindicated because the teeth should be functional during healing. With significant bone loss, excessive forces may jeopardize dental stability and contribute to additional tooth loosening. The same applies in a patient with bone loss associated with either advanced periodontal disease or osteoporosis and a strong bite. Bite force is not diminished with reduced alveolar bone support. The use of BOTOX may offer an alternative to conventional splint therapy.[5, 7]

Oromandibular Dystonia (OD), is considered a rare focal neurological disorder that affects an individual's lower facial muscles. Muscle groups affected by the disorder include the masticatory, tongue, and facial muscles. The documented prevalence of OD is 6.9 out of 100,000 individuals and occurs predominantly in women between the ages of forty to seventy years. Patients who suffer from this disorder display involuntary, repetitive, and sustained spastic movements of these muscles. This results in parafunctional movements such as bruxing and clenching. OD patients often have painful opening, closing and deflecting of the mandible related to temporomandibular joint pain. In particular, those affected may be predisposed to early edentulism and occlusal alterations that may worsen dystonic movements and contribute to temporomandibular joint disorder. This combination may present a challenging scenario for those rehabilitating the edentulous patient with OD. The patient reported with parafunctional habits improved after the Botox therapy.[28, 29] Intramuscular Botox injections have been utilized as the treatment of choice for symptom relief for OD and resolve some of these muscle dysfunctions.[12]

**Removable Prosthesis:**While it is true that more and more patients are receiving implant treatment to help stabilize dentures, there will always be patients who either cannot afford or are not candidates for implant therapy. Many of these patients have hyperactive muscles, which then create a challenge for retaining dentures in their mouths. The facial muscles of patients are studied carefully, often a hypertrophic masseter, lateral and medial pterygoid muscles can be felt that causes this situation. Muscle treated via Botox might provide relief.[12]

**Limitations of Botox:**The therapeutic approach using Botox inhibits masticatory function temporarily and the masticatory forces will eventually return to previous levels once the effect of the drug has subsided.[7]

**Discussion:**Research has certainly shown that Botox products, such as Botox and Dysport, are a viable treatment for many facial, TMD and oral

dysfunctions, when they are based in the musculature.Botox therapy is appropriate for patients in whom other preventive treatments and modifications are poorly tolerated or contraindicated, patients who are refractory to other treatments, special patient populations, and patients who simply prefer this treatment.[5]Before injecting Botox into the muscle and/or joint and/or skin, the skin has to be cleaned with an alcohol/betadine/chlorhexidine swab. For muscle injections, the site to be injected should be determined by using a small electric recorder or a larger machine called an EMG machine, which helps in correctly locating the area of the muscle to be injected. Ultrasound-guided injections may also be used for deeper joints or muscles. BOTOX is injected using 1 ml tuberculin syringe and 0.30 gauge half inch needle. Injections of a small amount of this toxin into a muscle produces atrophy and weakness within one to twenty days and recovers over two to four months as new terminal axons sprout and restore transmission. Injections are spaced out for a minimum of three months to minimize the risk of antibody formation to the protein, which would prevent BOTOX from working the subsequent time.[7, 30, 31]

**Conclusion:**The use of BTX in dentistry offers the dentist another extremely effective tool to add to the armamentarium for treating conditions that derive from masticatory and other pericranial muscular conditions. Most dentists are familiar with the oral anatomy and are comfortable injecting into the oral musculature. The treatment protocols and injection techniques require essential, yet minimal training for the general dentist. Botox in dentistry will offer the general dentist who is not an expert in gnathology and occlusion a safe, effective treatment for controlling the symptoms of masticatory muscle hypertonicity, bruxism, TMD, sialorrhea, gummy smile, secondary pain and myofacial pain.

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