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Mini Review

# Role of Botulinium Toxin for the Treatment of Oraofacial Diseases

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**Abstract**

Justinus Kerner described botulinum toxin as a "sausage poison". In 1928, P. Tessmer Snipe and Hermann Sommer for the first time purified the toxin. Botulinum toxin is the strong bacterial toxin created by fermentation of clostridium botulinum. Eight different serotype of botulinum are known. Botulinum toxin causes prolong inhibition of the neurotransmitter release at the neuromuscular junction and autonomic sympathetic and parasympathetic nerve terminals. Botulinum is presynaptic neuromuscular blocking agent triggers chemical denervation by temporary suppressing secretion of acetylcholine. So botulinum toxin is useful for diseases with increased involuntary muscle activity or tension. Botulinum toxin serotype A, however, inhibits the release of acetylcholine at the neuromuscular junction. This neurotoxin, therefore, interrupts a vital step in the contraction process of a skeletal muscle and causes temporary muscle paralysis. It can be useful in various orofacial conditions like bruxism, masseteric hypertrophy, temporomandibular joint disorder, myofacial pain syndrome, hemifacial spasm, neuropathic pain and oromandibular dystonia and also effective in severe case of sialorrohea. A growing number of dentists are providing botulinum toxin to patients. Botox may serve as a valuable treatment a dentist can provide to patient. Although other traditional solutions are available, research shows botox is a viable treatment for many facial and oral musculature dysfunctions. Adverse reactions are uncommon, relatively mild and transient. This paper describes about botulinum toxin and its applications in various orofacial disease.

**Keywords:** Clostridium Botulinum; Botulinum toxin; Botox

## Introduction

Clostridium botulinum 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 but only two, types A and B, have been made commercially available. Initially, only botulinum toxin A was available commercially on prescription but more recently, type B also came on the market [1].

More recently, botulinum toxin has been suggested as part of the armamentarium for the management/treatment of various orofacial conditions and a considerable body of literature has been developed describing or investigating its efficacy and safety [1].

## Mechanism of Action

The botulinum 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].

Botulinum toxin has certainly been demonstrated to have significant value in the management of some orofacial diseases.

## Temporomandibular Joint Disorder

Temporomandibular Disorders (TMD) involve a set of craniofacial changes with multifactorial or biopsychosocial etiology, which may involve the Temporomandibular Joint (TMJ), masticatory muscles and/or musculoskeletal structures associated to head and neck [2].

The first line treatment approach for temporomandibular disorders includes physiotherapy, exercises, behavioural type therapy, oral appliances (most often stabilizing type), anti-inflammatory medications, muscle relaxants, analgesics or some combination of these. Rarely surgical intervention is indicated. Botulinum toxin can be a useful adjunct, particularly when these have failed to provide adequate relief, particularly in cases involving muscular hyperactivity [1].

## Treatment Protocol for Temporomandibular Joint Disorder

The temporalis component of pain is treated with bilateral injections of 7.5 U into the anterior vertical fibers of each temporalis muscle. In more severe cases, 2.5 U are given into the middle and posterior third of the temporalis muscles. Pain relief for the tendon of temporalis is achieved with multiple injections of 2.5 U equidistantly spaced in the temple area outside the orbital rim [3]. The masseter




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component of pain is treated with 5 U injected into the belly of the masseter below an imaginary line joining the tragus of the ear and the corner of the mouth [3] Freund et al. conducted a study on 46 patients suffering from TMD and found that 150 U injections of BOTOX to the temporalis and masseter muscles significantly decreased pain and tenderness and improved function and mouth opening [4].

Bruxism (excessive eccentric grinding of teeth) can affect the muscles solely and/or lead to the formation of TMD causing joint damage. Chronic patients have headaches, bruxism induced TMJ derangement or arthritis and difficulty in speaking, swallowing, or chewing [5].

Possible current treatment for bruxism involves a bilateral injection of Botox into the masseter and temporalis muscles. Another method includes the injection of Botox bilaterally, solely into the masseter immediately superior to the angle of the mandible. Though it is not known as to which method is more effective, either of these treatments may provide relief for four to six months or, in some cases, may lead to a total resolution of bruxism [6].

## Dental Implants and Surgery

The muscular relaxation achieved with prophylactic use of BOTOX injections to the masticatory muscles can be beneficial by allowing implant structures better osseo-integrated. Maxillofacial fracture repair often requires multiple fixation sites and hardware to overcome the strong forces of masticatory musculature [5].

Overloading of these muscles can prevent fracture callus formation. The muscular relaxation achieved with prophylactic use of BOTOX injections to the masticatory muscles can be beneficial by allowing fracture healing in a more stable environment [5]. The Kayikvioglu group also found similar benefits of adjunct BOTOX treatment for surgical reduction of mandibular condylar bone fractures [7].

## Masseteric Hypertrophy

Patients who are chronic jaw clenchers frequently present with masseteric hypertrophy. The increased size of these muscles is evident in the patient's facial appearance, which is often altered. To treat this, surgical resection was commonly resorted to which often resulted in substantial contracture. In several small but well-documented clinical trials by injection of small aliquots of BOTOX into the masseter muscles resulted in a sustained reduction of masseter hyperactivity [5]. Botox is subcutaneously injected into the masseter muscles. This provides a denervation of the muscles that results in atrophy. Though the effects may last from 3 to 18 months, repeat injections may be required [6].

## 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. BOTOX treatment to the masticatory musculature diminishes the effects of hyper-functional or spastic muscles that can significantly improve function and mouth opening [5].

## Asymmetrical Smiles

Asymmetrical smile Facial asymmetries arise from a multitude of reasons. There are three basic types. Acquired facial asymmetry may be the result of a medical or physical accident. Parotidectomy or other surgeries may also cause injury to the facial nerve. An injection of Botox into the overactive muscle fibers of the depressor labiinferiororis (the muscle responsible for the asymmetry of the lower lip) produces a gentle relaxation of the muscle resulting in a symmetrical smile [6].

## Trigeminal Neuralgia

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 [8].

## Myofacial Pain and Neck Pain

The etiology 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. Injection of muscles with BOTOX has been reported to be effective for myofacial pain caused by trigger points [5].

## Recurrent Dislocation of the Mandibular Condyle

TMJ dislocation is a mandibular dislocation in which the condyle protrudes too far forward into the articular eminence and causes the jaw to lock in an open position [6]. Recurrent dislocation of the mandibular condyle poses a difficult problem for affected patients. In the course of time, dislocations often become more frequent and more difficult to avoid. Even with good patient compliance, conservative treatment is often not sufficient [5]. The injection of Botox into the muscles that cause dislocation of the TMJ will result in the atrophy and weakening of these muscles. Most commonly botox injections are given in the lateral pterygoid muscles. Results of injection last for a minimum of three months [6].

BTX-A injection is invasive, but is a relatively conservative option because it is a safe and effective treatment for dystonia. It can be used as an initial approach because injection into the lateral pterygoid muscle is straightforward and can be done in outpatients with few complications [9].

## Sialorrhea

Sialorrhea or excessive salivation, and drooling, are common and disabling manifestations in different neurological disorders such as Amyotrophic Lateral Sclerosis (ALS) or Parkinson's disease, and often coincide with alterations in swallowing reflex [10].

Botulinum toxin has been shown to be effective in the management of sialorrhea. This involves injection into the salivary glands, usually with electromyographic guidance [1]. Botox is injected into salivary glands, including the parotid and submaxillary glands, to inhibit the stimulation of the cholinergic receptors. This results in a reduction in saliva produced and secreted [6].

## Adverse Reaction and Safety

Adverse reactions are uncommon and relatively mild and

transient. They are more common at or near the site of injection. These include dry mouth, dysphagia, dysphonia, transient muscle paralysis, headache, urticaria and nausea. Often, but not always, these side effects are noted when the dose exceeds that recommended [1].

In 2008/2009, both Health Canada and the FDA revised the prescribing information for the commercially available botulinum toxin A. Products to include a "Boxed Warning" highlighting potentially adverse reactions related to distant spread of the toxin effect from the injection site. These highlight botulism-like symptoms such as muscle weakness, hoarseness or dysphonia, dysarthria, loss of bladder control, difficulty breathing, difficulty swallowing, double or blurred vision and drooping eyelids. These effects can occur anywhere from a day to several weeks after treatment at unrelated sites. Although rare, deaths have been reported [1].

## Discussion

BOTOX produces partial chemical denervation of the muscle resulting in localized reduction in muscle activity. BOTOX can be used as a sole therapy or as an adjunct to oral medication. Adding 4 ml of 0.9% preservative-free normal saline solution makes injections and the preparation should be used within 4 h. The potency of BOTOX is expressed as mouse units. A unit of BOTOX is defined as the LD50 for a colony of 20 gm Swiss-Webster mice, extrapolated to the 70 kg human and each 0.1 ml contain 2.5 U of BOTOX. It is dispensed in small vials containing 100 U or 500 U. The lethal dose of BOTOX in humans is not known. Although it has been estimated to be about 3000 U. The usual maximum dose recommended for dental applications at an injection session is about 80–100 U [2]. BOTOX is injected using 1 ml tuberculin syringe and 0.30 gauge half inch needle [5].

Botulinum toxin type A is marketed worldwide under the name BOTOX (Allergan, Inc. Irvine, CA, USA) and in Europe as Dysport (SpeyWood Pharmaceuticals Ltd., Maiden head, UK) [2].

Botulinum toxin has been suggested as part of the armamentarium for the management/treatment of various orofacial conditions and a considerable body of literature has been developed describing or investigating its efficacy and safety [1].

Botulinum toxin type A is a safe, effective and long-lasting method that can be effective in certain cases of facial pain syndromes associated with muscular hyperactivity and inflammatory phenomena [11]. BOTOX therapy is appropriate for patients in whom other preventive treatments and medications are poorly tolerated or contraindicated, patients who are refractory to other treatments [2].

## Conclusion

Botulinum toxin has certainly been demonstrated to have significant value in the management of some types of orofacial pain, particularly myogenous temporomandibular disorders in cases where the patient is unresponsive to the less invasive therapeutic modalities or, at times, in conjunction with them. Although the drug is considered generally safe, there are a number of uncommon, relatively mild adverse reactions but more recently, some severe, potentially life threatening side effects, distant from the site of injection have been described. Therefore, patients should be properly informed prior to consenting. Although other traditional treatment modalities are available, research shows Botox is a important treatment for many facial and oral musculature dysfunctions. It provides conservative, quick and painless approach. Though there may be some adverse effects with the use of Botox, they are minimal and, for the most part, uncommon. Because Botox provides a treatment that is reversible, it gives patients the option to stop the therapy at any time; therefore, botulinum toxin offers an array of valuable solutions in dentistry to problems related to both the oral cavity and the face.

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