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Applications of Botulinum Toxin in Dentistry - Literature Review

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Abstract

The Botulinum Neurotoxins are produced by the anaerobic bacterium *Clostridium botulinum* and are considered the most potent toxins known and its application has become useful and significant in the treatment of oral and maxillofacial injuries. The aim of this study was to review the literature showing the possible therapeutic uses of botulinum toxin in dentistry. There were used articles, that describe the injection of botulinum toxin type A (BTX-A) in areas related to the oral cavity and face, excluding cosmetic purposes. The results show that a toxin is a viable treatment alternative, with beneficial effects in dentistry, but in some cases should be associated with other types of treatment. Although the literature confirm the effectiveness of the BTX-A, these studies should be interpreted cautiously, and more research is needed to confirm the safety and effectiveness of this treatment in larger, well-controlled clinical studies.

Keywords: Botulinum toxin type A; Dentistry

Introduction

The application of botulinum toxin (BTX) has become a useful and significant tool in the control of oral and maxillofacial injuries. Its application began the aesthetic use but has been very effective in various other clinical or surgical medical specialties [1].

Botulinum neurotoxin is synthesized by the Gram-positive, anaerobic, bacterium *Clostridium botulinum* and is considered the most potent toxin known [2]. The neurotoxins produced are proteins, and seven different serological types have been identified (A, B, C1, D, E, F and G), but the most widely used is the Botulinum Type A Toxin (BTX-A) [3,4]. The United States was the first to produce BTX-A during World War II, but the development of Botulinum neurotoxin as drug began in 1981 with the description of the use of BTX-A for the treatment strabismus. In 1989, after thorough clinical and laboratory tests, the Food and Drug Administration (FDA) approved the therapeutic use of BTX-A, for treatment of strabismus, blepharospasm, and hemifacial spasm in patients over 12 years of age. In 2000 the FDA approved BTX for dystonia and in 2002 it was approved for the temporal management of glabellar lines [5,6].

Normally, the brain sends messages to the muscles to contract and to promote the movement. The message is transmitted through a substance called acetylcholine. Botulinum toxin blocks the presynaptic release of acetylcholine (Ach) into the end-plate of the neural junction by interfering with the activity of SNARE (soluble N-ethylmaleimide-sensitive factor attachment protein receptors) proteins [7] and as a result, the muscle does not receive the message to contract, but without any systemic effects [8,9]. BTX produces partial muscle chemical denervation, resulting in localized reduction of muscular activity and can be used as a single therapy or as an adjunct to another treatment [10].

It has been proposed that BTX reduces pain directly by producing molecular changes in nociceptive fibres function, blocking the release of neurotransmitters [11,12], and indirectly by reducing excess dysfunctional muscle activity has been reported to have analgesic effects independent of its action on muscle tone [7].

Clinical effects of BTX-A occur within approximately 24-48 h after administration, peaking at 2-3 weeks. Effects generally last about 4 months, then level off to a moderate plateau until eventually full nerve recovery occurs within 3 to 6 months [13,14].

In dentistry, the toxin is used as a form of control for temporomandibular disorders (TMD), headaches, trigeminal neuralgia, migrane, myofacial pain, gummy smile, asymmetrical smile,

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masseter hypertrophy, mandibular spasm, surgical procedures, and hemifacial spasm and also in sialorrhea. Its use is growing and appears to be quite varied, and you can use in patients with facial changes and those whose changes are related to oral health, with good results when compared to other forms of treatment [15].

The aim of this study was to review the literature showing the recent advances and possible therapeutic uses of botulinum toxin in dentistry.

Search Strategy

This study constitutes a Literature Review Narrative or Traditional, held between May and September 2016 and selected scientific articles through search using three electronic databases: Pubmed, Scielo, and Bireme. The main keywords used were Botulinum Toxin and Dentistry, adding-specific words for each type of change researched.

Literature Review

Temporomandibular Disorders (TMDs)

TMDs involve a set of craniofacial changes with nonodontogenic facial pain and multifactorial or biopsychosocial etiologies, which may involve the temporomandibular joint (TMJ), masticatory muscles, and the associated structures [16-20]. Due to its muscle activity reducing and pain relief effects, BTX-A has gained an emerging role as a potential therapy for TMDs [6,13,21-23], including TMJ dislocation, bruxism, orofacial dystonia and arthritis [13,24-30].

Headache, Migrane and Trigeminal Neuralgia

Headaches can be classified into primary and secondary types. Primary headaches occur without underlying organic diseases and can be further classified into migraine, tension-type headaches, and cluster headaches. Despite important advances in management of headache disorders, many patients remain treatment resistant. Such side effects of treatment are relatively rare BTX-A is emerging as a new therapeutic alternative in the preventative treatment of headaches [29,31,32]. Furthermore, there have been several studies supporting the safety and tolerability of BTX-A in the treatment of headache disorders [33,34]. Although additional large-scale studies are needed to clarify clinical predictors of response as well as optimal dosing, injection sites and mechanism of action [10,32].

Several studies have suggested that BTX-A injected into the hyperalgesic tissue may be helpful at reducing spontaneous and provoked pain of neurophatic origin. Furthermore, a few randomized clinical trials have also suggested that BTX-A may be helpful in the treatment of trigeminal neuralgia [35].

Myofacial Pain

Myofacial pain syndrome is a disorder caused by persistent acute or chronic muscle contraction, characterized identification of trigger points or fibrous bands that, when stimulated or pressed, transfer radiated pain to the distribution area of the affected muscle [36]. Such trigger points can result from direct trauma, strain, overuse, or repetitive micro-trauma [37]. Many treatment options have been used to arrest, stabilize, or reverse this muscle hyperactivity, although all have shown some degree of success, all have potential complications [38,39].

Several studies have investigated the use of BTX-A for the treatment of myofacial pain, with positive findings [22,40-43]. However, some studies have demonstrated that the sole use o BTX-A is not enough to relieve pain [44-47] and that, in addition to active treatment, physical therapy is fundamental [48]. Overall, insufficient prospective randomized clinical trials have been performed to prove the effectiveness of BTX-A to treat myofacial pain in the maxillofacial region [49].

Gummy Smile

Gummy smile is a term used to describe excessive display of gingival tissue in the maxilla upon smiling caused by hyper-functional muscles of the upper lip. Several surgical techniques have been reported for the correction of hyper-functional upper lip elevator muscles [31]. The BTX-A may be an effective treatment alternative for patients with excessive gum exposure caused by over activity of the lip elevator muscles [43,50-52], but should be used with caution. Muscles are injected close to the nasalis or orbicularis oculi, with some fibers intermeshing the elevator labii superioris, levator labii superioris alaeque nasi, levator anguli oris, and zygomaticus major and minor [53].

Sialorrhea

Hyper-salivation is the result of hyper-secretion of salivary glands, but it is commonly associated with the loss of neuromuscular control with impaired oral motor activity and increased saliva flow. It also occurs as a side effect of drugs that act in the secretomor pathway, resulting in hyper secretion [54]. There are several therapeutic approaches for treatment of sialorrhea and the application of BTX-A was first proposed in 1977 through intra-glandular injection, mainly to the parotid gland [55], because it is able to depress secretory activity of the salivary glands [56] and saliva production can be effectively reduced. However, some authors use BTX injection guided by ultrasound to improve the effectiveness and safety [57], although others have not found differences in effects associated with the method of drug application.

There are many clinical trials in the literature showing the efficacy of this drug, but more detailed studies are needed on its safety and effect on glandular tissue.

Hemifacial Spasm

Hemifacial spasm is is a chronic disorder characterized by repetitive synchronous contraction of facial nerve innervated muscles on one side of the face [58]. The use of BTX-A in hemifacial spasm was approved by the U.S. Food and Drug Administration in 1989 and since then, evidences supporting its efficacy in the treatment of this disorder [59,60], however only a small number of studies have described the long-term use.

Masseter Hypertrophy

Masseteric hypertrophy usually results from anatomical asymmetry of the jaw and may be unilateral or bilateral. The injection of BTX-A is a minimally invasive procedure and the results obtained with injections have been encouraging and satisfying to patients [61-63]. Many studies showed the effects of long-term treatment of BTX-A, analyzing the monitoring data of patients with hypertrophy of the masseter muscle. Excellent results were obtained with satisfactory regression of hypertrophied muscle after intramuscular injection of BTX [64,65].

Various side effects of a BTX-A injection for masseteric hypertrophy have been reported, including change in bite force, speech disturbance, muscle pain, facial asymmetry, and prominent zygoma [66-68]. The change in bite force is an inevitable side effect of muscle atrophy, although it is normally only temporary.

Mandibular Spasm (Trismus)

It is a motor disturbance of the trigeminal nerve when the mandibular musculature remains semi-contracted or in spasm, resulting in restricted mouth opening [69]. BTX-A is injected into each masseter muscle and temporalis muscle, improving function and mouth opening, and decrease pain and tenderness to palpation. BTX-A treatment to the masticatory musculature diminishes the effects of hyper-functional or spastic muscles [70].

Asymmetrical Smile

Facial asymmetry can result from different causes, which will determine whether or not it can be reversible. There are three basic types of facial asymmetries: asymmetry acquired, iatrogenic and idiosyncratic or familial. In the pilot study, five patients with idiosyncratic asymmetrical smiles were treated with injections of BTX-A, which produced a symmetrical, more balanced smile one week after treatment and lasted at least six months after [71].

Surgery Procedures

More recently, it has been reported the clinical use of BTX-A in implantology for prophylactic reduction of masseter and temporalis muscle strength after implantation immediate load protocols [72]. The failure in osseous integration can be impeded by excessive functional forces in patients with para-functional habits.

BTX-A can also be used as an adjunct in fracture maxillofacial repair such zygomatic fracture fixation surgery and surgical reduction of mandibular condyle [73]. The repair often requires multiple fixation sites and hardware to overcome the strong forces of masticatory musculature. Overloading of these muscles can prevent fracture callus formation [73-75].

In periodontal surgeries, BTX injection can reduce periodontal trauma due to excessive muscular function [31].

Contraindications and Drug Interactions

Few studies reveal systemic problems associated with the administration with plastic purpose. Contraindications to the use of BTX in pregnancy, breastfeeding, neuromuscular junction disorders, hypersensitivity and drug interactions with amino glycosides, antibiotics, quinidine, calcium channel blockers, magnesium sulfate, succinylcholine, and polymyxin [76,77].

Adverse Effects

The side effects of intramuscular injection of the BTX-A when in therapeutic applications were mostly local and relatively mild, however, may be present in some cases [76,77]. Normally, these effects are transient, disappearing a few weeks after the applications [21,22,78]. The effects of BTX in the body are related to the frequency and amount of dosage. It can be observed hypotension, nausea, dysphagia, impaired sphincter control, itching, and a flu-like symptoms, facial pain, pharyngitis, double or blurred vision, anaphylaxis, urticaria, erythema, difficulty in articulating words and lack of control salivation, transient weakness, fatigue at or near the site [79], etc.

Conclusions

From the literature, we conclude that BTX-A is a viable treatment alternative, with beneficial effects for dentistry, but in some cases should be associated with other types of treatment. BTX-A is a potent and specific muscle relaxant, it will promote relaxation of the masticatory muscles, reducing pain and allowing a proper jaw function. Side effects they are rare, and transient, not causing major problems for patients. Although the literature confirm the effectiveness of the BTX-A, these studies should be interpreted cautiously, and more research is needed to confirm the safety and effectiveness of this treatment in larger, well-controlled clinical studies.

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