



Indications, Contraindications and Care in the Botulinum Toxin Type A Application in Dentistry

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Abstract

Botulinum toxin type A has become widely known for its use in cosmetic and aesthetics. However, its use was started in Ophthalmology for therapeutic purposes. Botulinum toxin has been attracting new therapeutic and cosmetic indications in Medicine and Dentistry. The purpose of this paper is to present the indications in Medicine and consequently Dentistry, as well as the contraindications, discussing the care, warnings and precautions for its use.

Keywords: Botulinum Toxins, Type A; Drug Repositioning; Off-Label Use; Therapeutic Uses; Dentistry; Medicine

Introduction

Botulinum toxin was initially employed in ophthalmic muscle alterations such as strabismus and, due to the results presented in attenuating periorbital wrinkles, indications in aesthetic high regions (frontal, glabellar, and periorbicular regions) began [1].

Botulinum toxin presents a variety of therapeutic and cosmetic indications [2-4]. Undoubtedly, the cosmetic application has garnered botulinum toxin recognition and success, being initially indicated in cases of hyperfunctional facial lines, most commonly seen in the glabellar, frontal, and periorbital (latero-canthal) regions, deep wrinkles of the upper lip, nose, deep marionette lines, platysma band, and cheek undulations [2,4-6]. Frequently, as most of these applications can interfere with physiological functions, the prescriber professional should be careful [2].

Regardless of the goal - therapeutic or cosmetic - for the application of botulinum toxin, the patient and the professional should incessantly discuss the case to avoid disappointment and dissatisfaction. Generally men have greater muscle mass compared to women, requiring larger amounts of botulinum toxin [5].

Purpose of the Study

The purpose of this article is to present the indications in Medicine and consequently in Dentistry, as well as the contraindications, discussing the care, warnings, and precautions for its use.

Discussion

General indications

Among the movement disorders, botulinum toxin type A has been indicated in cases of focal dystonias, with involuntary and

spasmodic muscle activity, among them cervical, truncal, laryngeal, limb dystonia, hereditary muscle colic, tremor, tics, blepharospasm, strabismus, and nystagmus [1-4,7,8].

Conditions that have spasticity, such as stroke, traumatic brain injury, cerebral palsy, multiple sclerosis, spinal cord injury, botulinum toxin type A has benefits in reducing muscle tone [1,2,4,8].

The application of botulinum toxin has been reported in some smooth muscle hyperactivity disorders, such as detrusor muscle sphincter dyssynergia, achalasia cardia, and chronic anal fissure [2,8].

The application of botulinum toxin in cases of hyperlacrimation has been indicated [3,8].

In patients with allergic or intrinsic rhinitis who present rhinorrhea (runny nose), botulinum toxin can be injected into the mucosa covering the middle and lower nasal concha or, by topical application in sponges in position (absorption by the nasal mucosa). Reduction of nasal secretion was observed after 12 weeks. Epistaxis or nasal crusts were common adverse events [3].

Future indications of botulinum toxin application have been reported in reducing body weight and food intake within the gastric antrum to delay gastric emptying. The application of botulinum toxin to the sphincter of Oddi has been cited for the relief of biliary pain symptomatology after colescistectomy [8]. It is worth remembering that several indications recommended by Medicine can be transferred to the field of Dentistry, and that many of the stomatological indications were derived from medical ones.

Stomatological indications

Among the stomatological indications are oromandibular and orolingual dystonia, peripheral facial paralysis, myokinesis or synkinesis followed by poor facial nerve repair, hemifacial spasm, myoclonus, palatal tremor, and in the prevention of scar formation [1-4,7-10]. Synkinesis is an unavoidable sequela whose uncoordinated muscle movement is involuntary and caused by facial nerve reconstruction in patients who had tumors of the parotid glands. They are characterized by synchronized but involuntary movements of certain muscles of the mimic, including the platysma and are frequent in cases of facial paralysis [3,4]. In cases of oromandi-

bular dystonia affecting the lingual floor region, and depending on the type of movement disorder, intrinsic tongue muscles should be avoided because of the possibility of causing adverse events such as dysphagia, dysphonia and hyposalivation [3,4,8]. In palatal tremor, repetitive dystonic contractions of the soft palate muscles - palatoglossus, palatopharyngeal, salpingopharyngeal, tensor, and soft palate elevator muscles - cause rhythmic elevation of the soft palate, which can cause swallowing and phonation disorders, including tinnitus, due to velopharyngeal insufficiency. To optimize the correct detection of the target muscle, application of botulinum toxin must be made guided by electromyography [3,8].

Botulinum toxin can be applied in conditions under the Autonomic Nervous System regency, such as hypersalivation or sialorrhea, in which patients lack the ability to correctly swallow saliva (this can be caused by neurological diseases, Parkinson's disease, amyotrophic lateral sclerosis, cerebral palsy, carcinoma of the upper digestive tract, Frey syndrome, sialoceles and parotiditis) or its containment in the oral cavity, and may aspirate it and cause aspiration pneumonia [1-4,8,10]. All applications, except in Frey's syndrome, are performed percutaneously, injected into the glandular or perileisional parenchyma. Xerostomia is the first manifestation of botulism, a characteristic that gave rise to investigations of the use of botulinum toxin in sialorrhea [4]. Gustatory sweating is a common sequela after parotid gland surgery. For the best outcome, it has been suggested to divide and apply in pits using Minor's test. Treatment of face or head hyperhidrosis follows the same principles as treatment of gustatory sweating [3].

Patients with chronic pain usually require multidisciplinary management. Botulinum toxin type A has shown several benefits in its use in cases of non-dystonic pain syndromes, such as orofacial pain, myofascial pain, chronic low back pain, torticollis, cervicogenic and tension headache, migraine, trigeminal nerve neuralgia, symptomatic bruxism, headache secondary to parafunctional habits, hemifacial contracture after injury of the seventh cranial nerve. Benefits have been shown by botulinum toxin in cases of postsurgical pain [1-4,6-8,10].

Several indications have been reported in Temporomandibular Joint (TMJ) dysfunctions, such as masticatory muscle pain, reduced ability in mouth opening, recurrent TMJ displacement, and mastica-

tory hyperactivity [1-4,6-8,10]. Temporomandibular dysfunctions (TMD) are a major cause of orofacial pain. They can be classified into myofascial (muscle action related) or arthrogenic (joint related) [4]. It has been indicated for TMJ dislocation when the mandibular condyle is displaced anterior to the articular eminence and caused by hyperactivity of the lateral pterygoid muscle [3,4]. It frequently occurs in patients with oromandibular dystonia, neuroleptically induced late or early dyskinesias, epilepsy, or truncocerebral syndromes [4]. Improved verbalization, mastication, and quality of life have also been reported in patients with TMJ dislocation who have suffered strokes, cerebrovascular events, or anoxic encephalopathy [4]. For accurate inspection, palpation and electromyography or ultrasound are indicated [3,4]. Patients who have reduced mouth opening (trismus) may have muscle relaxation and reduced muscle inflammation and pain after application of botulinum toxin type A to the masseter, temporalis, pterygoid, and digastric muscles [4,8]. Articular disc displacement, after botulinum toxin application, can show reduced clicking in the lateral pterygoid muscle [4]. As an adjunct to arthrocentesis, the application of botulinum toxin can be used, characterizing less invasive procedures compared to surgery [4]. Botulinum toxin has been widely used in cases of bruxism or clenching (Figure 1) and electromyography is indicated [1,3,4,8,10-13]. Additionally, these patients may have facial asymmetries caused by uni- or bilateral masseteric hypertrophy, and recurrent application may cause muscle hypotrophy with gain of facial symmetry [1,3-6,10].



Figure 1: Patient with bruxism receiving botulinum toxin application.

In patients with gummy smile (Figure 2 and 3), the application of botulinum toxin causes dehiscence of the upper lip, providing aesthetic and functional benefits [1,4,5,10,14]. The etiology of gummy smile should be evaluated, and the therapeutic modality to be instituted should be particularized. Usually, gingival growth is present, and prior to the application of botulinum toxin, resective gingival surgery (gingivoplasty) should be performed [10,15-20].



Figure 2: Patient presenting gummy smile.



Figure 3: Aesthetic result 15 days after the application of botulinum toxin.

Promising results have been reported in cases of facial paralysis, intentionally inducing ptosis for the purpose of protecting corneal dryness, in cases of upper eyelid levator muscle paralysis [1,4,9,10]. Synkinesis arising from facial paralysis has also been cited as a sequela treated by the application of botulinum toxin. In cases of patients with facial asymmetry, the injection contralateral to facial paralysis has been of great value in reducing relative hyperkinesis, resulting in better symmetrical facial function [4]. Additionally, in cases of excessive hyperlacrimation, the toxin has been used successfully [3,4]. Other causes of paralysis have been indicated, such as in cases of trauma [4].

In cases of elective oral surgery, with extraoral access, in which there may be involuntary movements by the patient, the application of botulinum toxin can help immobilizing the muscles in cases of fracture of the jaws, in which immobilization is not possible [4]. Recently, clinical use has been reported in Implant Dentistry, for the prophylactic reduction of the contraction force of the masseter and temporalis muscles, after immediate implant loading [1,7,10]. Improvements have been observed in the clinical appearance of keloids and hypertrophic scars by inhibiting their growth, caused by reducing muscle contraction adjacent to the wound, and the influence on cell apoptosis and proliferation is also reported [4].

Remission of oral lichen planus in a patient with low self-esteem has been reported by the application of botulinum toxin to facial aesthetics, favoring and increasing quality of life [21].

Contraindications

Like any other drug, botulinum toxin is contraindicated in cases of patients who are hypersensitive to the formula's components. Among the formula's constituents, the bovine milk protein (lactose) and albumin stand out. The latter has a function in the stability of the toxin-protein complex. From this perspective, botulinum toxin is contraindicated in patients with hypersensitivity to lactose and albumin [1,6,22].

The application of botulinum toxin is contraindicated in children under 2 years of age, given the possibility of comorbidities, low weight, and the lack of specific literature database in this subpopulation [1]. Dastoor, *et al.* (2007) [2] recommended that children under 12 years of age should not receive botulinum toxin applications.

Application in pregnant and lactating women is contraindicated - pregnancy risk category: C - in which no reproductive studies have been conducted, and there are no data on the safety of its use in pregnant or lactating women [1,2,4-6,8,22].

Patients with neuromuscular transmission deficiencies, such as myasthenia gravis, Eaton-Lambert Syndrome, and amyotrophic lateral sclerosis, may have increased sensitivity to botulinum toxin, resulting in excessive muscle weakness [1,2,4-6,22,23].

In patients with respiratory or swallowing disorders should also be avoided, given the possibility that the botulinum toxin, when applied in deep muscle planes, can reach the respective affected muscles. In low frequency, bronchoaspiration, pneumopathy, dysphagia, and anaphylaxis causing death in patients with significant asthenia have already been reported in the literature [1,6,24].

The formation of anti-botulinum toxin antibodies was a rare event. Clinically, the existence of significant amounts of neutralizing antibodies can be presumed by the substantial deterioration of therapeutic response and/or the constant need for dose escalation [1].

The application of botulinum toxin has been considered contraindicated in patients in whom aminoglycoside antibiotics (streptomycin, gentamicin, tobramycin, amikacin, netilmicin, paramycin, spectinomycin) and other drugs that interfere with neuromuscular transmission (non-depolarizing blockers like curare, quinidine, magnesium sulfate, succinylcholine) are administered [1,4-6,22].

Pre-existing local infection at the application site was also considered as relative contraindication [1,22].

Warnings and precautions for use

The application of botulinum toxin can cause allergic reactions, although there are no documented cases in the medical literature. The side effects potentially related to the application of botulinum toxin were headache, reactions at the application site, and eyelid ptosis, the latter being related to the volume of the injection, muscle topography injected, and professional experience [1].

Headache is usually transient and yields to the common analgesic. In our protocol, we recommend administration of Tromeptanol

ketorolac 10 mg (Toragesic™, EMS Sigma Pharma Ltda., Hortolândia, Brazil) [1]. In cases of skin nodules and edema in the application region, pressure and ice packs can be used [25,26]. The application of ice packs over the region before or after application showed no statistically significant difference regarding analgesia. However, the application of ice 5 minutes before the application of botulinum toxin showed a statistically significant reduction in bleeding after application [26]. However, we do not recommend the use of local pressure in order to avoid spreading the toxin to unwanted areas [1].

Commercial formulations of botulinum toxin (except Xeomin™, Merz-Biolab, São Paulo, Brazil) contain small amount of human serum albumin, aiming to increase the stability of the toxin-protein complex. Therefore, the possibility of transmission of prion disease (Creutzfeldt-Jakob Disease) should not be excluded [1,6,27]. Pedron, *et al.* (2009) [27] stressed the importance of biomaterial selection, as well as in Implant Dentistry and Periodontics, in the face of the possibility, even if small, of prion infection. However, these incidents have not been reported in the medical literature [1].

In patients with renal or hepatic impairment, there is no need for dose reduction [1].

The application in patients with alterations in platelet aggregation, coagulation, or under treatment with platelet antiaggregant or anticoagulant drugs should be considered when strictly necessary, considering intramuscular injection [1].

The effects of botulinum toxin can be potentiated by drugs that directly or indirectly interfere with neuromuscular function. Botulinum toxin application in patients under treatment with aminoglycoside antibiotics and muscle relaxants used in anesthetic procedures should be used avoided [1,28].

It is worth mentioning that, according to the manufacturer's orientation, the professionals who use botulinum toxin must have extensive knowledge about the anatomy of the region to be applied, concepts of electroneuromyography, ultrasound, and electrostimulation. The manufacturer also recommends the use of one vial per patient, which is unfeasible in Dentistry. Attention should be given to the destruction and special disposal of the vial [1].

Psychologically unstable patients with unrealistic expectations or unrealistic fear of the toxin should be avoided [1,22].

Conclusion

Despite botulinum toxin's fame for its applications for aesthetic purposes, its therapeutic potential in several general and stomatological indications must be known, since it is a drug. It is also important to emphasize the knowledge of its contraindications and care inherent to the applications of its use by dental surgeon or physician.

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