International Journal of Basic & Clinical Pharmacology
Kamarthi N et al. Int J Basic Clin Pharmacol. 2022 Jul;11(4):348-351
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20221603

Review Article

Botulinum toxin: a boon or bane in dentistry

Nagaraju Kamarthi, Sangeeta Malik, Sumit Goel, Swati Gupta, Shubham Sharma*

Department of Oral Medicine and Radiology, Subharti Dental College, Meerut, Uttar Pradesh, India

Received: 01 April 2022
Revised: 10 May 2022
Accepted: 11 May 2022

***Correspondence:**
Dr. Shubham Sharma,
Email: shubhamsharma11297@gmail.com

ABSTRACT

Botulinum toxin is a neurotoxin which is produced by the Clostridium botulinum bacteria. It is an anaerobic, gram-positive, spore-forming rod-shaped bacteria which is commonly found in soil, on plants, in water and in the intestinal tracts of animals. All the serotypes of botulinum toxin interfere with neural transmission by blocking the release of acetylcholine. The use of botulinum toxins has revolutionised the treatment of various ophthalmic spastic disorders, Orofacial pain conditions, facial dystonia and periocular wrinkles. A precise knowledge and understanding of the functional anatomy of the mimetic muscles is absolutely necessary to correctly use botulinum toxins in clinical practice. This article is an effort to understand Botulinum toxin and its applications in head and neck.

Keywords: Botulinum toxin, Treatment, Orofacial conditions

INTRODUCTION

One of the most poisonous biological substances known, Botulinum toxin (BTX) is a neurotoxic protein produced by the Clostridium botulinum bacteria and related species. It prevents the release of the neurotransmitter acetylcholine from axonendings at the neuromuscular junction, thus causing muscle paralysis. There are seven stereotype of botulinum toxin A, B, C1, C2, D, E, F, G, H, and I.[1] BTX is an organic macromolecule made up of amino acids linked together by peptide bonds (polypeptide chains). Biochemically it consists of a 50-kDa light chain and a 100-kDa heavy chain connected by protease-sensitive disulphide bridges; the bond of these chains results in a 150-kDa protein.[1]

All the serotypes of botulinum toxin interfere with neural transmission by blocking the release of acetylcholine. When the botox is injected in the muscle in the form of intra muscular injection, it acts on neuromuscular junction to cause paralysis if the muscle blocking the release of the acetylcholine from the pre sympathetic motor neurons.[2]

Botox can act at four different points in the body. These four different points are neuro muscular junction, postganglionic sympathetic and parasympathetic nerve endings, anatomic ganglia. The doses of all commercially available botox injection are presented in terms of units. The physiologic response to botulinum toxin injection is observed after 6 hours of its administration, and the clinical results of the injection are seen within 24 to 72 hours after the procedure.[2] While clinically paralysis is observed after 24 hours of the injection, the peak of the paralytic effect occurs after 14 days after. Depending on individual factors like doses and post blockage instructions, the effect of BTX injection can last from 2 weeks to 6 months. In very conditions, some individuals may take 5 days to develop symptoms and peak effect can be seen after a period of 10 days which last up to 8-12 weeks.[3]

From the number of patients who were injected serially with earlier preparation of Botox, 5-15% developed secondary non-responsiveness from the production of neutralising antibodies. Injection of more than 200 units per session and repeated booster injection is given within 1 month of treatment. New advancements have been taken

place and new Botox (BCB 2024) has reduced the immunogenicity and lower the rate of production of neutralizing antibody because of its decreased protein load, it has not been proven in clinical trial yet.[4]

The first commercially available Botulinum toxin type A in United States is BotoxR, it is very safe to use but only drawback of it is that if the content vial are dissolved then the reconditioned product loses its potency. That's why dermatologist tend to schedule the for sever number of patients on the same day so the entire content of the vial can be used.[1,4]

In Europe, the same stereotype A of botox is marketed by different company as Dysport; Speywood, U.K. The potency of disport is ¼ of 1 unit of botox.

Xeomin is an innovative botox type A formulation as the complexing protein is removed from it by extensive purification process from Btx complex. Xeomin contain pure 150 kD of neurotoxin. Without complexing protein Xeomin has lowest content of bacterial protein in comparison to all available botulinumtoxin and repeated application of Xeomin can be done even in high dose. In many clinical studies have found that Xeomin is similar to Botox and 1 unit of Xeomin is equal to 1 unit of Botox.[5]

Neurobloxc (myobloc) is a clostridium botulinum type B neurotoxic complex which become available in UK. There has been very limited clinical experience in the use of this stereotype and it is not approved for cosmetic use anywhere in the world.

Botulinum toxin is stored in freezer below -5ºC. It can be denatured easily by bubbling or agitation. The diluent injected gently onto the inside wall of vial. If vacuum inside the vial is absent and do not pull the diluent, then vial needs to be discarded.

After mixing of saline in the botox, the product is made to store at 2-8ºC and it should be used within 4 hours of dilution. A study showed that there is no loss of activity after 6 hour, but after 12 hours 44% and 1-2 week 70% of activity is lost with refiguration.[6] For injecting botox in the muscle or gland a 1-inch needle of 30-gauge is used to reduce the pain injection. Doses for injection are decided according to the mode of use, individual patient and the mass of muscle where being injected. A larger dose is required for a larger muscle and if there is a pre-existing weakness in the muscle then a lower dose is required. Many authors have suggested that administration of injection under the guidance of electromyography (EMG).[20]

Clinical application in head and neck

Laryngeal conditions

Spasmodic dysphoniaoccurs due to inappropriate glottic closure or opening due to spasm of intrinsic laryngeal muscles. Its symptoms include hoarseness and strangled speech breaks. A meta-analysis was done, 30 randomized controlled trials (RCTs) involving Botox therapy in adductor spasmodic dysphonia revealed an improvement to about one standard deviation across the dependent voice-related quality of life.[9]

Critical voice tremor is characterized by rhythmic activation of the intrinsic laryngeal muscles. Symptoms include break in pitch, diminished fluency and arrests. It occurs by aging but can be seen with spasmodic dystonia. Electromyography (EMG)-guided Botox injection into the thyroarytenoid muscles was shown to have beneficial effect.[10]

Pain

The use of Botox as a prophylactic therapy for migraine and other types of headaches is proved by many. In this technique, injections into muscles innervated by the facial or trigeminal nerves (e.g., procerus, suboccipital, frontalis, temporalis and corrugator) specific sites of pain distribution or a combination of both. Significant improvement from baseline were observed in patients who are under Botox trial arm with regard to headache and migraine days.[14]

Masticatory myalgia can be explained by chronic nociceptive irritation of the tendons and fascia of the masseter, temporalis and medial pterygoid muscles. Many RCT's studies shows that botox is more effective than saline in reducing the masticatory myalgia. Recent studies on EMG guided Botox injection concluded that action potential of masseter and temporalis muscle showed a significant decrease by nearly 80% on 14th day and 25% on 28th day.

Trigeminal neuralgia is an agonizing, enervating orofacial pain, also known as tic douloureux, owing to the facial expression or squinch that often accompanies the painful episode. The incidence of TN is more commonly seen in elderly patients. The pain is stabbing and sharp shooting like electric shock in nature, last for about seconds to minutes. Recent showed that BTX type A injections are as efficient as topical anaesthetics like bupivacaine 0.5%, lidocaine 0.5% in terms of the duration and function, magnitude of pain relief, and quality of life, but Botox is less cost effective.[15]

Other oral and facial conditions

The most common cosmetic indication of botulinum toxin A is in wrinkle therapy for glabella lines and platysmal bands, and in perioral cosmetic therapies such as gummy and asymmetry smile treatment Wrinkles such as glabellar lines are a spontaneous facial animation that develops when the lower facial muscles pull the skin, and they develop mainly by the action of the procerus and corrugator supercilia muscles. BTX-A has been used to temporarily treat not only glabellar lines but also lateral

cantonal lines called horizontal forehead lines, platysmal bands, perioral lines, and crow's feet. The efficacy of BTX-A in reducing facial wrinkles has been proven in randomized controlled trials.

Table 1: Side effects associated with botox injection.

Mechanisms of side effects	Type of side effects
Injuring a blood vessel	Erythema, ecchymosis Bruising, hematoma
The needle puncturing the skin	Tenderness at the site of injection
Decreased sweat gland activity	Dry skin
Contamination of the injection site	Local infection, abscess
Nerve injures	Paraesthesia or dysesthesia
Aesthetic in periorbital area	"Mephisto sign", exaggeration of wrinkles, brow ptosis, periorbital edema
Functional in periorbital area	Blepharoptosis, ptosis Ectropion, dry eyes, corneal irritation, corneal exposure Blurred vision, accommodation difficulties, retinal detachment, diplopia, strabismus
Aesthetic in perioral area	Asymmetric smile, lip ptosis, changes in facial expression
Functional in perioral area	Trismus
	Xerostomia
Localized	Redness, edema, urticaria,
Generalized	Generalized urticaria, diffuse edema, anaphylactic shock
Other mechanism	Headache
Diffuse spread of toxin (botulism)	Severe dysphagia Generalized muscle weakness

Blepharospasm can be defined as bilateral involuntary contraction of the eyelid muscles mainly seen elderly patients over 60 yrs. Most commonly affected muscle is orbicularis oculi. Botulinum toxin was first used in 1995 to treat blepharospasm. Since then, it become the treatment of choice.[16]

Botulinum toxin is also used to induce therapeutic ptosis, thereby protecting the cornea at the acute phase of facial nerve paralysis. To achieve this ptosis transcutaneous injection of botox are given into Mueller's muscle and levator palpebral superioris. Botox injection is beneficial in preventing damage as well as healing of the cornea.

An adjuvant for wound healing after oral and maxillofacial surgery

Inappropriate muscle movement near surgical site can inhibits healing immediately after the surgery. BTX-A injection pre and post operatively can facilitate healing by weaking the muscles. botox injection onto to the masticatory muscle of face also prevents displacement of the fractured bone of the jaw.[17]

Adverse effects

Injections with botulinum toxin are generally well tolerated and side effects are few. Generalized idiosyncratic reactions are uncommon, varying from mild and transient. There can be mild injection pain and local edema, erythema, transient numbness, headache, malaise or mild nausea (Table 1).

CONCLUSION

Botulinum toxin type A has wide range of clinical applications, but it also has a risk of developing antibodies limits the repeated use of high dose injections. The use of botulinum toxins in various ophthalmic spastic disorders, facial dystonia and periocular wrinkles has revolutionised the treatment. A precise knowledge is required to understand the functional anatomy of the mimetic muscles is for the correct use of botulinum toxins in clinical practice. Adverse effects are usually mild and transient. The most common complication that occurs is excessive or unwanted weakness, and this resolves when the action of the toxin is lost. High dose or injection at incorrect site can cause eyelid ptosis, neck weakness, brow ptosis, dysphagia, and diplopia. A good knowledge of the functional anatomy and experience with the procedure help the clinician avoid complications. In future, the development of new potent toxins with increasing duration of effect and effectiveness will further aid in this expanding and interesting field of chemo denervation.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Majid OW. Clinical use of botulinum toxins in oral and maxillofacial surgery. Int J Oral Maxillofac Surg. 2010; 39:197-207.
2. Hatheway CL. Clostridium botulinum and other clostridia that produce botulinum neurotoxins. In: Clostridium botulinum–Ecology and Control in Foods. Hauschild AHW, Dodds KL. New York, NY: Marcel Dekker, Inc. 1992;3-10.
3. Flynn TC. Myobloc. Dermatol Clin. 2004;22:207-11.
4. Huang W, Foster JA, Rogachefsky AS. Pharmacology of botulinum toxin. J Am AcadDermatol. 2000;43(1):249-59.
5. Freeman SR, Cohen JL. New Neurotoxins on the Horizon. J Aesth Surg. 2008;28:325-30.
6. Jaspers GW, Pijpe J, Jansma J. The use of botulinum toxin type A in cosmetic facial procedures. Int J Oral Maxillofac Surg. 2011;40:127-33.
7. Yoshida K. Botulinum Neurotoxin injection for the treatment of recurrent temporomandibular joint

dislocation with and without neurogenic muscular hyperactivity. Toxins. 2018;10:174.
8. Kim HS, Yun PY, Kim YK. A clinical evaluation of botulinum toxin-A injections in the temporomandibular disorder treatment. Maxillofac Plast Reconstr Surg. 2016;38:5.
9. Guarda-Nardini L, Manfredini D, Salamone M, Salmaso L, Tonello S, Ferronato G. Efficacy of botulinum toxin in treating myofascial pain in bruxers: a controlled placebo pilot study. Cranio. 2008;26(2):126-35.
10. Sidebottom AJ, Patel AA, Amin J. Botulinum injection for the management of myofascial pain in the masticatory muscles. A prospective outcome study. Br J Oral Maxillofac Surg. 2013;51:199-205.
11. Poewe W, Deuschl G, Nebe A, Feifel E, Wissel J, BeneckeR et al. What is the optimal dose of botulinum toxin A in the treatment of cervical dystonia? Results of a double blind, placebo controlled, dose ranging study using Dysport. The German Dystonia study Group – GDSG. J Neurol Neurosurg Psych. 1998;64(1):13-17.
12. Daelen B, Thorwirth V, Koch A. Treatment of recurrent dislocation of the temporomandibular joint with type A botulinum toxin. Int J Oral Maxillofac Surg. 1997;26(6):458-60.
13. Freund B, Schwartz M, Symington JM. The use of botulinum toxin for the treatment of temporomandibular disorders: preliminary findings. J Oral Maxillofac Surg. 1999;57(8): 916-20.
14. Schwartz M, Freund B. Treatment of temporomandibular disorders with botulinum toxin. Clin J Pain. 2002;18(6):198-203.
15. von Lindern JJ, Niederhagen B, Bergé S, Appel T. Type A botulinum toxin in the treatment of chronic facial pain associated with masticatory hyperactivity. J Oral Maxillofac Surg. 2003;61(7):774-8.
16. Castro WH, Gomez RS, da Silva Oliveira J, Moura MD, Gomez RS. Botulinum toxin type A in the management of masseter muscle hypertrophy. J Oral Maxillofac Surg. 2005;63(1):20-4.
17. Wang CC, Wang CP. Preliminary experience with botulinum toxin type A intracutaneous injection for Frey's syndrome. J Chin Med Assoc. 2005;68(10):463-67.
18. Farinelli I, Coloprisco G, De Filippis S, Martelletti P. Long-termbenefits of botulinum toxin type A (BOTOX) in chronic dailyheadache: a five-year long experience. J Headache Pain. 2006;7(6):407-12.
19. Ahn KY, Kim ST. The change of maximum bite force afterbotulinum toxin typea injection for treating masseterichypertrophy. Plast Reconstr Surg. 2007;120(6):1662-6.
20. Kim JH, Shin JH, Kim ST, Kim CY. Effects of two different units of botulinum toxin type a evaluated by computed tomography and electromyographic measurements of human masseter muscle. Plast Reconstr Surg. 2007;119(2):711-7.

Cite this article as: Kamarthi N, Malik S, Goel S, Gupta S. Botulinum toxin: a boon or bane in dentistry. Int J Basic Clin Pharmacol 2022;11:348-51.