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REVIEW ARTICLE

Botulinum toxin: A review article

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INTRODUCTION

Botulinum toxin (Botox) is a drug made from a toxin produced by the bacterium *Clostridium botulinum*. In large amounts, this toxin can cause botulism, an illness that affects the nerves. Botox has been used since the 1970s in the field of ophthalmology, and in the last 20 years, its use has expanded to various health scopes, especially dermatology.[1,2]

Botox consists of 7 types of neurotoxins; however, only toxins A and B are used clinically. Botox A is used for several disorders in the field of medicine, particularly in dermatology, for cosmetic purposes.[3] The first type of Botox introduced to the market was on a botulinum toxin A. In 2002, it was recommended to be used as a cosmetic treatment for glabellar frown lines by the Food and Drug Administration (FDA).[2,4,5] The second formulation of on a botulinum toxin A, which was produced in France, obtained its license to be used for esthetic purposes from the European Union in 2006 and was approved by the FDA in 2009.[5,6] Botox type A has become a term used by the society to describe all ingredients used in cosmetic treatments.[7]

Botox injections can be used to treat glabellar frown lines, wrinkles around the lips (smoker's lines) and marionette lines, platysmal bands in the neck, strabismus, blepharospasm, cervical dystonia, hyperhidrosis as well as synkinesis following facial surgery.[1,2,9]

MECHANISM OF ACTION

The mechanism of action of Botox includes the following four main steps:

The first step is binding of the toxin to specific receptors on the surface of the presynaptic cells, mediated by the C-terminal of the heavy chain. This step occurs over approximately 30 mins.[10]

The second step is internalization, which is an energy-dependent receptor-mediated endocytic process. In this step, the plasma membrane of nerve cells invaginates around the toxin-receptor complex, forming a vesicle containing a toxin in nerve terminal.[10]

The third step is translocation. Following internalization, the disulfide bond is cleaved and the 50-kDa light chain of the toxin is released across the endosomal membrane of the endocytic vesicle into the cytoplasm of the nerve terminal.[10]

The last step is blocking. The light chain of serotypes A and E inhibit the release of acetylcholine by cleaving the cytoplasmic protein (SNAP-25) needed for the docking of acetylcholine vesicles on the inner side of the nerve membrane of the nerve terminal.[10]
Following the injection, the toxin diffuses into the tissue until it binds selectively and reversibly in the presynaptic terminal of the neuromuscular junction and then attaches to the specific protein-membrane responsible for acetylcholine excretion.[5,6] The toxin immediately inhibits the release of acetylcholine in the neuromuscular junction causing relaxation of local muscles that is reversible, resulting in reduced facial wrinkles/lines, of which some are due to constant facial muscle contractions.[11,12]

INDICATION

In the field of dermatology, Botox is generally injected into the muscles of facial expression attached to soft tissues rather than bones, and by contracting, they pull across the skin to give facial expressions.[2,13]
In esthetics, Botox is used for reducing glabellar frown lines, crow's feet at the side of the eyes, horizontal forehead creases, wrinkles around the mouth, nasolabial folds and smoothing out neck and chest/cleavage wrinkles.[2,14] It also can be used to elevate the eyebrows and treat problems such as hyperhidrosis, lichen simplex, pompholyx (dyshidrotic eczema) and acne vulgaris.[7,15]
Botox cannot be used to prevent other signs of aging such as dry skin, pigmentation disorders and vascular abnormalities.[16]

CONTRAINDICATION

Contraindications with the use of Botox include patients with myasthenia gravis, amyotrophic lateral sclerosis, multiple sclerosis, Eaton Lambert syndrome, patients with focal and systemic infections, patients who are hypersensitive or allergic to Botox
Women who are pregnant and breastfeeding, neonate and children,
Patients who had previously undergone lower eyelid surgery.[17]

CLINICAL EFFECT

The clinical effects of Botox are seen on the first to the fourth days after injection, followed by 1–4 weeks of maximum effect, which will resolve after 3–4 months. In order to prolong the effects of Botox from six months to one year, the treatment should be repeated for one year or more.[24] The duration of Botox effect varies among individuals due to differences in muscle arrangements, meaning that different individuals may require different doses of Botox. The effect will last up to 120 days.[25,26]

SAFETY

Botox is a drug with a broad margin of safety (lethal dose 50% (LD50) in humans can reach up to 40 U/kg BW). Therefore, its use in cosmetics is relatively safe. Botox is relatively safe and effective for treating facial wrinkles.27,28 Botox A does not cause persistent changes at the nerve terminals and targeted muscles.

SIDE EFFECTS

The possible side effects of Botox include bleeding, swelling, erythema and pain at the injection sites.[31]These side effects can be avoided by using thinner needles and diluting Botox with saline. Headaches may also occur following Botox injections but will resolve after 2–4 weeks. This side effect can be treated using systemic analgesics.[27,28] Other side effects that have also been reported to occur include malaise, nausea, influenza-like symptoms and ptosis.[31]

COMPLICATIONS

The most common complications are ecchymosis and purpura, which could be minimized by compressing ice on the injection sites before and after Botox injection.[27,28] Botox should be injected in minimal concentrations, with the appropriate dose and injected at least 1 cm from the superior, inferior or lateral margin of the orbital bone. Following treatment, patients should not manipulate the injected sites for 2–3 hrs and should remain in an upright seating or standing position for 3–4 hrs.[35]

CONCLUSION

The clinical applications of BoNT are extensive as it is used across different medical specialties. The prevention of acetylcholine release at cholinergic junctions makes BoNT effective in the treatment and management of numerous conditions characterized by hyperactivity of muscles and glands.

REFERENCE

1. Trindade de Almeida AR, Secco LC, Carruthers A. Handling botulinum toxins: an updated literature review. Dermatol Surg. 2011;**37**(11):1553–1565.
2. Awan KH. The therapeutic usage of botulinum toxin (Botox) in non-cosmetic head and neck conditions – an evidence based review. Saudi Pharm J. 2017;**25**(1):18–24. doi: 10.1016/j.jsps.2016.04.024
3. Rohrer TE, Beer K. Background to botulinum toxin In: Carruthers A, Carruthers J, editors. Botulinum Toxin. USA: Elsevier Inc.; 2005:9–18
4. Carruthers A, Carruthers J. Botulinum toxin In: Bolognia JL, Jorizzo JL, Rapini RP, editors. Dermatology. 2nd ed. New York: Mosby Elsevier; 2008:2381–2390.
5. Glogau RG. Botulinum toxin In: Wolf K, Goldsmith LA, Kartz SI, Gilchrest BA, Paller AS, Leffell DJ, editors. Fitzpatrick's Dermatology in General Medicine. 7th ed. New York: McGraw Hill; 2008:2389–2395
6. Flynn TC. Advances in the use of botulinum neurotoxins in facial esthetics. J Cosmet Dermatol. 2012;**11**(1):42–50. doi: 10.1111/j.1473-2165.2011.00593.x
7. Klein AW. Complications with the use of botulinum toxin. Dermatol Clin. 2004;**22**(2):197–205
8. Markey AC. Botulinum A exotoxin in cosmetic dermatology. Clin Exp Dermatol. 2000;**25**(3):173–175.
9. Rzany B, Zielke H. Overview of botulinum toxin In: de Maio M, Rzany B, editors. Botulinum Toxin in Aesthetic Medicine. New York: Springer-Verlag Berlin Heidelberg; 2007:1–10
10. Wollina U, Konrad H, Petersen S. Botulinum toxin in dermatology–beyond wrinkles and sweat. J Cosmet Dermatol. 2005;**4**(4):223–227. doi: 10.1111/j.1473-2165.2005.00195.x
11. Khawaja HA, Hernandez-Perez E. Botox in dermatology. Int J Dermatol. 2001;**40**(5):311–317.
12. Lowe NJ. Minimally invasive treatments and procedures for aging skin In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rook's Textbook of Dermatology. 8th ed. London: Blackwell Publishing; 2010:80.1–80.14
13. Joel LC, Freeman SR. Botulinum toxins In: Draelos ZD, editor. Cosmetic Dermatology Products and Procedures. Oxford: Blackwell Publishing; 2010:342–351
14. Raspaldo H, Niforos F-R, Gassia V, et al.; Consensus Group. Lower-face and neck antiaging treatment and prevention using onabotulinumtoxin A: the 2010 multidisciplinary French consensus–part 2. J Cosmet Dermatol. 2011;**10**(2):131–149. doi: 10.1111/j.1473-2165.2011.00560.x.

15. Michael AC, Kane MD. Botox injections for lower facial rejuvenation. Oral Maxillofac Surg Clin North Am. 2005;**17**(1):41–49. doi: 10.1016/j.coms.2004.09.003
16. Cohen JL, Dayan SH, Cox SE, Yalamanchili R, Tardie G. Onabotulinumtoxin A dose-ranging study for hyperdynamic perioral lines. Dermatol Surg. 2012;**38**(9):1497–1505. doi: 10.1111/j.1524-4725.2012.02456.
17. Rzany B. Requirements and rules In: Philipp M, editor. Botulinum Toxin in Aesthetic Medicine. Berlin: Springer; 2007:21–24.
18. Gart MS, Gutowski KA. Overview of botulinum toxins for aesthetic uses. Clin Plast Surg. 2016;43(3):459–471. doi: 10.1016/j.cps.2016.03.003
19. Cula GO, Bargo PR, Nkengne A, Kollias N. Assessing facial wrinkles: automatic detection and quantification. Skin Res Technol. 2013;19(1):e243–e251. doi: 10.1111/j.1600-0846.2012.00635.
20. Simon C, Resto V, Quinn FB Jr, Quinn MS. Botulinum Toxin for Cosmetic Use. USA: UTMB Health ; 2010.
21. Bauman L. Botulinum toxin In: Baumann L, Elsaie ML, Grunebaum L, editors. Cosmetic Dermatology. 2nd ed. New York: McGraw Hill; 2009:169–190.
22. de Maio M, Rzany B. Injection technique In: Rzany B, editor. Botulinum Toxin in Aesthetic Medicine. New York: Springer-Verlag Berlin Heidelberg; 2007:25–26
23. Carruthers JA, Lowe NJ, Menter MA, et al. A multicenter, double-blind, randomized, placebo-controlled study of the efficacy and safety of botulinum toxin type A in the treatment of glabellar lines. J Am Acad Dermatol. 2002;**46**(6):840–849
24. Krishtul A, Waldorf HA, Blitzer A. Complications of cosmetic botulinum toxin therapy In: Carruthers A, Carruthers J, editors. Botulinum toxin. USA: Elsevier Inc.; 2005:12132
25. Klein AW. Contraindications and complications with the use of botulinum toxin. Clin Dermatol. 2004;**22**(1):66–75. doi: 10.1016/j.clindermatol.2003.12.026
26. Carruthers A, Carruthers J. Upper face treatment In: Carruthers A, Carruthers J, editors. Botulinum Toxin. 1st ed. Philadelphia: Elsevier Saunders; 2005:31–43
27. Ascher B, Talarico S, Cassuto D, et al. International consensus recommendations on the aesthetic usage of botulinum toxin type A (Speywood Unit)–part II: wrinkles on the middle and lower face, neck and chest. J Eur Acad Dermatol Venereol. 2010;**24**(11):1285–1295. doi: 10.1111/j.1468-3083.2010.03728.
28. Maio M, Rzany B. Patient selection In: Acquilla R, Patel T, Gonzales M, editors. Botulinum Toxin in Aesthetic Medicine. New York: Springer; 2007:11–19.
29. Carruthers A, Carruthers J, Said S. Dose-ranging study of botulinum toxin type A in the treatment of glabellar rhytids in females. Dermatol Surg. 2005;**31**(4):414–422.
30. Hexsel C, Hexsel D, Porto MD, Schilling J, Siega C. Botulinum toxin type A for aging face and aesthetic uses. Dermatol Ther. 2011;**24**(1):54–61. doi: 10.1111/j.1529-8019.2010.01378.x
31. Cohen JL, Freeman SR. Botulinum toxins In: Draelos ZD, editor. Cosmetic Dermatology Products & Procedures. U: nited Kingdom: Wiley-Blackwell Publishing Ltd; 2010.