

RISK OF COMPLICATIONS ASSOCIATED WITH BOTULINUM TOXIN (BoNT) INJECTIONS

People ask, Should I get a Botulinum Toxin Treatment? It's always a risk vs benefit decision.



Figure 1. Concerned Woman

This question may relate to either cosmetic/aesthetic procedure or medical/therapeutic procedures. What's the difference? And what should I know?

Botulinum neurotoxins [BoNT or BTX] are commonly referred to by their brand names, the most common being Botox® [Allergan/Abbvie]. Others approved for use in the US include Dysport® [Galderma/Ipsen], Xeomin® [Merz] or Jeaveau® [Evolus].

We often think of the cosmetic use of BoNT for reducing the appearance of wrinkles. However over 55% of sales are used to treat medical conditions (1). BoNT is approved for use in

12 indications (2). The most common medical uses cover muscle spasticity, migraine headache, hyperhidrosis (over-active sweating), bladder dysfunction (over-active bladder – OAB) or other muscle disorders such as cervical dystonia, blepharospasm, strabismus, and cerebral palsy.

For rare but serious life-threatening conditions, the FDA requires that commercial BoNT products carry a Black Box Warning (3). Conversely, the most common afflictions are transient and considered mild. In both instances, many of the adverse effects (AEs) are due to spread of toxin. In less concerning AE's, spread is localized and limited to nearby muscles. Other side effects may include headache, injection site reactions and bruising.

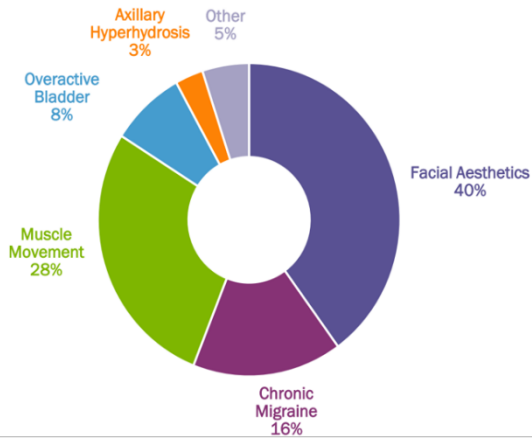


Figure 2. Split of Revenues 2017, Worldwide (1)

BoNTs cause muscle paralysis or muscle weakness by blocking neurotransmitter release. Neuromuscular complications may arise either from poor injection technique, excessive dosing or unexpected toxin diffusion. Whether it's an aesthetic or therapeutic procedure, the spread of toxin may result in some distressing conditions. Albeit, temporary, these may last weeks to months, with no available remedy (4).

Ultimately, the patient has no control over recovery and must wait for the paralytic effect of the toxin to dissipate or wear off.

Concern over AEs hinders the adoption of BoNT procedures. Did you know that in aesthetic uses, market penetration is only 7%? (5). This means, only a small fraction of the population that would qualify for a procedure, commits to a treatment. Hesitancy is attributed to many factors including cost, risk, and overall uncertainty or fear. According to , [Fortune Business Insights](#), the growth of the market for BoNTs is expected to be restrained by the relative side effects (6). In therapeutic uses, the dose of BoNT is higher and the risk of an adverse event is 33 times greater! (7).ⁱ

In addition to the common adverse effects associated with any injection, such as allergic reactions, bruising or mild pain; the longer lasting, undesirable conditions are associated with the action of the drug itself causing off-target or undesirable paralysis or muscle weakness.

Although the literature reports varying incidence of such adverse effects, the skill of the injector (medical professional) is significant, along with superior knowledge of muscle function and location. I have been told that even in the most expert hands, things can go wrong. As noted by Dr. Levine “I always advise my patients that you can always add to Botox but you can’t take away,” According to Dr. [Levine](#) “It is better to inject less and return in two weeks for more than put too much to begin with and then need to wait a full three months for the effects to wear off.”(8) Furthermore, not only is there an intuitive notion that complication rates are underestimated – ie nobody wants to admit to having a botched case or bring attention to it; there is clinical evidence of an underestimation. (9) (11) In aesthetic treatments the most common neuromuscular adverse effect is ptosis (droopy eye). Other reported complications and side-effects are listed in the table below, including those in medical/therapeutic procedures.

Possible Transient Adverse Effects following a BoNT(e.g. Botox®) Treatment			
Cosmetic/Aesthetic Applications	Incidence %	Medical/Therapeutic Applications	Incidence %
Ptosis (drooping) of the eye (or eyebrow)	5.4 (11)	Muscle weakness (requiring a brace)	19-39 (12)
Elevated (Spock Brow) eyebrow	-	Difficulty Swallowing, Difficulty Chewing	19-27 (13)
Misalignment (eg. Lips)	-	Difficulty Breathing (dyspnea)	18 (14)
Drooling (Lips)	-	Difficulty Gripping – post hyperhidrosis therapy	25-30 (15)
Un-natural look (Frozen Face)	-	Urinary Retention (requiring catheterization) – post OAB therapy	9-35 (16)

You should be aware, that many publications in the medical community, suggest such complications are mild and short-lived – yes, even though these can last weeks to months! (17) What if it happens to you?

Would you say – not a problem? Really? Let’s reflect on the negative experience posted by influencer and blogger, Whitney Buha, which made headlines in 2021 (18) and is depicted in her Instagram post (@somethingwhitty) .



A straightforward review is published by the [Huffington Post](#), (19)“What to do if you got botox and hate it”. The article (updated 2018) quotes, Dr. Stafford Broumand, of 740 Park Plastic Surgery in New York. “Botox can’t be removed or dissolved, Broumand said “There is not a way to undo [its effects], but rather we have to wait for the body to create new receptors when the Botox wears off,” he explained. Just as the treatment gradually

kicks in, the effects of Botox gradually fade. It can take anywhere from three to five months, according to Yagoda. But eventually, the muscle activity comes back. The concluding recommendation is to consult with a certified plastic surgeon.

Much to consider>> Wouldn’t it be nice to have a Do-Over? Just in Case? >>>>>>>



References

- (1) Revance Investor Presentation, 2017
- (2) Brin, M. F., James, C., & Maltman, J. (2014). Botulinum toxin type A products are not interchangeable: a review of the evidence. *Biologics : targets & therapy*, 8, 227–241. <https://doi.org/10.2147/BTT.S65603>
- (3) Kuehn B. M. (2009). FDA requires black box warnings on labeling for botulinum toxin products. *JAMA*, 301(22), 2316. <https://doi.org/10.1001/jama.2009.780>
- (4) Walker, T. J., & Dayan, S. H. (2014). Comparison and overview of currently available neurotoxins. *The Journal of clinical and aesthetic dermatology*, 7(2), 31–39.
- (5) Revance, Investor Presentation March 2019, p. 13
- (6) <https://www.fortunebusinessinsights.com/industry-reports/botulinum-toxin-market-100996>
- (7) Witmanowski, H., & Błochowiak, K. (2020). The whole truth about botulinum toxin - a review. *Postepy dermatologii i alergologii*, 37(6), 853–861. <https://doi.org/10.5114/ada.2019.82795>
- (8) New Beauty. Liz Ritter, Executive Editor · Nov 11, 2021, 11 Signs You Just Got ‘Bad Botox’ <https://www.newbeauty.com/signs-of-bad-botox>
- (9) Zargaran, D., Zoller, F. E., Zargaran, A., & Mosahebi, A. (2022). Complications of facial cosmetic botulinum toxin A injection: analysis of the UK Medicines & Healthcare Products Regulatory Agency registry and literature review. *Journal of plastic, reconstructive & aesthetic surgery : JPRAS*, 75(1), 392–401. <https://doi.org/10.1016/j.bjps.2021.05.074>
- (10) Yiannakopoulou E. (2015). Serious and long-term adverse events associated with the therapeutic and cosmetic use of botulinum toxin. *Pharmacology*, 95(1-2), 65–69. <https://doi.org/10.1159/000370245>
- (11) Dayan S. H. (2013). Complications from toxins and fillers in the dermatology clinic: recognition, prevention, and treatment. *Facial plastic surgery clinics of North America*, 21(4), 663–673. <https://doi.org/10.1016/j.fsc.2013.07.008>
- (12) Phadke, C. P., Balasubramanian, C. K., Holz, A., Davidson, C., Ismail, F., & Boulias, C. (2016). Adverse Clinical Effects of Botulinum Toxin Intramuscular Injections for Spasticity. *The Canadian journal of neurological sciences. Le journal canadien des sciences neurologiques*, 43(2), 298–310. <https://doi.org/10.1017/cjn.2015.314>
- (13) Patterson, A., Almeida, L., Hess, C. W., Martinez-Ramirez, D., Okun, M. S., Rodriguez, R. L., Rundle-Gonzalez, V., Wagle Shukla, A., & Malaty, I. A. (2016). Occurrence of Dysphagia Following Botulinum Toxin Injection in Parkinsonism-related Cervical Dystonia: A Retrospective Study. *Tremor and other hyperkinetic movements (New York, N.Y.)*, 6, 379. <https://doi.org/10.7916/D8GB24C5>
- (14) Coté, T. R., Mohan, A. K., Polder, J. A., Walton, M. K., & Braun, M. M. (2005). Botulinum toxin type A injections: adverse events reported to the US Food and Drug Administration in therapeutic and cosmetic cases. *Journal of the American Academy of Dermatology*, 53(3), 407–415. <https://doi.org/10.1016/j.jaad.2005.06.011>
- (15) Swartling, C., Färnstrand, C., Abt, G., Stålberg, E., & Naver, H. (2001). Side-effects of intradermal injections of botulinum A toxin in the treatment of palmar hyperhidrosis: a neurophysiological study. *European journal of neurology*, 8(5), 451–456. <https://doi.org/10.1046/j.1468-1331.2001.00261.x>
- (16) Osborn, D. J., Kaufman, M. R., Mock, S., Guan, M. J., Dmochowski, R. R., & Reynolds, W. S. (2015). Urinary retention rates after intravesical onabotulinumtoxinA injection for idiopathic overactive bladder in clinical practice and predictors of this outcome. *Neurourology and urodynamics*, 34(7), 675–678. <https://doi.org/10.1002/nau.22642>
- (17) <https://www.glowday.com/blog/what-is-ptosis>
- (18) BuzzFeed News Mar 26 2021, <https://www.buzzfeednews.com/article/stephaniemcneal/influencer-botched-botox>
- (19) HuffPost, Julia Brucculierin Sep. 25, 2018, https://www.huffpost.com/entry/what-to-do-if-you-got-botox-and-hate-it_n_5ba2a159e4b0181540d9b349



¹ See DelNova WhitePaper, <https://www.lifesciencesreview.com/whitepaper/>
<https://www.ciowhitepapersreview.com/pharma-life-sciences/risk-of-complications-associated-with-botulinum-toxin-bont-injections-1019.html>