

COMPLICATIONS AND SAFETY IN THE USE OF BOTULINUM TOXIN TYPE-A (BoNT-A) FOR AESTHETIC PURPOSES

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Abstract: Botulinum toxin type-A (BoNT-A) is used to treat an increasingly wide range of indications. Although the toxin is generally considered healthy in controlled doses, its extensive use raises safety concerns. The main objective of this study was to present a guide on complications and safety measures when injecting botulinum toxin type-A for aesthetic purposes. This is a bibliographic review study. Searches were carried out in the PubMed, SciElo and LILACS databases to identify articles on the topic. Articles on complications and safety in the use of BoNT-A in the last 10 years (2012 to 2022) were considered eligible for the review. It was possible to observe that several factors must be taken into consideration by professionals working in the area of aesthetic health. Starting with the choice of products to be used, always looking for the best inputs from trusted brands and companies, the esthete must seek the best for his patients, carrying out a quality anamnesis, investigating clinical and psychological issues, thus getting to know the individual to be treated as thoroughly as possible. It is extremely important for professional success to have mastery of the techniques used, theoretical-practical knowledge of possible complications and, also, of the protocols that must be adopted in the different possibilities, resulting in safe and effective procedures for all parties involved.

Keywords: Botulinum toxin type-A. BoNT-A. Complications. Security. Aesthetics.

INTRODUCTION

Since the first reports in 1994 of the effectiveness of botulinum toxin type-A (BoNT-A) in reducing the appearance of facial wrinkles, it has been widely used for various cosmetic indications (Rohrer and Beer, 2005). BoNT-A is a potent neurotoxin produced by the bacteria *Clostridium botulinum* that causes muscle paralysis by blocking

synaptic neurotransmission. Its therapeutic and aesthetic use arises from this ability to selectively weaken or paralyze the injected muscle group. As the effects of BoNT-A diminish over time, repeated injections are required to maintain the treatment effect (Erickson et al, 2015).

Currently, botulinum toxin injections are the most commonly performed non-invasive procedure for facial rejuvenation (Klein, 2004; Sethi et al, 2021). The therapeutic use of botulinum toxin has generally been safe and well tolerated. In most cases, the adverse effects caused by the use of the substance are considered mild, transient and self-limited. However, like all other injectable procedures, this is also susceptible to adverse events and more serious complications (Sundaram et al, 2016).

Botulinum toxin type-A is used to treat an increasing range of indications, including glabellar frown lines, smile lines, horizontal forehead lines, wrinkles around the lips (smoker's lines), marionette lines, platysmal bands on the neck, in addition to being used for therapeutic indications such as strabismus, blepharospasm, cervical dystonia, hyperhidrosis and synkinesis after facial surgery. Although the toxin is generally considered healthy in controlled doses, its extensive use raises safety concerns (Trindade de Almeida et al, 2011; Awan, 2017; Rzany and Zielke, 2007).

The main objective of this study was to present a guide on complications and safety measures when injecting botulinum toxin type-A for aesthetic purposes. To this purpose, we carried out a review on the topic based on a systematic search of the literature.

MATERIAL AND METHODS

This is a bibliographic review study. Searches were carried out in the databases of PubMed, SciElo (Scientific Electronic Library Online)

and LILACS (Latin American and Caribbean Literature in Health Sciences) to identify articles on the topic. The review protocol was defined a priori to standardize the search. In this sense, the following descriptors were selected: Botulinum toxin type-A or BoNT-A, Complications, Safety and Aesthetic. These descriptors were used in the search in English accompanied by Boolean operators: (AND) and (OR). The complete search in the databases was constructed using the following combination: Botulinum toxin type-A OR BoNT-A AND Complications AND Safety AND Aesthetic. Articles on complications and safety in the use of BoNT-A in the last 10 years (2012 to 2022) were considered eligible for the review.

RESULTS

In the SciELO and LILACS databases, only one article was found in each of them, both in Portuguese and were therefore excluded from the research. In the Pubmed database, 81 articles were found, however, 61 were not available for free, leaving 20 articles. After reading all the abstracts, it was found that 10 of them were not appropriate to the topic, leaving 10 works, which were read in full. After this stage, two more articles were excluded for not covering the topic broadly, reaching the final number of 8 selected articles (Figure 1).

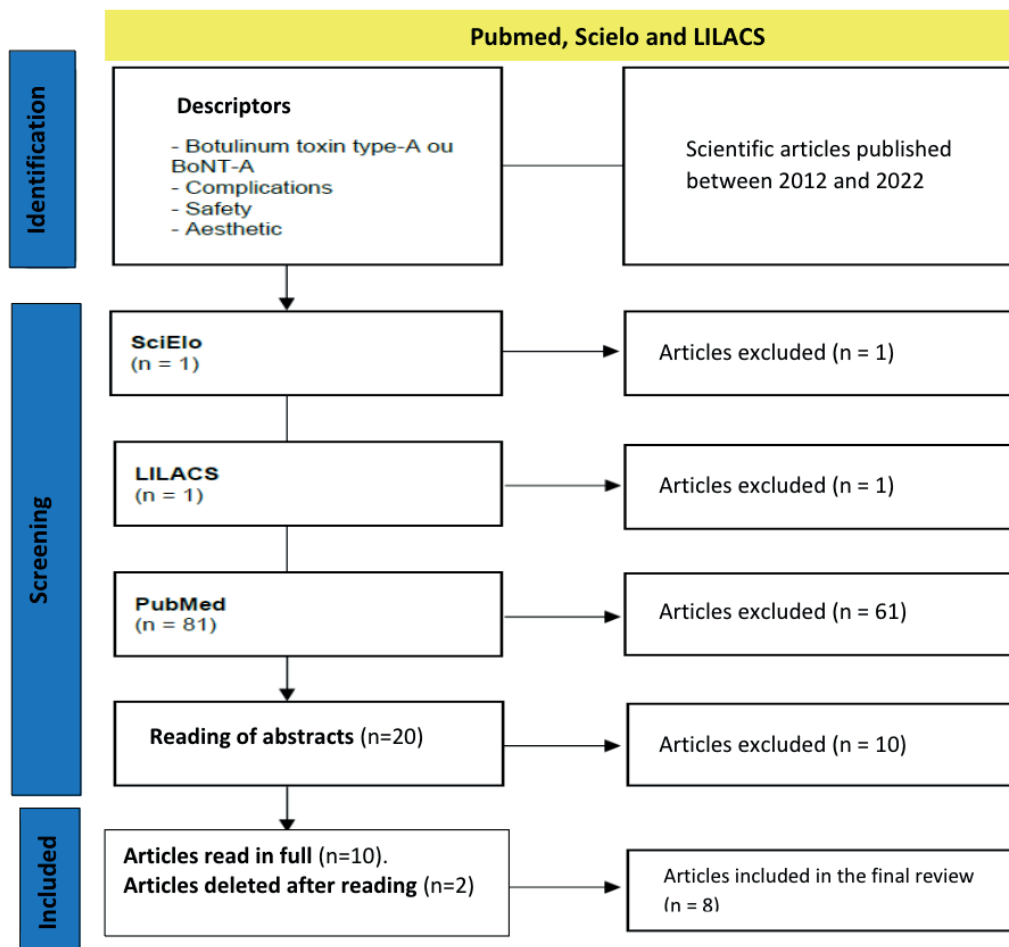


Figure 1: PRISMA flowchart for article selection.

DISCUSSION

In the literature there are few reports on serious or fatal complications resulting from the cosmetic use of botulinum toxin type-A. Complications basically depend on the technique and inputs used, which is why it is important to have adequate knowledge and training to carry out the applications. According to Borba and collaborators (2022), when safety zones are respected, the chance of complications is practically zero. However, the effects of the toxin may spread to non-target muscles, depending on the product used and the area treated. This may alter the location of the clinical effect and increase adverse effects. As reported by the same authors, the main complications secondary to BoNT-A injections in the upper face are: eyelid or superciliary ptosis, eyebrow asymmetry, diplopia, lagophthalmos, eyelid ectropion and prominence of the eyelid bags. To avoid such complications, it is important to have a vast knowledge of the anatomy of this region and adequate and individualized planning based on the existing patterns of the frontal, procerus and orbicularis oculi muscles (Borba et al, 2022).

In another study that aimed to provide an overview of the side effects related to BoNT-A, in addition to advising and outlining preventive strategies, it was reported that there are two classes of adverse events related to the use of the toxin: benign transient events and potentially serious. Benign side effects are well-localized, reversible, and self-limited complications that develop within a few days of injection and usually disappear without any treatment. Serious events basically consist of anaphylactic reactions and/or sequelae resulting from the systemic dissemination of the toxin leading to botulism, which is a rare, non-contagious neuroparalytic disease caused by the action of the toxin produced by the bacterium *Clostridium botulinum*, from

which the drug. The authors also highlight that aesthetic and functional adverse effects are associated with different muscular responses to botulinum toxin or poor positioning of the substance at the injection site and that the frequency of serious side effects is 33 times greater for therapeutic cases than for cosmetic uses. (Henryk Witmanowski and Katarzyna Błochowiak, 2020).

Sethi and collaborators (2021) published an interesting review article, where a large number of cases (9,398) were analyzed to study the safety of the toxin when used for aesthetic indications. They reinforced that the incidence of most complications remains low and, in most cases, these complications are mild, reversible and self-limited, corroborating other articles cited previously (Borba, et al, 2022; Henryk Witmanowski and Katarzyna Błochowiak, 2020). Headache was the most commonly reported adverse condition (5.38%), followed by nasopharyngitis (3.08%) and hypersensitivity reaction (2.90%). The frequently reported headache may be related to the injection procedure for different causes, such as periosteal trauma, intramuscular hematomas, anxiety in new patients and temporary muscle spasm. Nasopharyngitis may possibly occur as an acute immunological response to the inoculation of the toxin in regions close to the nose. Furthermore, in many cases, this is already a previous clinical condition of the patient, in which the condition is chronic. Hypersensitivity reactions, although rarely reported, need to be determined whether they are type I or type IV hypersensitivity reactions or pseudo-allergy reactions. Other confounding factors such as reactions to benzyl alcohol, bacteriostatic serum or antiseptic solutions used to disinfect the skin before the procedure need to be taken into consideration (Sethi et al, 2021).

A study carried out in 2020 addressed the complications of injectable procedures, such

as the application of BoNT-A, in another way, separating them into early and late reactions. The authors considered early complications at the injection site, such as bruising, edema, hypersensitivity, Tyndall effect and intravascular injection. Late complications included type IV hypersensitivity and acute infections such as cellulitis, abscesses, herpes, granulomas, biofilms, and atypical mycobacterial infections. The study highlights that an understanding of detailed facial anatomy, knowledge of the characteristics of all substances used, early identification and treatment options for complications will guarantee optimal results. Furthermore, it ratifies that mastery of injection techniques, awareness of the various complications and their management protocols, means that most complications can be avoided and their incidence minimized, allowing the inevitable to be treated effectively (Kuldeep Singh and Shahin Nooreydzan, 2020).

Some articles addressed the complications of using botulinum toxin type-A in a more specific way, as is the case of the study carried out by Ho and collaborators (2022), where the immunogenicity caused by the use of the medication for both aesthetic and therapeutic purposes was evaluated. There was a consensus that as doses used in aesthetic practice become similar to those in therapeutics, rates of NAb (neutralizing antibodies) formation can be expected to increase. However, the true extent of NAb formation in aesthetics is likely underestimated due to limitations in published evidence and variability in treatment patterns of aesthetic patients. Since BoNT-A therapy is typically lifelong, practitioners using the substance need to recognize immunogenicity as a potential complication that may affect future therapeutic use and strive to minimize risk factors. The selection and use of a brand with proven lower immunogenic potential from the beginning can be advantageous,

especially when a treatment with high doses of the product is planned (Ho et al, 2022).

In the case of Wang and colleagues (2022), a meta-analysis was performed to evaluate the efficacy and safety of BoNT-A injection therapy in the treatment of facial scars. This study demonstrated that the toxin has the potential to improve facial scars with an acceptable safety profile. Only three studies recorded three mild adverse events, two of which occurred in the BoNT-A group and the other in the control group. None of the studies reported serious adverse events. Based on the results, botulinum toxin type-A showed favorable safety when used to treat facial scars (Wang et al, 2022). In another work carried out by Goodman and collaborators (2020), the safety assessment of the use of botulinum toxin for aesthetic purposes was also positive. The authors confirm that the majority of adverse reactions are transient, self-resolving and mild to moderate in severity. They make it clear that injecting professionals must be fully aware of all possible complications, employ known prevention strategies and be able to carry out appropriate corrective treatment. Furthermore, they strongly recommend that treatment with BoNT-A be avoided during pregnancy and breastfeeding due to the lack of adequate data on the developmental risk to a human fetus from use of the toxin in pregnant women. They also highlight that it is not known whether botulinum toxin is excreted in human breast milk (Goodman et al, 2020).

Kattimani and collaborators (2019) briefly point out in their work an issue that is little analyzed, but which has important relevance, which is the professional's sensitivity to the patient's psychological issues. Avoiding this type of treatment in people who have mental comorbidities such as cognitive impairment, severe depression, dysmorphic disorder and even individuals who create

irrational expectations are crucial factors for the successful treatment of aesthetic patients (Kattimani et al, 2019).

When analyzing the possible complications arising from the use of botulinum toxin type-A, it was possible to observe that several factors must be taken into consideration by professionals working in the area of aesthetic health. Starting with the choice of products to be used, always looking for the best inputs from trusted brands and companies, the esthete must seek the best for his patients, carrying out a quality anamnesis, investigating clinical and psychological issues, thus getting to know the individual to be treated as thoroughly as possible. Some aspects, despite seeming irrelevant at first glance, can be crucial for solving problems that may arise during the process. Furthermore, as highlighted several times by all the studies evaluated, in-depth knowledge of the various

possible complications and the anatomy of the area that will undergo intervention will help aesthetic professionals to become increasingly safer injectors.

CONCLUSION

Botulinum toxin type-A used for aesthetic indications is gaining considerable popularity in recent years due to relatively consistent clinical effects with minimal complications and rapid recovery time compared to cosmetic surgery. As toxin use becomes increasingly common, the absolute number of different types of adverse events is expected to increase. Therefore, it is extremely important for professional success to have mastery of the techniques used, theoretical-practical knowledge of possible complications and, also, of the protocols that must be adopted in the different possibilities, resulting in safe and effective procedures for all involved parties.

REFERENCES

- Awan KH. The therapeutic usage of botulinum toxin (Botox) in non-cosmetic head and neck conditions—an evidencebased review. **Saudi Pharm J.** 2017. 25(1):18–24.
- Borba A, Matayoshi S, Rodrigues M. Avoiding Complications on the Upper Face Treatment With Botulinum Toxin: A Practical Guide. **Aesthetic Plast Surg.** 2022 Feb;46(1):385-394. doi: 10.1007/s00266-021-02483-1. Epub 2021 Aug 2. PMID: 34341857; PMCID: PMC8328485.
- Erickson BP, Lee WW, Cohen J, Grunebaum LD. The role of neurotoxins in the periorbital and midfacial areas. **Facial Plast Surg Clin North Am.** 2015;23:243–255. doi: 10.1016/j.fsc.2015.01.010.
- Goodman GJ, Liew S, Callan P, Hart S. Facial aesthetic injections in clinical practice: Pretreatment and posttreatment consensus recommendations to minimise adverse outcomes. **Australas J Dermatol.** 2020 Aug;61(3):217-225. doi: 10.1111/ajd.13273. Epub 2020 Mar 22. PMID: 32201935; PMCID: PMC7497045.
- Ho WWS, Albrecht P, Calderon PE, Corduff N, Loh D, Martin MU, Park JY, Suseno LS, Tseng FW, Vachiramon V, Wanitphakdeedecha R, Won CH, Yu JNT, Dingley M. Emerging Trends in Botulinum Neurotoxin A Resistance: An International Multidisciplinary Review and Consensus. **Plast Reconstr Surg Glob Open.** 2022 Jun 20;10(6):e4407. doi: 10.1097/GOX.0000000000004407. PMID: 35747253; PMCID: PMC9208887.
- Kattimani V, Tiwari RVC, Gufran K, Wasan B, Shilpa PH, Khader AA. Botulinum Toxin Application in Facial Esthetics and Recent Treatment Indications (2013-2018). **J Int Soc Prev Community Dent.** 2019 Mar-Apr;9(2):99-105. doi: 10.4103/jispcd.JISPCD_430_18. Epub 2019 Apr 12. PMID: 31058058; PMCID: PMC6489509.
- Klein AW. Contraindications and complications with the use of botulinum toxin. **Clin Dermatol.** 2004 Jan-Feb;22(1):66-75. doi: 10.1016/j.clindermatol.2003.12.026. PMID: 15158548.

Rohrer TE, Beer K. Background to botulinum toxin In: Carruthers A, Carruthers J, editors. **Botulinum Toxin. USA**: Elsevier Inc.; 2005:9–18.

Rzany, B., Zielke, H. Overview of Botulinum Toxin. In: de Maio, M., Rzany, B. (eds) **Botulinum Toxin in Aesthetic Medicine**. Springer, Berlin, Heidelberg. 2007. https://doi.org/10.1007/978-3-540-34095-9_1

Sethi N, Singh S, DeBouille K, Rahman E. A Review of Complications Due to the Use of Botulinum Toxin A for Cosmetic Indications. **Aesthetic Plast Surg**. 2021 Jun;45(3):1210-1220. doi: 10.1007/s00266-020-01983-w. Epub 2020 Oct 13. Erratum in: **Aesthetic Plast Surg**. 2022 Feb;46(1):595. PMID: 33051718.

Singh K, Nooreydzan S. Nonvascular Complications of Injectable Fillers- Prevention and Management. **Indian J Plast Surg**. 2020 Dec;53(3):335-343. doi: 10.1055/s-0040-1721872. Epub 2020 Dec 24. PMID: 33500603; PMCID: PMC7822713.

Sundaram H, Signorini M, Liew S, Trindade de Almeida AR, Wu Y, Vieira Braz A, Fagien S, Goodman GJ, Monheit G, Raspaldo H; Global Aesthetics Consensus Group. Global Aesthetics Consensus: Botulinum Toxin Type A--Evidence-Based Review, Emerging Concepts, and Consensus Recommendations for Aesthetic Use, Including Updates on Complications. **Plast Reconstr Surg**. 2016 Mar;137(3):518e-529e. doi: 10.1097/01.prs.0000475758.63709.23. PMID: 26910696; PMCID: PMC5242214.

Trindade de Almeida AR, Secco LC, Carruthers A (2011) Handling botulinum toxins: an updated literature review. **Dermatol Surg**. 37(11):1553–1565.

Wang W, Liu G, Li X. The Efficacy and Safety of Botulinum Toxin Type A Injections in Improving Facial Scars: A Systematic Review and Meta-Analysis. **Pharmacology**. 2022;107(5-6):241-249. doi: 10.1159/000522396. Epub 2022 Mar 30. PMID: 35354154.

Witmanowski H, Błochowiak K. The whole truth about botulinum toxin – a review. **Postepy Dermatol Alergol**. 2020 Dec;37(6):853-861. doi: 10.5114/ada.2019.82795. Epub 2019 Feb 5. PMID: 33603602; PMCID: PMC7874868.