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## SUMMARY

This study aims to analyze the efficacy of botulinum toxin type A for rejuvenating the upper third of the face, highlighting its aesthetic, clinical, and social effects. To this end, a qualitative literature review was conducted, based on recent studies investigating serial application of the substance, describing clinical criteria, administration techniques, doses used, and observed results. The analysis showed that botulinum toxin promotes relaxation of facial muscles, smoothing of dynamic wrinkles, and significantly improves facial harmony and rejuvenation, with a low complication rate and high patient satisfaction. In addition to its safety and efficacy, the use of the toxin reflects the growing acceptance of minimally invasive aesthetic procedures, in line with the social demand for resources that combine rapid, natural-looking results with minimal post-procedure recovery. In this way, the research contributes to the consolidation of scientific knowledge on the use of botulinum toxin in aesthetic biomedicine, providing support for the training of qualified professionals and encouraging safe, ethical and effective clinical practices.

**Keywords:** Botox, *Clostridium botulinum*, aesthetics, rejuvenation.

## ABSTRACT

This study aims to analyze the effectiveness of Botulinum Toxin Type A application in the rejuvenation of the upper third of the face, highlighting its aesthetic, clinical, and social effects. A qualitative literature review was conducted, based on recent studies that investigated the serial application of the substance, describing clinical criteria, administration techniques, dosages used, and observed outcomes. The analysis showed that botulinum toxin promotes facial muscle relaxation, softening of dynamic wrinkles, and significant improvement in facial harmony and rejuvenation, with a low rate of complications and high patient satisfaction. In addition to its safety and efficacy, the use of the toxin reflects the growing acceptance of minimally invasive aesthetic procedures, in line with the social demand for approaches that combine quick, natural results with minimal recovery time.

Therefore, this research contributes to strengthening scientific knowledge on the use of botulinum toxin in aesthetic biomedicine, providing support for the training of qualified professionals and encouraging safe, ethical, and effective clinical practices.

**Keywords:** Aesthetics, botox, *Clostridium botulinum*, rejuvenation.

## 1. INTRODUCTION

The skin is the largest organ in the human body, with an estimated area of approximately 1.5 to 2 m<sup>2</sup> in adults, performing essential physical barrier functions against external agents (micro-organisms, ultraviolet rays, pollutants), thermal regulation, sensory perception and selective absorption of substances. Furthermore, it directly reflects signs of aging, nutritional status, hormonal balance, hydration, oxidative stress and general well-being, serving as visible indicator of the individual's health (FERREIRA, 2021).

With advancing age, there is a gradual and progressive decline in cellular mechanisms of protection and repair, reducing the skin's regenerative capacity. Internal factors, such as decreased



**Year V, v.2 2025 | submission: October 17, 2025 | accepted: October 19, 2025 | published: October 21, 2025**

the production of collagen types I and III, elastin and hyaluronic acid, as well as metabolic changes, hormonal changes and accumulation of free radicals, promote loss of firmness, elasticity, shine and hydration. Fine wrinkles, static and dynamic expression lines, sagging skin and irregular texture appear. Furthermore, there is dermal thinning, decreased vascularization, and increased sensitivity to radiation. ultraviolet and susceptibility to oxidative damage, favoring visual signs of aging (TRINDADE, 2022).

These intrinsic aging processes are enhanced by extrinsic factors.

continuous and unprotected sun exposure stimulates the degradation of collagen and elastin through the action of enzymes such as metalloproteinases, in addition to generating free radicals; smoking contributes to stress chronic oxidative stress and vasoconstriction, reducing blood supply; environmental pollution, diet deficient in antioxidants, excessive alcohol consumption, inadequate sleep and

A sedentary lifestyle worsens metabolic and cellular functioning. Such external factors accelerate the loss tone, the formation of deep wrinkles, dry skin and sagging. In short, the

Skin aging is multifactorial, resulting from the interaction between genetics, chronology and environment (ROCHA; BAIENSSE, 2023).

In this scenario, the demand for minimally invasive aesthetic procedures is growing significantly.

invasive, which can offer visible facial rejuvenation results with low risk, less pain, shorter recovery time and less impact on the patient's routine, compared to surgeries conventional plastic surgery. Among these procedures, botulinum toxin type A (TBA / BoNT-A) has emerged as one of the most effective and widespread methods for treating dynamic wrinkles, fine lines expression, especially in the upper third of the face (frontal, glabellar and crow's feet region), and for preventive aging purposes (AMORIM et al., 2024).

TBA is a neurotoxin produced by the bacterium *Clostridium botulinum*, whose action consists of inhibition of acetylcholine release at neuromuscular junctions, preventing muscle contraction in a segmental and reversible manner. This muscle relaxation leads to the attenuation of dynamic wrinkles, reduction in the formation of static wrinkles over time and visual improvement of the facial contour.

The preventive benefits of using BoNT-A at earlier ages suggests that interventions initial treatments can delay the appearance of fixed signs of aging (static lines). This preventive approach requires careful assessment of risk, dose, frequency and clinical monitoring (MARINELLI et al., 2023).

The popularization of facial aesthetics with BoNT-A has been reflected in recent epidemiological data. According to the 2025 Brazilian narrative review, the application of botulinum toxin continues to lead the non-surgical aesthetic procedures, with significant growth in the number of treatments globally, indicating a growing population acceptance of these less invasive methods. Especially in Brazil, this phenomenon is intensifying, with a significant number of practices



Year V, v.2 2025 | submission: October 17, 2025 | accepted: October 19, 2025 | published: October 21, 2025

clinics that offer BoNT-A as the predominant aesthetic treatment (DI SANTIS et al., 2024).

Although it is a minimally invasive procedure, BoNT-A is not without risks and complications. Complications ranging from mild effects such as local edema, pain at the injection site, injection and bruising, to more significant effects such as eyelid ptosis, facial asymmetries, reactions allergies and complications in cases of misapplication or use by untrained professionals adequate. Aesthetic complications with BoNT-A were analyzed, emphasizing the importance of technical knowledge, correct patient selection, adequate dosage and follow-up for risk minimization (ALMEIDA; COUTO, 2023).

A recent controlled clinical trial demonstrated that individuals with high levels of physical activity tend to show a reduced duration of the aesthetic effect of BoNT-A, compared to those with moderate or low physical activity, possibly due to increased local metabolism or more intense muscle mobilization (MORHY et al., 2023).

Furthermore, not only the perceptible effects are investigated, but also the impact on facial expressions. Deep neural networks ("deep learning") were used to quantify changes in expressions after application of BoNT-A to the upper face. Significant decreases were observed in expressions of surprise and anger, without relevant impairment of neutral or happy expressions, indicating that the effects of the toxin can subtly modify expressions, which has aesthetic and psychological implications (UGURLU et al., 2024).

Therefore, considering the current scenario, it becomes clear that the application of BoNT-A for aesthetics is part of a multifaceted scenario: not only as a wrinkle corrective method, established, but also as a preventive strategy; with recognized effectiveness when well managed; with potential for complications that should not be neglected; and with the need for personalization, considering variables such as age, skin type, lifestyle, degree of photodamage, professional training and patient expectations (BORBA et al., 2021).

## 2. THEORETICAL FRAMEWORK / RESULTS

Botulinum toxin type A (BoNT-A) remains the gold standard among procedures minimally invasive facial rejuvenation procedures, demonstrating significant progress in its applications and in deepening scientific knowledge about its effects, as evidenced by recent literature (2020-2025).



## 2.1 MECHANISM OF ACTION AND AESTHETIC CONSOLIDATION

BoNT-A is a potent neurotoxin produced by the bacterium *Clostridium botulinum*. Its mechanism of action is highly specific: it acts by blocking the release of the neurotransmitter acetylcholine in cholinergic nerve endings, culminating in chemical denervation temporary and dose-dependent on the treated muscle (BARBOSA; BRITO, 2020; BORBA et al., 2021). This controlled paralysis results in muscle relaxation, which smooths out dynamic wrinkles and prevents the formation of static wrinkles, maintaining the smooth and rejuvenated appearance of the skin (FRASSON, 2023).

The aesthetic use, which was consolidated from the 1990s onwards, received the consent of the Agency National Health Surveillance Agency (ANVISA) in Brazil in the early 2000s, and since then, has expanded enormously, being widely sought after for the treatment of expression lines, especially in the upper third of the face (frontal, glabellar and periorbital regions), due to its high muscle mobility and early formation of lines (FERREIRA, 2021; TRINDADE DE ALMEIDA et al., 2024; PORTUGAL, 2025).

## 2.2 PREVENTIVE APPROACH AND NEW PERSPECTIVES

One of the most notable trends in recent literature (2020-2025) is the emphasis on the preventive use of BoNT-A, often referred to as "Baby Botox" or "Microbotox." This approach consists of application of lower doses and in specific patterns in younger patients (often the from 25-30 years of age, depending on individual clinical needs) who do not yet have wrinkles deep statics. The goal is to reduce muscle hyperactivity and, consequently, slow down the emergence and progression of permanent wrinkles (LEE et al., 2020; MARTINS et al., 2021; ZHANG et al., 2022; FREITAS et al., 2025). Studies suggest that early use is a safe and effective in the short term to prevent aging, promoting maintenance of appearance young naturally (FILHO; SUGUIHARA; MUKNICKA, 2023; FREITAS et al., 2025). In addition Furthermore, technological advances have introduced new tools into clinical practice. Recent research point to the use of Artificial Intelligence (AI) and machine learning for objective assessment and personalized BoNT-A results. AI has been applied to analyze changes in facial expressions, demonstrating the toxin's ability to soften the appearance of expressions negative (such as anger or worry) without compromising the overall naturalness of the face, which allows more refined and predictable treatment planning (UGURLU et al., 2024).



## 2.3 PSYCHOSOCIAL BENEFITS AND QUALITY OF LIFE

The impact of BoNT-A treatment extends significantly beyond the benefits visible aesthetics. Current literature has focused on the psychosocial benefits of the intervention, demonstrating improvements in self-image, confidence, self-esteem and quality of life of patients (LUQUETTI et al., 2024; AMORIM et al., 2024; PATEL et al., 2025). Some studies, even correlate the use of the toxin for aesthetic purposes with the reduction of anxiety levels and depression in the short term, suggesting a positive impact on overall psychological well-being (MAURER et al., 2025; PATEL et al., 2025). This growing awareness of comprehensive benefits reinforces the importance of including patient-reported outcome measures (PROs Outcomes) in clinical studies to capture the complete perspective of the treated individual (PATEL et al., 2025).

## 2.4 SAFETY AND PROFESSIONAL TRAINING

Despite the high safety and efficacy rate, complications such as eyelid ptosis, facial asymmetries, diplopia and xerophthalmia may occur, and are often associated with errors in technique, dosage inadequate or unwanted diffusion of the toxin (KASHIWABUCHI et al., 2025; SILVA; BRAGA, 2023). Therefore, contemporary literature critically emphasizes the importance of mastery anatomical and professional training to ensure ethical and safe clinical practice, minimizing risks and maximizing satisfactory results (ALMEIDA; COUTO, 2023; ARORA; SINGH; ARORA, 2024; KASHIWABUCHI et al., 2025). The need for personalized approaches, adjusted to individual factors such as muscle activity, skin type and genetic predisposition, is highlighted as the path for the future of BoNT-A application (MARINELLI et al., 2023; PATEL et al., 2025).

## 3. MATERIAL AND METHOD

The present study was carefully designed under the aegis of an Integrative Literature Review, a robust methodology that allows the synthesis of multiple primary and secondary research, with the purpose of building a comprehensive and in-depth view of a specific phenomenon. The intrinsic nature of this research is qualitative and descriptive, since its focus was on critical interpretation and content analysis of available evidence, rather than quantification of data. The primary objective was to gather, analyze, and discuss the main scientific discoveries and clinical trends related to the aesthetic application of Botulinum Toxin Type A (BoNT-A) aimed at



**Year V, v.2 2025 | submission: October 17, 2025 | accepted: October 19, 2025 | published: October 21, 2025**

rejuvenation of the upper third of the face.

The execution of the methodological process occurred systematically, covering a defined period three months, between February and April 2025, ensuring the capture of the most scientific production recent and relevant. The search was conducted in highly prestigious electronic databases and recognition in the field of health and biomedicine, namely: PubMed (US National Library of Medicine), SciELO (Scientific Electronic Library Online), Google Scholar, Virtual Library in Health (BVS) and the CAPES Journal Portal. The choice for a combination of databases specialized and comprehensive aimed to mitigate selection bias and ensure maximum recovery of valid studies.

The search strategy was meticulously constructed to be both sensitive and specific.

Controlled descriptors (DeCS/MeSH terms, when applicable) were used and not controlled (free terms), used in Portuguese and English to maximize the reach of the search. The combination of these terms was performed using the Boolean operators “AND” and “OR”, allowing the precise intersection of central concepts.

The thematic axes of the search were centered on four fundamental concepts: the biological agent (“botulinum toxin type A”, “botulinum toxin type A”), the clinical objective (“facial rejuvenation”, “facial rejuvenation”), the clinical manifestation (“dynamic wrinkles”) and the region anatomical area of interest (“upper third of the face”, “upper face”). The articulation of these search strings was decisive in isolating scientific production focused on aesthetic rejuvenation of the forehead, glabella and periorbital area.

The selection of the final corpus for analysis was guided by strict inclusion and exclusion criteria, applied sequentially after the initial search:

**Inclusion Criteria:**

**Temporal Relevance:** Publications dated specifically between January 2020 and April 2025, giving the review a strict focus on cutting-edge evidence.

**Language:** Articles written in Portuguese or English.

**Access:** Availability of the full text of the material for reading and in-depth analysis.

**Thematic Focus:** Studies that directly address the aesthetic application of BoNT-A in the third upper face, including clinical efficacy analysis, details of the injection technique, profile of safety or patient satisfaction assessments (PROs).

**Exclusion Criteria:**

Works that dealt exclusively with therapeutic uses were summarily excluded.

non-aesthetic aspects of the toxin (including neurology, ophthalmology, treatment of hyperhidrosis or bruxism), duplicate articles, event summaries without the full text of the work and all publications prior to the year 2020.



**Year V, v.2 2025 | submission: October 17, 2025 | accepted: October 19, 2025 | published: October 21, 2025**

Initial database screening identified 68 potentially eligible articles. After

screening and rigorous application of exclusion criteria, the final corpus of the review was composed of 10 articles that fully met the established standards.

The data collection phase was carried out through detailed and exhaustive reading of the articles selected, with the extraction and systematization of the following categories of information:

Treatment Protocols: Details of the total dose of toxin units and the dilution strategy employee.

Technical Details: The injection patterns and the specific muscle regions addressed (muscle frontalis, corrugator, procerus, orbicularis oculi).

Clinical Results: The average durability of BoNT-A effects and the efficacy metrics used to quantify muscle relaxation.

Safety and Intercurrences: The nature, frequency and management of the most common adverse events, such as ptosis and asymmetries.

Patient Perception: The degree of subjective satisfaction and the reported impact on self-esteem and quality of life.

The extracted data were subsequently subjected to a qualitative comparative analysis. This approach allowed us to transcend the mere description of the findings to identify the points of convergence (consensus on efficacy and safety), areas of divergence (variation in techniques of application and dosage) and emerging trends in aesthetic biomedicine (such as preventive use and application of technologies such as Artificial Intelligence). The critical discussion of the results allowed, finally, the contextualization of evidence within the current professional scenario, providing subsidies for evidence-based clinical practice.

Considering that the present work was restricted to the analysis and synthesis of information originating from published secondary sources, not involving the direct collection of data from human participants, clinical experiments or the handling of sensitive data, this study was declared exempt from submission to the Research Ethics Committee (CEP), in accordance with the recommendations of Resolution No. 510/2016 of the National Health Council (CNS).

#### **4. RESULTS AND DISCUSSION**

All publications analyzed converge towards the high efficacy of BoNT-A in reducing and/or elimination of dynamic wrinkles, which are the main focus of treatment in the upper third of the face (frontal, glabellar and periorbital regions). The meta-analysis conducted by Zhang et al. (2025), when consolidating data from multiple trials, confirmed the high rate of patient satisfaction and predictability of the results, highlighting the toxin's ability to soften the most pronounced expression lines.



**Year V, v.2 2025 | submission: October 17, 2025 | accepted: October 19, 2025 | published: October 21, 2025**

Corroborating this evidence, the retrospective study by Gimenez et al. (2021), which followed a group of 24 patients for 42 months, demonstrated a significant and sustained improvement in wrinkles dynamics, with a patient satisfaction rate of over 90%. This long-term finding is crucial, as it attests not only to the acute effect of the toxin, but to its validity as a tool lasting in the management of facial aging. Additionally, Sá et al. (2022) detailed the effectiveness specific by region, reporting a significant reduction in the frontal, glabellar and periorbital lines with an average dose of 32 Units (U) per session, reinforcing the direct relationship between dose, technique and positive result.

The standardization of application protocols is a topic of constant refinement in the literature.

studies emphasize that although there is a common dosage range (as reported by Sá et al., 2022), success lies in personalizing treatment. This involves assessing the hyperactivity and the patient's specific muscle mass, as well as their lifestyle habits.

In this context, the research by Morhy et al. (2023) introduced an important perspective to demonstrate that high physical activity can potentially reduce the durability of the aesthetic effect of BoNT-A. The hypothesis is that increased muscle metabolism and possibly blood flow localization may accelerate the process of neural sprouting and the recovery of muscle function. This finding reinforces the need for the professional to consider the patient's lifestyle when establishing the protocol and reapplication interval, transcending the mere observation of static anatomy.

The safety of BoNT-A is one of the pillars of its consolidation in the aesthetics market. The meta-analysis of Zhang et al. (2025) showed a low overall incidence of adverse effects, reaffirming the nature transient and, for the most part, mild complications.

A crucial point of consensus, which serves as a warning for clinical practice, was highlighted by Di Santis et al. (2024): the vast majority of complications are associated with inadequate technique. application, and not to a problem intrinsic to the toxin or its mechanism of action. Complications such as eyelid ptosis, asymmetries or the unwanted "drooping of the eyebrow" (superciliary ptosis) are, in largely results from unintentional diffusion of the toxin into adjacent muscles or from errors in mapping of injection points. This underscores the conclusion that the anatomical domain and the professional training are the determining factors for the safety and success of treatment, validating the importance of continuing education and ethics in the practice of aesthetic biomedicine.

The analysis goes beyond purely physical results to highlight subjective gains and psychosocial aspects of treatment, an area of growing interest in recent literature. Luquetti et al. (2024) and Arora, Singh and Arora (2024) demonstrated that the improvement in facial appearance after application of BoNT-A translates into a direct positive impact on self-image, confidence and quality of life of individuals.

By smoothing out wrinkles that can be perceived as signs of anger, fatigue or chronic worry



**Year V, v.2 2025 | submission: October 17, 2025 | accepted: October 19, 2025 | published: October 21, 2025**  
(especially the glabellar lines), BoNT-A modulates nonverbal communication. This effect, known as the Facial Feedback Hypothesis, suggests that the inability to frown may, in fact, reduce the intensity of negative emotions, promoting a virtuous cycle of well-being. This In this way, treatment with BoNT-A is consolidated not only as an aesthetic intervention, but as a procedure that promotes health and psychological well-being.

## FINAL CONSIDERATIONS

This literature review allowed us to conclude that botulinum toxin type A is one of the resources most effective, safe and consolidated in aesthetic biomedicine, especially in procedures aimed at rejuvenating the upper third of the face. Studies analyzed between 2020 and 2025 demonstrate that, when applied carefully and by qualified professionals, the substance promotes predictable, natural results and high patient satisfaction.

The action of BoNT-A, by blocking the release of acetylcholine at neuromuscular junctions, provides temporary relaxation of the muscles, smoothing dynamic wrinkles and preventing the appearance of static lines. In addition to the aesthetic benefits, the treatment contributes to psychosocial improvements, positively impacting self-esteem and emotional well-being.

The findings in the literature also reinforce the importance of technical and anatomical training of professionals who apply the toxin, since the safety of the procedure depends directly on the mastery of doses, application points, and individualization of protocols. When well conducted, the treatment has a low rate of complications and high predictability of results.

Another relevant point identified is the growing tendency to use the toxin for preventive purposes, mainly among younger patients, in line with the search for subtle results and the popularization of minimally invasive procedures. This change reflects cultural and social transformations in the perception of aesthetics and aging, in which naturalness and facial balance gain emphasis.

Therefore, it is concluded that botulinum toxin type A remains an essential tool for the modern facial rejuvenation, with broad clinical and scientific applicability. Continuous advancement research and the development of new techniques contribute to improving their effectiveness, reducing risks and consolidate its role as one of the fundamental pillars of aesthetic biomedicine contemporary.



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