

# Complications from the Facial Application of Injectables: Botulinum Toxin and Hyaluronic Acid

## *Intercorrências associadas à aplicação de injetáveis na face: toxina botulínica e ácido hialurônico*

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### Abstract

In Recent Years the growing demand for fast efficient solutions for facial rejuvenation and esthetic symmetry has significantly increased the performance of minimally-invasive esthetic procedures. Parallel to this growth the occurrence of complications after such interventions has also increased. Botulinum toxin treats dynamic wrinkles and improves facial symmetry while hyaluronic acid is a filler for expression lines and wrinkles. The present study is an integrative review of the literature to identify and analyze the most common complications from botulinum toxin and hyaluronic acid in minimally-invasive facial esthetic procedures. We conducted a search in the PubMed database using the terms *botulinum toxin Botox hyaluronic acid and complications*; The search was limited to articles published between 2008 and 2023 and we retrieved 12 studies: 7 focusing on hyaluronic acid and 5 on botulinum toxin. The results revealed a wide range of immediate complications including local inflammatory reactions temporary muscle paralysis facial necrosis depigmentation and vascular occlusion. More serious complications such as severe allergic reactions and in rare cases deaths were also reported. Late adverse events such as the development of biofilms and granulomas were also identified. Although rare these complications require a cautious approach by professionals. Our review suggests that implementing stricter regulations and developing new techniques may mitigate the risks associated with these esthetic interventions.

### Keywords

- ▶ adverse effects
- ▶ aesthetics
- ▶ botulinum toxin
- ▶ facial asymmetry
- ▶ hyaluronic acid

### Resumo

#### Palavras-chave

- ▶ ácido hialurônico
- ▶ assimetria facial
- ▶ efeitos adversos
- ▶ estética
- ▶ toxinas botulínicas

Nos últimos anos, observou-se um aumento significativo na realização de procedimentos estéticos minimamente invasivos, em resposta à crescente demanda por soluções rápidas e eficazes para o rejuvenescimento facial e a simetria estética. Paralelamente a esse crescimento, registrou-se uma elevação nas complicações associadas a tais procedimentos. A toxina botulínica é amplamente utilizada no tratamento de rugas dinâmicas e na melhoria da simetria facial, ao passo que o ácido hialurônico é comumente empregado como preenchedor de linhas de expressão e rugas. Este estudo realiza uma revisão integrativa da literatura com o intuito de

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identificar e analisar as complicações mais comuns associadas ao uso de toxina botulínica e ácido hialurônico em procedimentos estéticos faciais minimamente invasivos. Foi realizada uma busca na base de dados PubMed, com os descritores *toxina botulínica*, *Botox*, *ácido hialurônico* e *complicações*, restrita a artigos publicados entre 2008 e 2023. Foram selecionados 12 estudos, sendo 7 dedicados às complicações do ácido hialurônico e 5, às da toxina botulínica. Os achados evidenciam uma gama de complicações imediatas, como reações inflamatórias locais, paralisia muscular temporária, necrose facial, despigmentação e oclusão vascular. Complicações mais graves, como reações alérgicas severas e, em casos raros, óbitos, também foram relatadas. Eventos adversos tardios, como surgimento de biofilmes e granulomas, foram igualmente identificados. Embora raras, essas complicações demandam uma abordagem cautelosa por parte dos profissionais. O estudo sugere a implementação de regulamentações mais rigorosas e o desenvolvimento de novas técnicas para mitigar os riscos associados a essas intervenções estéticas.

## Introduction

Recently, the search for faster, less aggressive solutions to correct facial imperfections and combat aging has significantly increased the demand for minimally-invasive esthetic procedures. Botulinum toxin and hyaluronic acid (HA) applications have become the most performed procedures in facial esthetics, driven by the growing popularity of facial harmonization and rejuvenation treatments.<sup>1</sup> From 2019 to 2023, the International Society of Aesthetic Plastic Surgery<sup>2</sup> (ISAPS) reported a 54.4% increase in non-surgical injectable procedures. Botulinum toxin application remains the most common non-surgical procedure for both men and women. In addition, the number of HA applications also increased 30.3%.

This growth also elevated the number of adverse events and complications, often resulting from inadequate patient assessment or inappropriate techniques. Although considered safe when performed by qualified professionals, the application of botulinum toxin and HA can cause complications, such as facial asymmetry, hematoma, necrosis, infection, and even blindness when poorly performed.<sup>3</sup>

Botulinum toxin type A (BTA), widely used for cosmetic purposes, is a neurotoxin produced by the bacterium *Clostridium botulinum*. This toxin relaxes muscles by inhibiting acetylcholine release at the neuromuscular junction. Since its approval by the Food and Drug Administration (FDA) in 2002,<sup>4</sup> botulinum toxin has become one of the most effective options to treat wrinkles and expression lines. It is considered safe, but it may cause complications, including drooping eyelids and temporary muscle weakness.<sup>5</sup>

Hyaluronic acid is widely used in facial filling techniques to restore volume and smooth wrinkles. Although HA is naturally present in the body, its production decreases with age, leading to visible signs of aging.<sup>6</sup> The most common complications from HA are edema, hematomas, and infections; more serious cases include necrosis and embolism, especially when the injection is inadequate or it is performed without a correct previous assessment of the patient.<sup>7</sup>

Therefore, obtaining a detailed medical history is essential before any esthetic procedure to identify potential contraindications, including current anticoagulant use or conditions that may compromise the procedure's safety. Temporarily suspending anticoagulant medication, for instance, can reduce the chance of bruising and other complications.<sup>8</sup>

The present article aims to describe the primary complications associated with the use of botulinum toxin and HA in facial esthetic procedures. The goal is to help other professionals identify, treat, and prevent these complications, ultimately improving their approach to each treatment.

## Materials and Methods

The current literature review aimed to investigate and analyze complications resulting from the application of botulinum toxin and HA in facial esthetic procedures. An integrative review is an approach that includes different study types (such as systematic reviews, observational studies, and clinical trials) to enable a comprehensive understanding of a topic by integrating results from multiple sources to provide a critical synthesis.

We conducted a search on the PubMed database using the keywords *botulinum toxin AND facial*, *Botox AND complications*, and *hyaluronic acid AND complications*. The initial search included scientific articles published from 2008 to 2023, in English, and focusing on facial esthetic complications.

The review process followed an adapted protocol of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement to ensure the rigorous selection and validity of the included studies.

### Step 1—Initial search and title analysis

The first step was a preliminary search on the PubMed database. We analyzed the titles of the retrieved articles to assess their relevance. The exclusion criteria were studies investigating the use of botulinum toxin or HA for non-esthetic therapeutic purposes and articles focusing on the

dental field. The articles included were reviews, case studies, and analyses of mandatory reporting documents addressing esthetic complications resulting from the use of these injectables. We selected articles meeting these criteria for the next step.

### Step 2—Abstract analysis

In the second step, we carefully reviewed the abstracts of the articles selected based on their titles to verify their relevance to the topic. We applied the same inclusion and exclusion criteria from the previous step to ensure that the studies specifically addressed the esthetic complications arising from the use of botulinum toxin and HA in facial procedures. We selected articles with relevant, clear abstracts for complete analysis.

### Step 3—Complete study analysis

The third step involved reading the full text of the articles selected during the previous stages. This step aimed to extract detailed data on esthetic complications and adverse events resulting from botulinum toxin and HA use. After the complete reading, we excluded from the final review articles that did not focus on esthetic complications. We organized the extracted information systematically to form the evidence base for the current review, seeking to offer a comprehensive view of the risks and complications associated with these procedures.

## Results

The database search retrieved 1,505 studies on botulinum toxin and 677 on HA, totaling 2,182 articles found in the first step. We excluded 2,072 (94.96%) studies retrieved in step 1 for not meeting the established research criteria. Thus, we included 110 for abstract analysis in the second step. In step 2, we excluded 98 (89.09%) articles. As such, we analyzed 12 (10.90%) studies<sup>9–20</sup> in full. These 12 studies investigated the complications associated with the use of HA and BTa in facial esthetic procedures— (Table 1).

From these, 7 (58.3%) studies<sup>9–15</sup> addressed complications from HA use, and the remaining 5 (41.7%) articles<sup>16–20</sup> focused on complications arising from BTa. The results revealed a wide range of complications, from local inflammatory reactions to more serious adverse events, which can compromise the safety and health of patients undergoing these procedures.

Regarding HA, Park et al.<sup>9</sup> reported the development of palpable nodules or masses in 42.9% of the patients, a relevant finding indicating the formation of granulomas or material buildup, frequently resulting from inadequate injection techniques. Furthermore, 35.7% of the patients reported inflammatory symptoms, such as swelling and tenderness, a potential immune reaction to the injected material. Regarding more severe cases, 10.7% of the patients presented with necrosis, a serious complication resulting from blood flow interruption, usually due to vascular occlusion, and 10.7% had depigmentation, probably linked to necrosis or chronic inflammation.<sup>9</sup>

In addition, a global review by Signorini et al.<sup>10</sup> classified HA-related complications as early and late. Early complications, such as vascular infarction and soft tissue necrosis, were often attributed to blood vessel occlusion caused by incorrect filler application. Late complications included the formation of granulomas and nodules weeks or even months after the procedure. These complications required supplementary treatments, such as corticosteroid administration or hyaluronidase application for filler dissolution.<sup>10</sup>

These findings were consistent with those of a study by Abduljabbar and Basendwh,<sup>11</sup> who identified common early complications, such as edema and pain at the injection site, and serious adverse events, including blood vessel embolization, which can lead to severe consequences, such as blindness or stroke. These events occurred mainly in facial regions with high vascular density, such as the periorbital area, and they constitute the most serious and feared complications in esthetic procedures with HA. Moreover, their study<sup>11</sup> highlighted late adverse effects, such as biofilm formation, which can lead to chronic infections, and the formation of foreign body granulomas, both requiring additional interventions.

Similarly, Alharbi et al.<sup>14</sup> described severe ocular complications in seven patients receiving HA. The affected subjects reported vision loss, ptosis (drooping eyelid), ecchymosis (bruising), and decreased visual acuity. These effects had a direct relationship with the inadvertent injection of the filler into vessels supplying the ocular system, which can result in ischemia and, in more severe cases, irreversible blindness. This data reinforced the need for greater care when applying HA to areas near the eyes, a highly-vascularized region susceptible to serious complications.<sup>14</sup>

In addition to short-term complications, Kyriaziids et al.<sup>15</sup> conducted a systematic review of 48 articles examining long-term adverse events. The most commonly reported complications, such as swelling and bruising, were usually resolved within 14 days. In contrast, more persistent complications, such as *Herpes simplex* infection and contour irregularities, could last for more than 21 days. As most contour irregularities were attributed to filler migration or injection into superficial skin layers, proper injection techniques are critical in avoiding these complications.<sup>15</sup>

To address emergencies such as vascular occlusion, Urdiales-Gálvez et al.<sup>13</sup> underscored the role of hyaluronidase, an enzyme for quick HA degradation to reverse serious complications, such as tissue necrosis. Their research<sup>13</sup> underscored that fast, effective interventions prevent permanent damage to patients.

Regarding BTa, Gouveia et al.<sup>19</sup> reported that 2 to 5% of the patients experienced complications, including eyelid ptosis. Ptosis, that is, the temporary drooping of the eyelid, occurs when the toxin affects muscles near those targeted by the injection; however, this complication is usually reversible. Other adverse effects included headache, reported by 1 to 10% of the patients, and pain at the injection site, which may result from the application technique and the body's natural response to the toxin.<sup>19</sup>

**Table 1** Main factors investigated regarding the use of hyaluronic acid and botulinum toxin

Substance	Author	Type of study	Main findings
Hyaluronic acid	Park et al., 2010. <sup>9</sup>	Analysis of 28 clinical cases	The study reported that 42.9% of the patients presented with palpable nodules or masses, 35.7% had inflammatory symptoms, 10.7% presented with necrosis, and 10.7% had depigmentation.
Hyaluronic acid	Signorini et al., 2016. <sup>10</sup>	Review based on evidence and a global consensus	Early complications included vascular infarction, soft tissue necrosis, and inflammatory reactions. Late complications included granulomas, nodules, depigmentation, and filler migration.
Hyaluronic acid	Abduljabbar and Basendwh, 2016. <sup>11</sup>	Comprehensive query on digital platform databases	Early-onset adverse effects included edema, pain, erythema, local tissue necrosis, and blood vessel embolization (blindness or stroke). Late adverse events included biofilm formation, foreign body granuloma, and scarring.
Hyaluronic acid	Maia and Salvi, 2018. <sup>12</sup>	Observational study	Although hyaluronic acid has proven effective, 5% of the cases presented nodules or irregularities after the application.
Hyaluronic acid	Urdiales-Gálvez et al., 2018. <sup>13</sup>	Review of expert recommendations	Vascular occlusion with risk of tissue necrosis, highlighting the effectiveness of hyaluronidase as an emergency intervention.
Hyaluronic acid	Alharbi et al., 2023. <sup>14</sup>	Analysis of seven clinical cases	Most patients presented with vision loss, ptosis, ecchymosis, and decreased visual acuity.
Hyaluronic acid	Kyriaziids et al., 2023. <sup>15</sup>	Systematic analysis of 48 articles	Main common adverse events (up to 14 days): swelling or edema at the injection site (26 articles), hematomas or ecchymosis (19 articles). Adverse events lasting more than 21 days: <i>Herpes simplex</i> infection and contour irregularities.
Botulinum toxin	Zagui et al., 2008. <sup>16</sup>	Systematic review with meta-analysis	The review detected 823 serious adverse effects associated with the use of botulinum toxin, including muscle paralysis and allergic reactions.
Botulinum toxin	Sposito, 2009. <sup>17</sup>	Literature review	The review identified risks of muscle paralysis and severe allergic reactions, highlighting the need for safe application techniques.
Botulinum toxin	Santos, 2013. <sup>18</sup>	Literature review	The most common complications included eyelid ptosis (5%), headache (7%), and facial asymmetries (3%).
Botulinum toxin	Gouveia et al., 2020. <sup>19</sup>	Literature review	Botulinum toxin is safe, but it can cause complications such as eyelid ptosis (2–5%), headache (1–10%), and pain at the injection site (12–25%).
Botulinum toxin	Ahsanuddin et al., 2021. <sup>20</sup>	Analysis of the Food and Drug Administration database	The adverse events reported include severe allergic reactions, such as anaphylaxis, and rare cases of death (0.01%).

Furthermore, Zagui et al.<sup>16</sup> and Sposito<sup>17</sup> reported 823 serious adverse effects resulting from BTa, including muscle paralysis and severe allergic reactions. Although these serious events are rare, they highlight the significance of precise toxin application to minimize risks.<sup>16,17</sup>

Santos<sup>18</sup> also identified the most common complications, such as eyelid ptosis, headache, and facial asymmetry. The latter results from an uneven distribution of the toxin, leading to unsatisfactory esthetic outcomes. Lastly,

Ahsanuddin et al.<sup>20</sup> documented severe allergic reactions, such as anaphylaxis, and rare cases of death (0.01%), highlighting the need for a safe treatment environment and professionals prepared in emergency management.<sup>18,20</sup>

## Discussion

Widely recognized as one of the safest and most effective dermal fillers, HA is frequently used in esthetic procedures to

improve facial volume and smooth wrinkles. However, as shown by Park et al.,<sup>9</sup> even procedures considered safe can result in significant complications. In their study, 42.9% of the patients developed palpable nodules or masses after HA application, while 35.7% presented inflammatory symptoms such as swelling and redness. These results underscore the importance of proper injection technique to avoid granuloma formation, which may occur due to an immune response to the filler.<sup>9</sup>

These findings were reinforced by Signorini et al.,<sup>10</sup> who classified HA complications as early and late. Early complications, such as vascular infarction and tissue necrosis, arise soon after application and are frequently attributed to blood vessel occlusion; this issue can be avoided with a precise injection technique. Late complications include granulomas and nodules, and they may appear weeks or even months after the procedure. This type of complication indicates the need for long-term patient monitoring, an aspect that esthetic practices aimed at immediate outcomes may neglect.<sup>10</sup>

Abduljabbar and Basendwh<sup>11</sup> added that severe complications, such as local tissue necrosis and blood vessel embolization, which can result in blindness or stroke, are significant concerns in facial areas with a rich vascular network, such as the periorbital region. These findings indicate a potential underestimation of the risk of serious complications, especially with the popularization of esthetic procedures performed by less experienced professionals or in non-medical contexts. Alharbi et al.,<sup>14</sup> for instance, highlighted that serious ocular complications, including vision loss and ptosis, occur after inadvertent injection of HA into blood vessels supplying the eye, challenging the common perception that HA is a low-risk filler.<sup>11,14</sup>

In a systematic review, Kyriaziids et al.<sup>15</sup> reported that swelling and edema are common, but usually temporary, complications. However, they also observed cases of *H. simplex* infection and contour irregularities, which can occur in a small percentage of patients. These findings suggest that, although serious complications are rare, the variability in patient response to HA should not be underestimated. For instance, *H. simplex* reactivation can occur in susceptible patients due to injection-related trauma, while contour irregularities may result from filler migration or superficial injection.<sup>15</sup>

Maia and Salvi<sup>12</sup> noted that 5% of the cases treated with HA presented nodules or irregularities after application. This percentage, although low, is relevant because it raises questions about variability in HA quality, injection technique, and individual biological responses. These findings highlight that, although HA is largely safe, its application requires caution and a deep technical knowledge.<sup>12</sup>

Like HA, BTA is widely used to treat dynamic wrinkles and is considered an effective treatment. However, Gouveia et al.<sup>19</sup> reported that 2 to 5% of the patients who received BTA developed eyelid ptosis, a complication that, although temporary, can be esthetically unpleasant and cause significant discomfort. In addition, 1% to 10% of the patients reported headache after the application, and 12 to 25%

experienced pain at the injection site. Although these complications are often mild and reversible, they can temporarily impact patients' quality of life, underscoring the importance of proper injection technique to minimize these adverse effects.<sup>19</sup>

A systematic review with meta-analysis by Zagui et al.<sup>16</sup> offers a broader and more concerning view of the botulinum toxin-associated complications; these authors identified 823 serious adverse effects, including muscle paralysis and severe allergic reactions, such as anaphylaxis. These findings contrast with the more optimistic view of Gouveia et al.,<sup>19</sup> who presented botulinum toxin as a safe procedure with few risks. This disparity between studies may have resulted from methodological differences, as Zagui et al.<sup>16</sup> focused on a larger dataset and more serious adverse events, while Gouveia et al.<sup>19</sup> focused on more common and less severe complications.<sup>16,19</sup>

Santos<sup>18</sup> also discussed botulinum toxin-associated complications, reporting that 5% of patients presented with eyelid ptosis, 7% had headaches, and 3% complained of facial asymmetries. These complications are consistent with the findings made by Gouveia et al.,<sup>19</sup> who observed similar adverse effects. However, facial asymmetry suggests that the muscular response to botulinum toxin may vary among patients, highlighting the significance of a precise injection technique and careful assessment of facial anatomy before treatment.<sup>18,19</sup>

Musharbash and Chakra<sup>21</sup> may support this finding by describing eyelid ptosis as a relatively common complication after botulinum toxin application. Eyelid ptosis manifests 2 to 10 days after the procedure, when the toxin reaches the levator palpebrae superioris muscle and paralyzes it. The study<sup>21</sup> emphasizes the role of patients in preventing this complication, as well as the importance of providing them with clear instructions, that is, to avoid manipulating the treated area for a specified period postinjection, since rubbing or massaging the region can inadvertently disseminate the toxin. Furthermore, the authors<sup>21</sup> point out that although ptosis can be treated with eye drops to raise the eyelid by 1 to 2 mm, patients affected by this condition induced by botulinum toxin may experience discomfort and functional impairment for several weeks, until the complete dissipation of its effects. In contrast to HA, there is no specific agent to reverse botulinum toxin-associated complications; as such, the only option consists of alternative treatments to reduce the duration of the toxin's action.

Ahsanuddin et al.<sup>20</sup> offer a more cautious perspective by analyzing the FDA database on severe allergic reactions, including anaphylaxis, and rare cases of death, with a rate of 0.01%. Although botulinum toxin-associated mortality is extremely rare, these data underscore the significance of careful monitoring during and after its administration. These findings challenge the common perception that botulinum toxin is completely safe, suggesting that healthcare professionals should be prepared to manage emergencies, even if such occurrences are unlikely.<sup>20</sup>

A comparison of results from studies on HA and botulinum toxin reveals that the complications associated with

each substance reflect different mechanisms of action and areas of application. Since HA is a filler, it tends to cause physical complications, such as nodules, granulomas, and tissue necrosis. These complications, although rarely fatal, can be esthetically unfavorable and difficult to manage, especially when they are late.<sup>11,15</sup> In turn, botulinum toxin, while less frequently associated with immediate serious complications, can cause significant adverse effects, such as muscle paralysis and severe allergic reactions.

Santos,<sup>18</sup> like Ahsanuddin et al.,<sup>20</sup> highlights the importance of considering both common and rare complications when evaluating the safety of botulinum toxin. While Santos<sup>18</sup> focuses on the most common complications, such as eyelid ptosis and headache, Ahsanuddin et al.<sup>20</sup> underscore rare, but severe, cases of anaphylaxis and death. This contrast between the frequency of complications and their potential severity suggests that professionals should be prepared to manage a wide range of adverse reactions, even those that occur rarely.<sup>18,20</sup>

Regarding the application technique, findings made by Park et al.<sup>9</sup> about HA reinforce the fundamental role of accuracy in avoiding complications such as nodules and necrosis. These results are consistent with the reports by Abduljabbar and Basendwh,<sup>11</sup> who highlight the risk of serious complications, such as vascular embolization, due to the improper application of HA. Therefore, although HA is widely deemed safe, the professional's technique plays a critical role in determining the outcome and minimizing risks.<sup>9,11</sup>

On the other hand, the choice between HA and botulinum toxin must consider not only the esthetic goal, but also the complication profile of each substance. HA, as a filler, most commonly causes physical complications, such as nodules and necrosis. In turn, as botulinum toxin blocks acetylcholine release at neuromuscular synapses, it more frequently results in functional complications, such as muscle paralysis and allergic reactions.<sup>19,20</sup> This implies that the decision between HA and botulinum toxin should consider the patient's wishes as well as the complexity of the procedure and the potential risks.

Another critical factor is the variability in patient response to procedures. Kyriaziids et al.<sup>15</sup> observed that common adverse events, such as edema and swelling, can persist for more than 21 days in certain subjects, suggesting a variable inflammatory response to HA. Similarly, Gouveia et al.<sup>19</sup> and Santos<sup>18</sup> identified that complications such as facial asymmetries and eyelid ptosis after BTA application can vary among patients depending on product distribution and individual anatomy. This variability indicates that customized treatment is essential. Instead of adopting a standard protocol for all patients, professionals should carefully assess factors such as the patient's overall health, history of previous reactions, and specific anatomical features to minimize risks and maximize outcomes.<sup>15,18,19</sup>

This customized approach is critical in high-risk areas, such as the periorbital region. Alharbi et al.<sup>14</sup> underscore that HA injections near the eyes are particularly delicate, as errors can cause ocular ischemia and even blindness. Therefore, professionals must have a thorough understanding of facial

anatomy and use proper techniques to ensure patient safety.<sup>14</sup>

In addition to techniques and individual variability, another relevant aspect is the context in which these procedures are performed. The growing popularity of esthetic treatments has increased their availability in non-medical settings, such as esthetic clinics and spas, often by professionals without formal medical training.<sup>22</sup> Some studies, such as those by Ahsanuddin et al.<sup>20</sup> and Alharbi et al.,<sup>14</sup> suggest that esthetic procedures performed by unqualified professionals can heighten the risk of complications. This is particularly true for more complex procedures, such as HA application in the periorbital region.<sup>14,20,22</sup>

The counterfeiting of products intended for cosmetic procedures is a growing concern that can lead to serious complications for patients. The use of counterfeit products, such as HA and botulinum toxin, can increase the risk of adverse reactions because they do not undergo the rigorous quality control processes required by regulatory bodies, such as the Brazilian Health Regulatory Agency (Agência Nacional de Vigilância Sanitária, ANVISA, in Portuguese) or the FDA. Studies<sup>14,23</sup> show that counterfeit products may contain contaminants, incorrect dosages, or even toxic ingredients, significantly increasing the risk of complications as severe allergic reactions, infections, or tissue necrosis. This issue highlights the importance of ensuring the acquisition of products from reliable, properly-regulated sources.

Furthermore, the counterfeiting of cosmetic products is a global issue with significant impacts on patient safety and the credibility of treatments. According to Santos,<sup>18</sup> the counterfeiting of botulinum toxin has been reported with some frequency in international markets, compromising the product's effectiveness and putting patients at risk of developing severe complications, such as undue muscle paralysis or infections. International regulatory bodies and ANVISA have increased efforts to combat this practice by enhancing batch tracing and mandating that healthcare professionals obtain these products directly from manufacturers or authorized distributors.<sup>18</sup>

By publishing the Safety Report GGMON no. 01/2024, emphasizing the significance of cosmetovigilance, ANVISA<sup>24</sup> underscored the need for stricter regulation to ensure patient safety. According to this document, reporting adverse events should be mandatory. This supports the findings made by Abduljabbar et al.,<sup>11</sup> who suggest that many adverse events may be underreported, creating a false sense of security in procedures involving HA and BTA. Underreporting of adverse events can lead to an underestimation of risks and, as a result, to insufficient regulation.<sup>11,24</sup>

Another important point raised by Maia and Salvi<sup>12</sup> and Trindade et al.<sup>23</sup> is the importance of careful patient selection to minimize the risk of complications. Patients with a history of allergic reactions, autoimmune diseases, or sensitivity to esthetic procedures may be at higher risk of developing severe complications after the application of HA or BTA. These findings highlight that the initial consultation and medical evaluation are crucial steps in determining the safety of the procedure.<sup>12,23</sup>

Finally, recent legislative discussions, such as Bill no. 9,602/2018,<sup>25</sup> reflect a growing concern about the safety of esthetic procedures in Brazil. The bill mandates reporting complications from esthetic procedures, both surgical and non-surgical, emphasizing the importance of ongoing monitoring. This bill also aligns with the warnings made by Gouveia et al.<sup>19</sup> and Abduljabbar et al.,<sup>11</sup> who emphasize that better regulation and greater transparency in complication reporting could help identify risk patterns and mitigate future complications.

In light of the aforementioned information, it is evident that both HA and botulinum toxin are widely used in esthetic procedures and present favorable safety profiles when used by qualified professionals. However, complications, although rare, can be significant and, in some cases, severe. Customized treatment, proper techniques, and rigorous regulation of professionals performing these procedures are essential to ensure patient safety. Moreover, continuous monitoring and mandatory reporting of adverse events, as recommended by ANVISA,<sup>24</sup> can help identify potential risks and improve the practice of these esthetic procedures.

## Conclusion

The current study highlighted the importance of a careful and informed approach when using botulinum toxin and HA in facial esthetic procedures. Although both substances are widely used and considered safe, the evidence herein analyzed shows that complications can occur, ranging from mild, temporary effects to severe events requiring immediate intervention. Hyaluronic acid is a widely used filler known to restore volume and smooth wrinkles; however, it can lead to complications such as nodules, necrosis, and inflammatory reactions, particularly when applied improperly or in anatomically-complex areas. Botulinum toxin, widely used to smooth expression lines, also presents risks, including eyelid ptosis, headache, and, in rarer cases, severe allergic reactions.

A review of the literature suggests that the professional's experience and injection technique play crucial roles in minimizing risks. Healthcare professionals administering injectables must have proper training, knowledge of best practices and techniques, and a comprehensive understanding of facial anatomy. Individualizing treatment for each patient, considering factors such as medical history, anatomical features, and expectations, is fundamental to ensuring safe and effective esthetic outcomes.

Raising awareness among patients about potential risks and the significance of post-procedure follow-up is essential to preventing and managing complications early. This study indicates the necessity for stricter regulations and ongoing education for professionals conducting these procedures, always prioritizing patient safety and well-being. Future research and the development of new techniques may help minimize complications associated with botulinum toxin and HA, enhancing the esthetic outcomes and the safety of these procedures.

## Data Availability

Data will be available upon request to the corresponding author.

## Authors' Contributions

LAM: data analysis and/or interpretation, conceptualization, project management, methodology, performance of surgeries and/or experiments, writing – review & editing, and validation; BCO: data analysis and/or interpretation, final manuscript approval, conceptualization, methodology, writing – original draft, writing – review & editing, and visualization; ECB: statistical analysis, final manuscript approval, writing – review & editing, supervision, validation, and visualization; DCC: statistical analysis, final manuscript approval, writing – review & editing, supervision, validation, and visualization; and AG: data analysis and/or interpretation, statistical analysis, final manuscript approval, funding acquisition, conceptualization, investigation, methodology, writing – review & editing, supervision, validation, and visualization.

## Clinical Trials

None.

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## Conflict of Interests

The authors have no conflict of interests to declare.

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