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Impacts of SARS-CoV-2 Infection and COVID-19 Vaccination on The Duration of Botulinum Toxin Effects: A Review of The Evidence

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Facial rejuvenation has gained substantial prominence in contemporary clinical practice, particularly with the widespread use of botulinum toxin type A due to its well-established neuromuscular blocking effects and favorable safety profile. However, the emergence of COVID-19, caused by SARS-CoV-2, has introduced new challenges regarding potential interactions between infection, vaccine-induced immune responses, and aesthetic procedures. Current evidence suggests that these immunological alterations may influence the therapeutic response to botulinum toxin, potentially affecting its duration and clinical efficacy. In this context, this study aims to analyze the possible interactions between SARS-CoV-2 infection, COVID-19 vaccination, and the effects of botulinum toxin type A. The findings indicate that immune activation, inflammatory mediators, and antibody production may act as modifying factors in treatment outcomes. These results highlight the importance of a cautious and individualized clinical approach, as well as the need for further scientific investigation to better understand these interactions.

Keywords: Botulinum Toxin Type A, COVID-19 Vaccines, COVID-19

I. INTRODUCTION

The COVID-19 pandemic, caused by SARS-CoV-2, has had significant global impacts since 2019, raising concerns about possible changes in human physiology and its interactions with different therapies. In this context, botulinum toxin type A stands out, being widely used for both therapeutic and aesthetic purposes, especially in facial rejuvenation, whose demand has increased considerably in recent decades. Its mechanism of action is based on the inhibition of acetylcholine release, promoting temporary muscle relaxation, and it is recognized for its efficacy and safety (HUANG et al., 2020; DRESSLER, 2008).

In addition to its aesthetic applications, botulinum toxin has been widely used in dentistry, contributing to the treatment of various clinical conditions, such as temporomandibular disorders and bruxism, and is regulated by specific guidelines that ensure its safe use by qualified professionals (JOHNSON, 2008). However, with the emergence of COVID-19 and the development of vaccines, questions have arisen regarding possible interactions between infection, immune response, and the effects of botulinum toxin (LEE et al., 2021).

Immunological alterations associated with SARS-CoV-2 infection, such as the excessive release of inflammatory cytokines, may influence the therapeutic response, raising hypotheses about potential interference in treatment effectiveness (LIU et al., 2021; HADJIVASSILIOU et al., 2020). Therefore, it is essential to investigate the relationship between botulinum toxin, SARS-CoV-2 infection, and COVID-19 vaccination, aiming to ensure greater safety, effectiveness, and scientific support in clinical practice (GONZALEZ-LATAPI et al., 2021; GOURLEY et al., 2021).

II. LITERATURE SURVEY

Botulinum toxin type A is one of the main therapeutic and aesthetic tools in current practice, acting by inhibiting the release of acetylcholine at the neuromuscular junction, resulting in temporary muscle paralysis. Its use is widely established in several clinical fields, especially in orofacial harmonization, due to its efficacy, safety, and

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predictability (JOHNSON, 2008; DRESSLER, 2008).

With the emergence of the COVID-19 pandemic, new questions have arisen regarding possible interactions between botulinum toxin, the immune system, and SARS-CoV-2. Infection with the virus triggers a significant systemic inflammatory response, characterized by the release of pro-inflammatory cytokines, intense immune activation, and neuromuscular alterations. This scenario may directly impact the action of botulinum toxin, since its effectiveness depends on the integrity of neuromuscular transmission (HUANG et al., 2020; LIU et al., 2021).

From a molecular and immunological perspective, the SARS-CoV-2 spike protein plays a central role in host cell entry through its interaction with ACE2 receptors, initiating a cascade of immune responses. This process activates both innate and adaptive immunity, particularly T lymphocytes (CD4+ and CD8+), and promotes the release of inflammatory mediators such as interleukin-6 (IL-6), interleukin-1β (IL-1β), and tumor necrosis factor-alpha (TNF-α). These cytokines are directly associated with systemic inflammation, muscle catabolism, and alterations in neuromuscular junction physiology, potentially affecting synaptic transmission and muscle responsiveness.

In this context, immune hyperactivation may interfere with the pharmacodynamics of botulinum toxin. The inflammatory environment may accelerate neuromuscular recovery, alter receptor sensitivity, and modify the internalization or activity of the toxin at cholinergic nerve terminals. Additionally, the production of antibodies and immune mediators may contribute to reduced duration of effect or variability in clinical response. The neurotropic potential of SARS-CoV-2 further supports the hypothesis of direct or indirect interference in neuromuscular function (LIU et al., 2021; HADJIVASSILIOU et al., 2020).

In parallel, COVID-19 vaccination also emerges as a relevant factor in this context. Vaccines based on mRNA or viral vectors induce the expression of the spike protein, triggering a controlled immune response that includes activation of T cells and cytokine production. Although beneficial for protective immunity, this response may transiently reproduce inflammatory and immunological conditions similar to those observed during infection. Consequently, this may influence the interaction with botulinum toxin, particularly in terms of antibody formation, local inflammation, and possible modulation of therapeutic efficacy (GONZALEZ-LATAPI et al., 2021; LEE et al., 2021).

Recent studies report variability in the duration of botulinum toxin effects in post-COVID-19 or vaccinated patients, suggesting a possible correlation between immune status and therapeutic response. These findings highlight the need for an individualized clinical approach, considering the patient's infection history, vaccination status, and immunological condition (GONZALEZ-LATAPI et al., 2021; GOURLEY et al., 2021).

In this context, it becomes evident that the interaction between botulinum toxin, SARS-CoV-2 infection, and immune response represents an emerging field of great clinical relevance. Understanding these mechanisms is essential to ensure patient safety, optimize therapeutic outcomes, and guide evidence-based clinical protocols. However, the literature still presents important gaps, emphasizing the need for further studies to deepen this relationship and provide more robust guidelines for professional practice (GOURLEY et al., 2021; HUANG et al., 2020).

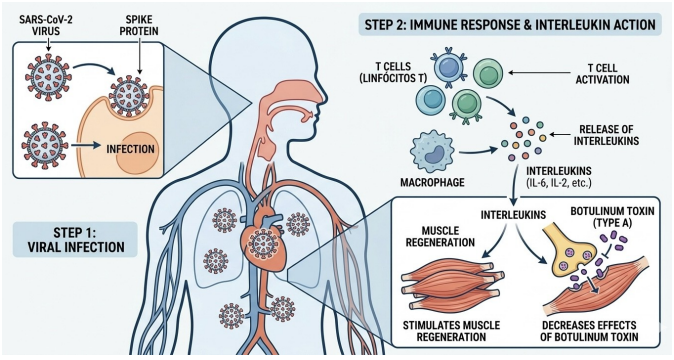

Figure 1: Schematic representation of the interactions between SARS-CoV-2 infection, interleukin-mediated immune response, and their potential effects on the action of botulinum toxin type A. Source: Author's own work (2026).

III. METHODOLOGY

The study was conducted through a qualitative and explanatory literature review, using databases such as PubMed, SciELO, and Google Scholar.

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Scientific articles, case studies, and clinical reports related to the use of botulinum toxin in patients with a history of SARS-CoV-2 infection and/or COVID-19 vaccination were included. Data analysis allowed the identification of possible changes in treatment effectiveness, as well as patterns and gaps in the literature, contributing to a better understanding of the interactions between botulinum toxin and post-COVID-19 effects.

IV. RESULTS

The analysis of the selected studies revealed a consistent pattern suggesting that the immunological status of patients, particularly in the context of recent SARS-CoV-2 infection or COVID-19 vaccination, may significantly influence the clinical performance of botulinum toxin type A. Across multiple reports, there was a recurrent observation of variability in both the onset and duration of the toxin's effects, with a notable tendency toward reduced longevity in patients who had recent immune activation.

Evidence indicates that SARS-CoV-2 infection is associated with a pronounced inflammatory response, characterized by elevated levels of cytokines such as IL-6, IL-1β, and TNF-α, as well as alterations in neuromuscular function. These changes appear to interfere with the pharmacodynamic action of botulinum toxin, particularly by affecting synaptic transmission and neuromuscular junction stability. Studies included in this review reported cases in which patients experienced a shorter duration of effect or required higher doses to achieve similar clinical outcomes following COVID-19 infection (GONZALEZ-LATAPI et al., 2021; HADJIVASSILIOU et al., 2020).

Similarly, vaccination against COVID-19, although essential for public health, induces a controlled but significant immune response, involving activation of T lymphocytes and production of pro-inflammatory mediators. This transient immunological state may partially mimic aspects of the inflammatory environment observed during infection, potentially influencing the interaction between botulinum toxin and neural tissue. Some studies suggested that patients vaccinated shortly before or after toxin application exhibited subtle reductions in treatment duration and increased variability in clinical response (GOURLEY et al., 2021; MALHOTRA et al., 2021).

From a mechanistic perspective, the findings support the hypothesis that immune-mediated processes may accelerate neuromuscular recovery or interfere with the internalization and activity of botulinum toxin at presynaptic terminals. Additionally, the potential formation of neutralizing antibodies or modulation of receptor sensitivity may contribute to decreased efficacy or shorter duration of action. Although direct causality has not yet been definitively established, the convergence of clinical observations and immunological evidence strongly suggests a biologically plausible interaction.

Overall, the results of this review reinforce the notion that recent infection or vaccination may act as modifying factors in botulinum toxin treatments, influencing both efficacy and duration. These findings highlight the importance of considering the patient's immunological status as a relevant variable in clinical decision-making. Furthermore, they underscore the need for individualized treatment planning, including the possible adjustment of application timing in relation to vaccination or recent infectious events, in order to optimize therapeutic outcomes and minimize variability in response.

V. CONCLUSION

This study highlights that, although botulinum toxin type A remains a well-established, safe, and effective therapeutic tool, its clinical performance may be influenced by the patient's immunological status, particularly in the context of recent SARS-CoV-2 infection and COVID-19 vaccination. Current evidence suggests that immune activation, characterized by increased production of pro-inflammatory cytokines and modulation of adaptive immune responses, may interfere with the pharmacodynamic mechanisms of the toxin. These alterations may contribute to reduced duration of action, variability in clinical response, and decreased predictability of therapeutic outcomes.

From a biological standpoint, the inflammatory microenvironment and immune-mediated processes associated with infection and vaccination may impact neuromuscular transmission, receptor sensitivity, and the internalization of botulinum toxin at presynaptic terminals. Additionally, the

potential formation of neutralizing antibodies and changes in synaptic recovery mechanisms further support the hypothesis of a clinically relevant interaction. The convergence of these factors reinforces the plausibility that recent immune challenges may act as modulators of toxin efficacy.

Although definitive causal relationships have not yet been fully established, the consistency of emerging clinical observations supports the need for a cautious and individualized approach in aesthetic and therapeutic practice. Consideration of recent infection or vaccination history may be essential for optimizing treatment planning and outcomes. Therefore, further well-designed studies are required to better elucidate these interactions and to establish evidence-based protocols that enhance safety, efficacy, and predictability in the use of botulinum toxin in the post-COVID-19 era.

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