

Botulinum Toxin in Treatments for Abnormal Movements

Revisión sistemática sobre: Toxina Botulínica en tratamientos para movimientos Anormales

<https://doi.org/10.47606/ACVEN/MV0235>

María Gabriela González Chico^{1*}

<https://orcid.org/0000-0001-9445-9004>
maria.gonzalez@iste.edu.ec

Miliana Esperanza Estupiñan Bazurto²

<https://orcid.org/0009-0009-7331-8590>
milianaestupinan640@gmail.com

Xaviera Elizabeth Medina Godoy²

<https://orcid.org/0009-0007-0613-0016>
xmedina@uees.edu.ec

María José López Becerra²

<https://orcid.org/0009-0001-3813-5790>
lopezmariajose@uees.edu.ec

Recibido: 20/01/2024

Aceptado: 15/03/2024

ABSTRACT

Introduction: Botulinum toxin is crucial for reducing sequelae in movement disorders such as Parkinson's. It blocks muscle contractions and improves quality of life, being used in both aesthetic and medical treatments. **Methodology:** A non-experimental longitudinal design was adopted, observing variables at multiple time points without manipulation. A mixed approach (qualitative and quantitative) was used with adults over 30 years old without Parkinson's history. The review included documents from PubMed, Scopus, and Scielo, applying rigorous inclusion and exclusion criteria. **Objective:** To evaluate the efficacy of botulinum toxin in treating abnormal movements in Parkinson's and understand its long-term effects. **Results:** Botulinum toxin type A reduces tremors by blocking acetylcholine. It improves motor symptoms of Parkinson's and essential tremor but requires frequent and costly treatments. There is a risk of developing antibodies that decrease its effectiveness. **Discussion:** It offers significant benefits, but its high cost and the need for frequent treatments are challenges. Patients report satisfaction in short-term studies, but more long-term research is needed. **Conclusions:** Promising for movement disorders, especially Parkinson's, although limited by cost and duration of effect. Future research should seek to extend therapeutic effects and reduce costs.

Keywords: botulinum toxin, movement disorders, parkinson's disease.

1. Instituto Tecnológico Superior Universitario España.
 2. Universidad de Especialidades Espíritu Santo.
- * **Autor de correspondencia:** maria.gonzalez@iste.edu.ec

RESUMEN

Introducción: La toxina botulínica es crucial para reducir secuelas en trastornos de movimientos anormales, como el Parkinson. Bloquea contracciones musculares y mejora la calidad de vida, usándose tanto en tratamientos estéticos como médicos. **Metodología:** Se adoptó un diseño longitudinal no experimental, observando variables en múltiples puntos temporales sin manipularlas. Se utilizó un enfoque mixto (cualitativo y cuantitativo) con adultos mayores de 30 años sin antecedentes de Parkinson. La revisión incluyó documentos de PubMed, Scopus y Scielo, aplicando criterios rigurosos de inclusión y exclusión. **Objetivo:** Evaluar la eficacia de la toxina botulínica en el tratamiento de movimientos anormales en Parkinson y entender sus efectos a largo plazo. **Resultados:** La toxina botulínica tipo A reduce temblores bloqueando acetilcolina. Mejora síntomas motores del Parkinson y temblor esencial, pero requiere tratamientos frecuentes y costosos. Existe riesgo de desarrollar anticuerpos que disminuyen su eficacia. **Discusión:** Ofrece beneficios significativos, pero su alto costo y la necesidad de tratamientos frecuentes son desafíos. Los pacientes reportan satisfacción en estudios a corto plazo, pero se necesitan más investigaciones a largo plazo. **Conclusiones:** Prometedora para trastornos del movimiento, especialmente Parkinson, aunque limitada por costo y duración del efecto. Futuras investigaciones deben buscar extender efectos terapéuticos y reducir costos.

Palabras claves: toxina botulínica, trastornos del movimiento, enfermedad de parkinson.

INTRODUCCION

What therapeutic approach is categorized as crucial in the long term for reducing the sequelae caused by disorders involving abnormal or degenerative movements in Parkinson's disease? Botulinum toxin is responsible for blocking muscle contractions and is commonly used for aesthetic treatments as well as for diseases that cause abnormal movements(1). It helps control symptoms and improve the quality of life for individuals(2). Essential tremor is one of the most common diseases, affecting 1% of the population with an incidence of approximately 300 cases per 100,000 inhabitants. Parkinson's tremor, typically occurring at a frequency of 4-6 Hz and initially affecting the limbs asymmetrically, is also commonly treated with botulinum toxin(3). Reviewing studies conducted in recent years, there is an expectation of increased implementation of this treatment in diseases with a degenerative neural background, preserving both the physical and psychological integrity of the individuals undergoing this treatment (4).

METHODOLOGY

The methodology of this study focuses on the use of botulinum toxin, more commonly known as Botox, which has been widely used for aesthetic purposes and is increasingly utilized for therapeutic applications.

This research will adopt a non-experimental longitudinal design, meaning that researchers will observe and analyze the variables over two or more time points without manipulating them. This approach allows for a naturalistic observation of changes and trends over time, providing a robust framework for understanding the effects of Botox in a therapeutic context.

The study will employ a mixed-category approach, integrating both qualitative and quantitative variables. This comprehensive method ensures that the research addresses multiple dimensions of the problem, capturing not only numerical data but also subjective experiences and insights. By combining these two approaches, the study aims to provide a more holistic understanding of the therapeutic use of Botox. The qualitative aspect will explore the subjective experiences and perceptions of the participants, while the quantitative aspect will focus on measurable outcomes and statistical analysis.

The population targeted in this research comprises adults over 30 years of age who do not have a pathological history of underlying Parkinson's disease or its degenerative effects on movement. A non-probabilistic sampling method will be used, where participants are selected based on specific non-random criteria, ensuring that the sample meets the study's inclusion and exclusion criteria. Data collection will be conducted through a thorough review of documents available on platforms such as PubMed, Scopus, and Scielo. During the data analysis phase, these criteria will be meticulously applied to ensure the reliability and validity of the findings. This structured and detailed approach will facilitate a comprehensive understanding of the therapeutic potential of Botox in the specified population.

Inclusion and exclusion criteria

The inclusion criteria for this review are designed to ensure that the selected articles provide relevant and high-quality data for our analysis. Articles included in this review must involve individuals over the age of 30 who exhibit symptomatology directly related to the treatment under investigation. Additionally, the studies must have been conducted within the past five years to ensure that the data reflects the most current findings and advancements in the field. This criterion helps maintain the relevance and applicability of the research outcomes to current clinical practices and therapeutic approaches.

Conversely, the exclusion criteria are equally important in maintaining the integrity and focus of the review. Articles will be excluded if they involve individuals under the age of 30. This age restriction is crucial as it ensures the study population is more homogeneous and relevant to the treatment effects observed in adults. Furthermore, studies involving participants with a history of other pathologies will be excluded to avoid confounding factors that could influence the treatment outcomes.

This helps to isolate the effects of the treatment on the specific symptomatology being investigated, providing clearer insights into its efficacy and safety. Lastly, any articles that do not involve prior history or symptomatology related to the treatment will also be excluded. This criterion ensures that the review focuses only on studies where the treatment's impact on existing symptoms is evaluated. By applying these stringent inclusion and exclusion criteria, the review aims to compile a body of evidence that is both specific and relevant, thereby enhancing the reliability and validity of the conclusions drawn from the analyzed data. This methodical approach helps ensure that the findings are robust and applicable to real-world clinical settings.

Search criteria.

The search criteria for this review were meticulously designed to ensure the extraction of relevant and high-quality information from certified sources on the internet. The primary databases utilized for this purpose were PubMed, Scopus, and Scielo, which are well-regarded platforms in the academic and scientific communities.

The search process was guided by criteria determined in consultation with the supervising teacher, ensuring that the approach was methodologically sound and aligned with the research objectives. This collaborative effort helped in defining clear and precise search parameters that were crucial for obtaining relevant results.

To conduct the search, a detailed and systematic approach was employed. This involved the integration of various search parameters, including the strategic use of keywords related to the study's focus. Keywords were carefully selected to encompass a broad spectrum of relevant terms, ensuring that the search was comprehensive and inclusive of all pertinent studies.

The use of Boolean operators and filters further refined the search process, allowing for the exclusion of irrelevant results and the inclusion of studies that met the specific criteria established for the review. This detailed search strategy was instrumental in obtaining a robust dataset for analysis.

The effectiveness of the search criteria was evidenced by the quality and relevance of the results obtained. By employing a structured approach and leveraging the capabilities of these well-established databases, the research was able to gather a substantial body of literature that met the predetermined criteria.

The integration of different search parameters and the use of precise keywords facilitated the identification of studies that were most relevant to the research questions. This thorough and methodical search process was fundamental in ensuring that the review was based on reliable and pertinent data, thereby enhancing the validity and reliability of the research findings.

Study selection.

The study selection process began with an extensive search across multiple platforms. From the PubMed platform, we retrieved a total of 196 titles. Unfortunately, the Scielo platform did not yield any results. However, the Scopus platform provided an additional 35 search results, bringing the initial total to 231 articles. The first step in refining these results was to eliminate duplicate entries, which reduced the number of articles to 153.

Following the removal of duplicates, we proceeded to apply the inclusion and exclusion criteria previously established. This rigorous filtering process was crucial to ensure that only the most relevant articles were considered. As a result, we further narrowed down the selection to 31 articles. To ensure the articles' relevance and adherence to our criteria, we carefully read the abstracts of these 31 articles. This step led to the exclusion of those that did not meet the necessary criteria, leaving us with 10 articles to determine their full availability.

In the final phase of the study selection process, we checked the availability of these 10 articles. Despite the comprehensive search and screening efforts, only 8 articles were found to be accessible. This outcome highlights the challenges of obtaining complete datasets but also underscores the importance of a thorough and systematic approach in the study selection process. The final 8 articles will serve as the foundation for our subsequent analysis, providing a solid basis for our research objectives.

Data extraction process

The data extraction process from the post-screening articles involves developing a comprehensive table that captures key details from each study. This table includes columns for the titles, authors, journal names, types of articles, the number of patients involved, specific data to be extracted, and the conclusions drawn. By systematically organizing this information, we ensure a structured approach to data collection, allowing for a thorough and consistent review of each article's content.

Through this meticulous process, we were able to compile several reviews. Each review was examined carefully to extract relevant data points that contribute to the overall analysis. Interestingly, none of the reviews mentioned direct patient interaction, highlighting a potential gap in the existing literature. However, the reviews did provide substantial characteristic data that could be valuable for future research and clinical applications.

The data extraction method proved to be an effective way to synthesize information from a variety of sources. By focusing on specific attributes and outcomes, we were able to create a detailed overview that enhances our understanding of the subject matter. This approach not only helps in identifying trends and patterns but also in pinpointing areas that require further investigation.

General Bias Risk

Among the general risks, the search was limited to Spanish and English languages, leading to a potential error by excluding research records in other languages or unavailable articles containing relevant information for the review.

Individual Study Bias Risk

The work may have risks due to reviewers omitting important information during reading or errors in translating necessary information.

RESULTS

Botulinum toxin has been studied, as shown in Table 1. Men and women over 30 years old participated in the study, except those related to diseases other than Parkinson's. Similarly, BoNT type A has been found to influence and have a better effect on people suffering from these abnormal movements.

Table 1.
Characterization of the Articles

Study	H Index	Age	Amount	Analysis
Naeem et al.	102	N/A	72	Protocols were identified, which are the Yale protocol and the Western University- London (ON, Canada) protocol, which have introduced effective methodologies for the treatment of EP.
Liao et al.	102	N/A	40	While BoNT A and B have been recognized to successfully treat involuntary movement disorders, four BoNTs are currently available: three type A toxins and one type B toxin.
Jabbari et al.	-	N/A	26	BoNT and saline groups after initial injections, improvement was seen in 75% of onabotulinumtoxinA-treated patients, 25% of control group
Li et al.	95	N/A	37	It was identified that two serotypes of botulinum toxin are commonly used: A (BoNT-A) and B (BoNT-B), although the efficacy of A is proven in most studies.
Abusrair et al.	-	N/A	169	The characteristic or conduction of pain is defined or studied in a way that seeks to alleviate the tremor, understanding the pathway by which it is produced.
Tater et al.	53	N/A	144	From this article the administration plan of the medication is rescued to understand the distinct functions of the botulinum toxin and its immersion in the different tremors.
Cardoso et al.	140	N/A	30	This article explains the different benefits such as the definition of the central problem considering factors necessary for the administration of the medication.
Bruno et al.	74	+30	24	In this study, the medication and placebo were administered to patients over 30 years of age, with confusing results due to time limits.

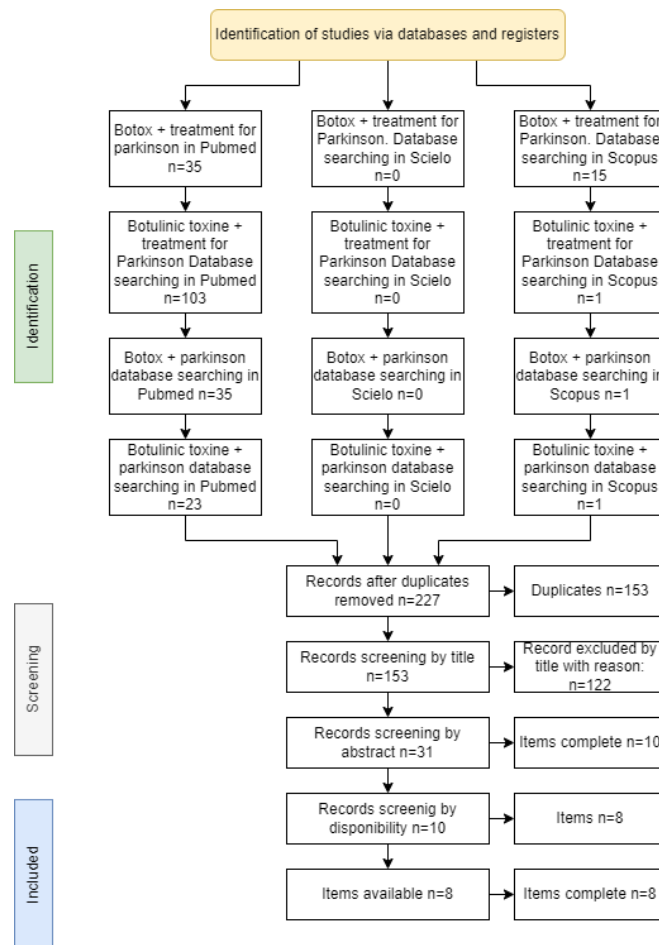


In four of the articles, it is stated that botulinum toxin (BoNT) is produced by the bacterium *Clostridium botulinum*, which promotes the blockade of the release of the neurotransmitter acetylcholine, “which will mainly cause movements or, in turn, paralysis in the upper extremities such as the hands, originating in most cases, followed by the lower extremities. For this reason, due to the application of Botulinum Toxin Type A and Type B, with Type A being the most used due to its high effectiveness, it has become very helpful in treating abnormal movements in Parkinson's disease. Botulinum toxin has a wide range of benefits, being considered an effective treatment for disorders involving abnormal movements or tremors. However, although it is considered a quite safe treatment without notable adverse effects, it should be considered that it is not a fully viable treatment due to its many limitations regarding its short duration response and high cost.

Flow diagram.

Figure 1:

Identification of studies via databases and registers. Source: Own elaboration (2023)



DISCUSSION

This article reports on the action of botulinum toxin in the abnormal movements of Parkinson's disease, which comply with pathophysiological mechanisms in which the cerebro-thalamo-cortical and ganglio-basal-cortical pathways are involved, being affected and therefore eventually triggering episodes of tremor, in the case of botulinum toxin it will act at the level of both pathways, its main mechanism of action being the prevention of acetyl release. lina from the presynaptic vesicles, thus suppressing the tremor of these abnormal movements. According to Anandan, he determines that treatment with botulinum toxin has an average duration of 2.5 to 2.8 months (1, 2), while Niemann, J. determines that this occurs between 29.6 months and 3-88 months, this being a determining factor for implementing treatment with botulinum toxin (5, 6) since according to Shivam, patients who are constantly receiving botulinum toxin treatment have deficiencies in terms of their results, these being much less effective (7, 8).

For its part, the Interdisciplinary Group (GTI) was one of the first organizations to focus on movement disorders, including parkinsonian syndromes, dystonia, tremors, chorea, tics, and many rare syndromes, with botulinum toxin considered the main treatment for dystonia, which Jabbari corroborates (9). The abnormal movements in Parkinson's were in turn considered as motor symptoms which are of the utmost importance for a clinical analysis (10, 11).

On the other hand, according to Alvarado, botulinum toxin acts on sialorrhea, this being one of the main symptoms present in Parkinson's and which are great triggers to obtain a better lifestyle, which results have shown that botulinum toxin type A to reduce the accumulation of saliva, due to infiltration in the parotid and submandibular glands, which stopped movements. In comparison, Santos determines that a person suffering from Sialorrhea should stop its treatment before implementing botulinum toxin for Parkinson's as it can aggravate it (12, 13). Research by Honk et al. (14) points out the satisfaction of patients when maintaining treatment with botulinum toxin. Also, in the following articles: Mojica et.al (15); Wissel and Kiwi (16), Fernández (17) the satisfaction demonstrated by the patients who integrated into the use of this medication during the first weeks of its use is confirmed, considering that the studies were only conducted during a brief time in which the efficacy against the symptoms was evaluated.

Considering that the studies had a not so long duration, satisfaction on the part of the patients could be demonstrated, however, the existence of studies that show long-term results should be mentioned; As Berardelli and Conte (18) mentions, the short duration of this treatment over six weeks after its application, patients begin to have discomfort or a reappearance of this symptom. However, it should be considered that the cost of this treatment is quite high, for which many patients will not be able to use it as a therapeutic method as mentioned by Tambasco et.al (19), de Jongh et al. (20), Hassell and Charles (21), Zakim and Simpson (22) likewise, after recurrent

treatment, antibodies can be generated that reduce its effectiveness. Finally, it must be considered that botulinum toxin is an encouraging treatment for abnormal movements, however, the budget of the patients must be considered as well as the reactions generated, as well as its efficacy, due to its long-term use.

CONCLUSIONS

The research on the use of botulinum toxin in the treatment of abnormal movements, particularly those associated with Parkinson's disease, highlights its significant therapeutic potential. Botulinum toxin, commonly known for its aesthetic applications, has demonstrated efficacy in controlling symptoms and improving the quality of life for individuals with movement disorders. The non-experimental longitudinal design of this study allowed for a naturalistic observation of the therapeutic effects over time, providing valuable insights into the long-term benefits and challenges associated with this treatment.

The findings indicate that botulinum toxin, particularly Type A, effectively reduces tremors and other abnormal movements by blocking the release of the neurotransmitter acetylcholine. This mechanism of action is crucial in mitigating the motor symptoms associated with Parkinson's disease and essential tremor. The integration of qualitative and quantitative data in this study provided a comprehensive understanding of both the measurable outcomes and the subjective experiences of the participants, emphasizing the treatment's impact on their physical and psychological well-being.

However, the research also underscores several limitations and challenges. The short duration of the therapeutic effects, typically lasting only a few months, necessitates frequent treatments, which can be costly and burdensome for patients. Additionally, the potential development of antibodies against botulinum toxin after recurrent treatments may reduce its efficacy over time. These factors, coupled with the prohibitive cost of treatment, pose significant barriers to widespread and long-term use.

Despite these challenges, botulinum toxin remains a promising treatment option for individuals with movement disorders. The elevated level of patient satisfaction reported in the studies suggests that, when accessible, botulinum toxin can significantly enhance the quality of life for those affected by abnormal movements. Future research should focus on developing strategies to extend the duration of its therapeutic effects and reduce treatment costs, making this beneficial therapy more accessible to a broader population. By addressing these issues, botulinum toxin could become a more viable and sustainable option for managing movement disorders in clinical practice.

BIBLIOGRAPHIC

1. Tater P, Pandey S. Botulinum toxin in movement disorders. *Neurol India*. 2018;66(Supplement):S79-89.
2. Cardoso F. Botulinum toxin in parkinsonism: The when, how, and which for botulinum toxin injections. *Toxicon*. 1 de junio de 2018;147:107-10.
3. Bruno V, Freitas ME, Mancini D, Lui JP, Miyasaki J, Fox SH. Botulinum Toxin Type A for Pain in Advanced Parkinson's Disease. *Can J Neurol Sci*. enero de 2018;45(1):23-9.
4. Naeem F, Reid J, Bailey M, Reid A, Smyth C, Taylor-Rowan M, et al. Pharmacological Interventions for Sialorrhoea in People with Parkinson's Disease: A Systematic Review and Meta-Analysis. *Mov Disord Clin Pract*. abril de 2023;10(4):558-68.
5. Abusrair AH, Elsekaily W, Bohlega S. Tremor in Parkinson's Disease: From Pathophysiology to Advanced Therapies. *Tremor Other Hyperkinet Mov (N Y)*. 2022;12:29.
6. Jabbari B, Comtesse SM. Botulinum Toxin Treatment of Motor Disorders in Parkinson Disease-A Systematic Review. *Toxins (Basel)*. 17 de enero de 2023;15(2):81.
7. Liao YH, Hong CT, Huang TW. Botulinum Toxin for Essential Tremor and Hands Tremor in the Neurological Diseases: A Meta-Analysis of Randomized Controlled Trials. *Toxins (Basel)*. 10 de marzo de 2022;14(3):203.
8. Anandan C, Jankovic J. Botulinum Toxin in Movement Disorders: An Update. *Toxins*. enero de 2021;13(1):42.
9. Tyślerowicz M, Kiedrzyńska W, Adamkiewicz B, Jost WH, Sławek J. Cervical dystonia — improving the effectiveness of botulinum toxin therapy. *Neurologia i Neurochirurgia Polska*. 2020;54(3):232-42.
10. Rueda-Acevedo M, Fuquen FC. Disfunción autonómica en la enfermedad de Parkinson: enfoque práctico. *Acta Neurológica Colombiana*. 1 de septiembre de 2019;35(3 Supl 1):69-74.
11. Yıldız BT, Berktaş DT. Experiences on the administration of botulinum toxin in movement disorders. *Journal of Translational Internal Medicine*. 1 de marzo de 2021;9(1):52-6.
12. Aplicação de toxina botulínica no tratamento da sialorreia crônica em pacientes com doenças neurológicas [Internet]. *PubSaúde*. 2022 [citado 3 de junio de 2024]. Disponible en: <https://pubsaude.com.br/revista/aplicacao-de-toxina-botulinica-no-tratamento-da-sialorreia-cronica-em-pacientes-com-doencas-neurológicas/>
13. Li S, Francisco GE. The Use of Botulinum Toxin for Treatment of Spasticity. En: Whitcup SM, Hallett M, editores. *Botulinum Toxin Therapy* [Internet]. Cham: Springer International Publishing; 2021 [citado 3 de junio de 2024]. p. 127-46. Disponible en: https://doi.org/10.1007/164_2019_315
14. Hok P, Veverka T, Hlušík P, Nevrlý M, Kaňovský P. The Central Effects of Botulinum Toxin in Dystonia and Spasticity. *Toxins*. febrero de 2021;13(2):155.
15. Mojica YMR, García LCM, Ruíz DMC. Aplicación de toxina botulínica en el tratamiento de la distonía. Experiencia en un hospital de tercer nivel. *Revista Colombiana de Medicina Física y Rehabilitación*. 29 de junio de 2022;32(1):36-45.
16. Wissel J, Kivi A. Post-Stroke Spastic Movement Disorder and Botulinum Toxin A Therapy: Early Detection And Early Injection. *Ann Rehabil Med*. octubre de 2023;47(5):326-36.
17. Fernández García G. TOXINA BOTULÍNICA Y SUS APLICACIONES CLÍNICAS. TOXINA BOTULÍNICA Y SUS APLICACIONES CLÍNICAS. 27 de abril de 2022;126(126):1-126.
18. Berardelli A, Conte A. The Use of Botulinum Toxin for Treatment of the Dystonias. En: Whitcup SM, Hallett M, editores. *Botulinum Toxin Therapy* [Internet]. Cham: Springer International Publishing; 2021 [citado 3 de junio de 2024]. p. 107-26. Disponible en: https://doi.org/10.1007/164_2019_339

19. Tambasco N, Filidei M, Nigro P, Parnetti L, Simoni S. Botulinum Toxin for the Treatment of Hemifacial Spasm: An Update on Clinical Studies. *Toxins*. diciembre de 2021;13(12):881.
20. de Jongh FW, Schaeffers AWMA, Kooreman ZE, Ingels KJAO, van Heerbeek N, Beurskens C, et al. Botulinum toxin A treatment in facial palsy synkinesis: a systematic review and meta-analysis. *Eur Arch Otorhinolaryngol*. 1 de abril de 2023;280(4):1581-92.
21. Hassell TJW, Charles D. Treatment of Blepharospasm and Oromandibular Dystonia with Botulinum Toxins. *Toxins*. abril de 2020;12(4):269.
22. Zakin E, Simpson DM. Botulinum Toxin Therapy in Writer's Cramp and Musician's Dystonia. *Toxins*. diciembre de 2021;13(12):899.