

APLICAÇÕES TERAPÊUTICAS DA TOXINA BOTULÍNICA: REVISÃO DE LITERATURA

THERAPEUTIC APPLICATIONS OF BOTULINUM TOXIN: LITERATURE REVIEW

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Eixo Temático: 1

RESUMO

A toxina botulínica é uma neurotoxina produzida pela bactéria *Clostridium botulinum* capaz de reduzir temporariamente a atividade muscular através da inibição da liberação de acetilcolina. Este estudo teve como objetivo analisar suas principais aplicações terapêuticas, eficácia, segurança, duração dos efeitos, custo-efetividade e novas perspectivas na medicina. Foram realizadas revisões bibliográficas descritivas e analíticas, utilizando a base de dados PubMed, com os termos de busca "Botulinum Toxins" e "Therapeutic Uses" combinados pelo operador AND. Foram incluídos artigos em português e inglês relacionados ao tema, desde que você pode encontrá-los na versão inteira e gratuita. Os estudos trazem benefícios principalmente no tratamento de distúrbios musculares, enxaqueca crônica, hiperidrose e certas condições urológicas. Resultados promissores também foram apresentados em novas aplicações, como a depressão, ainda assim sendo necessários mais estudos. A duração dos efeitos (que duram por vários meses), ação localizada e boa tolerabilidade podem incrementar a praticidade e custo-efetividade do tratamento em situações específicas. Conclui-se que a toxina botulínica oferece amplo potencial terapêutico, mas são possíveis mais pesquisas para consolidar suas aplicações emergentes.

Palavras-chave: Toxinas Botulínicas. Uso Terapêutico. Doenças Neuromusculares. Enxaqueca. Hiperidrose.

ABSTRACT

Botulinum toxin is a neurotoxin produced by the bacterium *Clostridium botulinum* that is capable of temporarily reducing muscle activity by inhibiting the release of acetylcholine. This study aimed to analyze its main therapeutic applications, efficacy, safety, duration of effects, cost-effectiveness, and new perspectives in medicine. Descriptive and analytical literature reviews were conducted using the PubMed database, with the search terms "Botulinum Toxins" and "Therapeutic Uses" combined using the AND operator. Articles in Portuguese and English related to the topic were included, provided they were available in full-text, free-access versions. The studies highlight benefits primarily in the treatment of muscle disorders, chronic migraine, hyperhidrosis, and certain urological conditions. Promising results were also reported for new applications, such as depression, although further studies are still needed. The duration of effects (lasting several months), localized action, and good tolerability can enhance the practicality and cost-effectiveness of the treatment in specific situations. It is concluded that botulinum toxin offers broad therapeutic potential, though further research is warranted to consolidate its emerging applications.

Keywords: Botulinum Toxins. Therapeutic Use. Neuromuscular Diseases. Migraine. Hyperhidrosis.

INTRODUCTION

Botulinum toxin (BoNT) is a potent neurotoxin produced by the anaerobic, Gram-positive bacterium *Clostridium botulinum*. It acts primarily by inhibiting the release of acetylcholine at the neuromuscular junction, causing temporary, localized muscle paralysis.¹

Although initially associated mainly with its toxic effects, the substance gradually gained therapeutic value. In the 19th century, Justinus Kerner was among the first researchers to observe its effects on motor and autonomic functions. Subsequently, its clinical use expanded to treat conditions such as strabismus and other disorders linked to abnormal muscle activity.^{1,2}

Over the years, the therapeutic use of BoNT has expanded significantly. Currently, it is employed for conditions such as dystonias, spasticity, strabismus, hemifacial spasm, hyperhidrosis, and chronic migraine, in addition to aesthetic applications.¹⁻³ Its importance lies in its ability to act locally, alleviating symptoms while improving patients' functional capacity and quality of life. At the same time, the expansion of its applications has raised questions regarding appropriate dosages, administration techniques, duration of effects, adverse reactions, and the potential for treatment resistance. These aspects are becoming increasingly relevant as research into new therapeutic applications continues.^{2,4}

Thus, the growing number of clinical applications makes it essential to better understand the benefits and limitations of botulinum toxin. Such understanding facilitates better treatment selection and safer use of the substance in clinical practice. Therefore, this study examines the primary therapeutic applications of botulinum toxin, considering its mechanism of action, efficacy, safety, duration of effects, cost-benefit aspects, and potential future medical uses.

METHOD

This is an analytical and descriptive literature review conducted via searches in the PubMed database. Descriptors such as "Botulinum Toxins" and "Therapeutic Uses"—along with their derivatives—were used, combined with the Boolean operator AND.

Articles published within the last fifteen years in Portuguese or English were selected, provided they were available in full text at no cost and contained information relevant to the study's objectives—specifically regarding mechanism of action, therapeutic applications, efficacy, safety, duration of effects, and future perspectives. Duplicate articles, publications unrelated to the topic or research objectives, and studies lacking free full-text access were excluded.

Following the search, studies were initially evaluated by analyzing their titles and abstracts. Articles deemed relevant were subsequently selected for full-text reading. The information obtained was then analyzed and organized according to the key therapeutic

applications identified, enabling a comparison and discussion of the findings throughout the study.

RESULTS

Analysis of the selected studies demonstrated that botulinum toxin has a broad and constantly expanding therapeutic scope. Although its mechanism is traditionally associated with blocking neuromuscular transmission, studies have identified benefits across various systems and clinical conditions, including movement disorders, pain, autonomic disturbances, urological diseases, and, more recently, psychiatric disorders.¹⁻³

1. Muscle and neurological disorders

The most well-known applications of botulinum toxin involve conditions characterized by excessive or involuntary muscle activity. These include hyperkinetic disorders, such as dystonias, spasticity, blepharospasm, and hemifacial spasm. Because the toxin acts locally and directly on the muscles involved in these disorders, administration at these sites can reduce abnormal contractions and, consequently, alleviate symptoms and pain while improving functional limitations.¹⁻³

In patients with spasticity, for example, reducing the activity of specific muscles can facilitate movement and aid the rehabilitation process. Another instance involves dystonias; for the most clinically common type—cervical dystonia—the toxin is injected into the sternocleidomastoid muscle and is considered the first-line treatment, with 50% to 90% of patients showing improvement.³ Furthermore, a key advantage of this approach is its predominantly localized action, which can reduce the need for systemic exposure to medications.

Strabismus caused by an imbalance in eye muscle strength also represents a significant therapeutic application. In this instance, temporarily reducing the activity of specific eye muscles can alter the balance among the muscles responsible for eye movement.^{1,2} Its use for this condition was pivotal in the development and expansion of other therapeutic applications for BoNT; it also serves as an option when surgery is undesirable or when temporary treatment is appropriate.¹

2. Chronic migraine and pain

The use of botulinum toxin for chronic migraine represents a significant expansion of its therapeutic role. In this condition, its effect cannot be explained solely by muscle relaxation. Its action interferes with the release of substances involved in pain transmission and peripheral sensitization, thereby helping to reduce migraine symptoms.²

Periodic administration can reduce the frequency of headache episodes and thus serve as a preventive option for some patients; however, individual responses vary and may depend on the clinical characteristics of the case.²

Beyond migraine, botulinum toxin is also being investigated for other painful conditions, including certain neuropathic and musculoskeletal disorders—such as Parkinson's disease and camptocormia, among others. Although some studies show favorable results, the evidence is less consistent, and there are fewer studies on these indications compared to those where the toxin's use is already established.² Consequently, these applications should be viewed as promising areas of research rather than as established treatments for routine clinical practice.

3. Hyperhidrosis and glandular secretion

The neurotoxin is also used to treat hyperhidrosis, particularly when excessive sweating interferes with daily activities and negatively impacts quality of life. In this context, it works by inhibiting the neural stimulation responsible for activating sweat glands, resulting in reduced sweat production.^{1,2}

An important feature of this treatment is the duration of its effect. The reduction in sweating can last for several months, although this period varies depending on the treated area, the dosage used, and the individual's response. Once the effect wears off, a repeat application may be required.^{1,2}

The ability to maintain a therapeutic effect for months can make the treatment more convenient for patients, as it does not require daily administration. In some situations, it may also offer a favorable cost-benefit ratio, especially when compared to treatments requiring continuous use.

4. Overactive bladder and urological applications

In urology, botulinum toxin is primarily used to treat overactive bladder and detrusor overactivity, particularly in patients who have not achieved satisfactory results with conventional treatments. When injected into the bladder muscle, it reduces excessive

contractions and can improve symptoms such as urinary urgency, increased urinary frequency, and urinary incontinence.^{1,2}

Furthermore, the toxin offers the benefit of a long duration of action in the body—approximately 12 months—and side effects associated with its use are rare.^{1,2} However, while botulinum toxin can be an effective alternative for patients who do not respond adequately to other treatments, its benefits must be weighed against potential risks.

5. Use in depression

The use of botulinum toxin for depression is one of the more recently investigated areas in the literature. Research has focused primarily on the administration of onabotulinumtoxinA into facial muscles. One proposed hypothesis is that altering the activity of these muscles may influence emotional processing and, consequently, depressive symptoms.^{4,5}

The randomized clinical trial regarding depression selected for this study was published in 2024 and evaluated 58 patients with treatment-resistant major depression. Participants received onabotulinumtoxinA injections in different facial regions and were followed for 12 weeks. After six weeks, a greater therapeutic response was observed in the group treated in the glabellar region compared to the group treated in the crow's-feet area. The article also suggested that patients with higher levels of psychomotor agitation might be more likely to respond to treatment.⁵

These results are significant because they suggest that the effects of botulinum toxin may extend beyond its traditional action on muscles. However, evidence regarding its use for depression is still evolving. Therefore, further studies involving larger patient cohorts and longer follow-up periods are needed to determine the true magnitude of the effect, the most suitable injection sites, and which patients are most likely to benefit.⁵

6. Safety, duration, cost-effectiveness, and new perspectives

Overall, the studies analyzed describe botulinum toxin as a treatment with good tolerability and a favorable safety profile when administered correctly. Adverse effects are generally related to the treated area and tend to be temporary, although their occurrence and intensity may vary depending on the indication, dosage, and injection site.^{1,2,4}

Another important characteristic is the duration of the therapeutic effect. Unlike treatments requiring daily or continuous administration, the effects of botulinum toxin can last

for several months, depending on the clinical indication and individual response. After this period, a repeat injection may be necessary to maintain the effects.^{2,4}

This characteristic can be relevant from both practical and economic standpoints. A treatment that produces a prolonged effect may reduce the need for daily medications or frequent procedures and, in certain situations, offer a favorable cost-benefit ratio. However, the toxin should not automatically be considered a cheaper treatment. Its economic advantage depends on the cost of the procedure, the dosage, the duration of the benefit, the frequency of repeat injections, and the treatment against which it is being compared. In general, the findings indicate that botulinum toxin is a versatile therapeutic option.

CONCLUSION

The literature review demonstrated that botulinum toxin is an important therapeutic resource, particularly for disorders involving muscle activity, chronic migraine, hyperhidrosis, and certain urological conditions. Its localized action, good tolerability, and duration of effect lasting several months can enhance practicality and, in specific situations, yield a favorable cost-benefit ratio. New applications—especially in depression—show promising results but still require further scientific validation.

The review also highlights the expanding therapeutic use of the toxin and the need to tailor its application to each clinical condition. Future studies with larger samples and long-term follow-up are needed to evaluate new indications, safety, duration of effects, treatment resistance, and cost-benefit, thereby contributing to increasingly safe and effective use.

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