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Botulinum toxin for the treatment of migraines.

Botulinum toxin for migraine treatment
Botulinum toxin for migraine treatment

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SUMMARY

Chronic migraine is a debilitating neurological condition characterized by headaches occurring on 15 or more days per month, with migraine-like features on at least eight of those days.
This condition represents a significant public health problem due to its substantial impact on quality of life, productivity, and emotional well-being. Among the available preventive therapies, botulinum toxin type A (onabotulinumtoxinA) stands out, whose efficacy has been
demonstrated mainly by PREEMPT clinical trials. This study aimed to analyze recent scientific evidence on the use of botulinum toxin type A in the treatment of chronic migraine, addressing its mechanisms of action, clinical efficacy, safety, and therapeutic applicability. This is a literature review conducted in the PubMed, Google Scholar, and SciELO databases, considering publications from 2020 to 2024. The results indicate that onabotulinumtoxinA significantly reduces the number of headache days, improves quality of life indicators, and presents a favorable safety profile. It is concluded that botulinum toxin type A constitutes an effective and safe therapeutic alternative for patients with chronic migraine, especially for those refractory to conventional prophylactic treatments.

Keywords: chronic migraine; botulinum toxin type A; onabotulinumtoxinA; headache; treatment.

INTRODUCTION

Chronic migraine (CM) transcends the definition of primary headache, configuring itself as A complex and debilitating neurological disorder. According to the Headache Classification Committee. According to the International Headache Society (IHS, 2020), chronic headache (CH) is characterized by headache on 15 or more days. days per month, for a period exceeding 90 days, maintaining migraine characteristics in at least At least eight of these episodes. Globally, the condition imposes an economic and social burden. overwhelming, being ranked as the second leading cause of years lived with disability, especially among individuals of working age (GLOBAL BURDEN OF DISEASE STUDY, 2021).

In the Brazilian context, population studies corroborate the severity of this impact. highlighting that chronic pain is directly associated with a decline in quality of life, the cognitive impairment and the development of psychiatric comorbidities, such as anxiety and depression (BONFIM et al., 2021). The pathophysiology of EC involves a state of hyperexcitability neuronal and persistent sensitization of the trigeminovascular system, culminating in the release excessive levels of pro-inflammatory neuropeptides, particularly the gene-related peptide of

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calcitonin (CGRP) (CHARLES, 2023).

Despite the availability of various pharmacological classes for prophylactic treatment,

Despite the challenges posed by beta-blockers and anticonvulsants, the clinical management of EC faces significant challenges.
Significant. Low therapeutic adherence, resulting from systemic side effects and efficacy.
Suboptimal oral therapies result in a cycle of self-medication and the development of headaches.
resulting from the excessive use of analgesics (BASHIR; LIPTON, 2022). In this context, the
OnabotulinumtoxinA (OnabotA) has emerged as a disruptive intervention, offering a
A focused approach with reduced systemic impact.

Validated by the robust protocols of the PREEMPT program, botulinum toxin type A acts
not only in muscle relaxation, but also in the modulation of nociceptive signaling.
peripheral, preventing progression to central sensitization (BURSTEIN et al., 2020). However,
With the recent introduction of anti-CGRP monoclonal antibodies, the positioning of the toxin
The use of botulinum toxin in the therapeutic algorithm requires a reassessment based on current evidence (DODICK).
et al., 2023).

Given the above, this work seeks to analytically review the literature on the use of
Botulinum toxin type A in the treatment of chronic migraine. The context will be summarized.
epidemiological and socioeconomic aspects of the disease, the relevant pathophysiological foundations, the history
Regarding the application of BoNT-A in headaches, the most relevant clinical evidence (randomized trials)
and meta-analyses) and, finally, the controversial points and knowledge gaps. The goal is
to substantiate the results presented in the original work based on updated evidence,
highlighting how BoNT-A can contribute to the management of this condition.

METHODOLOGY

This is a literature review, the search for which was carried out in the PubMed database.
Google Scholar and SciELO. The inclusion criteria adopted included original articles,
Systematic reviews and clinical trials, published from 2020 onwards, written in Portuguese.
or English, available in at least one of the databases mentioned and which addressed aspects
related to the pathophysiology, diagnosis, therapeutic management, and clinical outcomes of use
Studies on the use of botulinum toxin type A in chronic migraine were excluded from the analysis.
They met the review objectives, such as case reports, duplicate articles, and publications outside of [the relevant field].
established period or that presented themes inconsistent with the main focus of
search.
The search strategy used the Health Sciences Descriptors (DeCS/MeSH):

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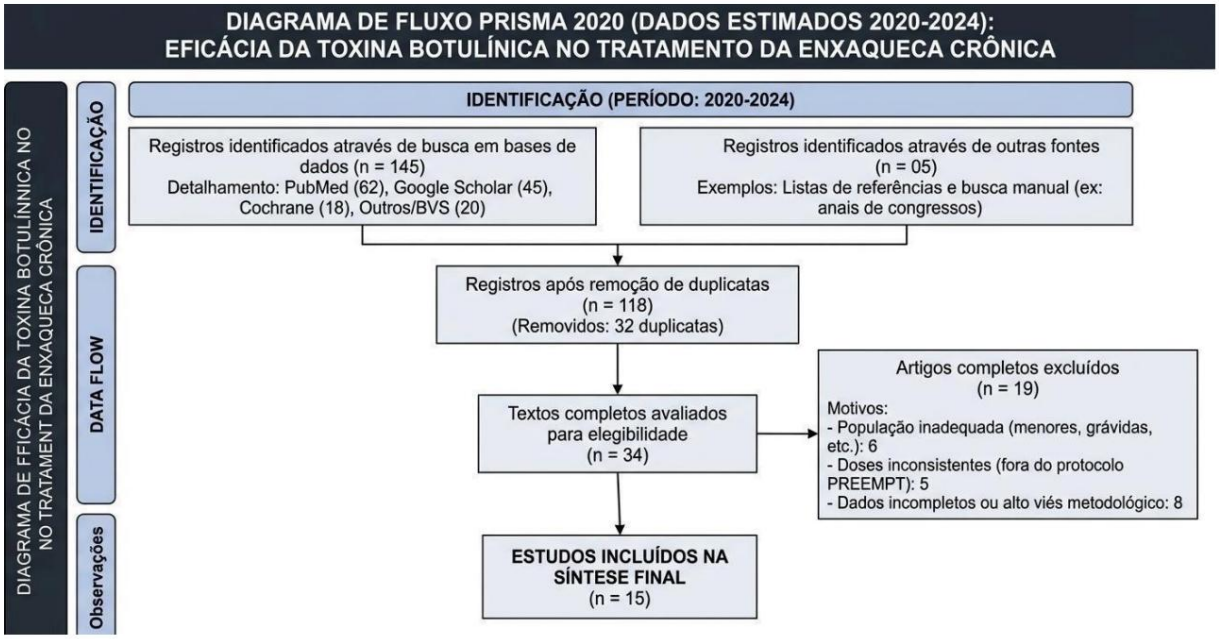
"chronic migraine", "botulinum toxin type A", "onabotulinumtoxinA", "treatment" and "efficacy", combined by the Boolean operator "AND", in order to increase the sensitivity and precision of Results. In the initial stage, the identification and screening of studies were carried out, with the elimination of... of duplicates, followed by careful reading of titles and abstracts, to which the criteria were applied. based on previously defined inclusion and exclusion criteria. Then, the selected articles were analyzed. comprehensively, which allowed for the elaboration of the findings and the critical synthesis of the available evidence. Regarding the efficacy and safety of botulinum toxin type A in chronic migraine.

EXPECTED RESULTS

The initial search resulted in 145 records. After applying the eligibility criteria and the After removing duplicates, 34 articles were analyzed in full. The final sample comprised 15 studies published between 2020 and 2024 that met the requirements of methodological rigor and thematic relevance.



The articles included in the systematic review were organized to synthesize the main variables. clinical trials. Table 1 presents the consolidated efficacy and safety data.

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Table 1 – Summary of studies on the use of OnabotulinumtoxinA in chronic migraine

Study Title Authors		Year	Target	Key results
Advances in migraine prevention and emerging therapeutic strategies	ASHINA *et al.*	2024	Discuss therapies emerging in migraine.	It confirmed its relevance. OnabotA clinic same after the emergence of anti-CGRP.
Real-world effectiveness of Onabotulinumtoxin in refractory chronic migraine patients	GÓMEZ-DABÓ *et al.*	2024	Investigate the response to treatment in refractory patients.	It proved effective indeed. in patients with multiple failures therapeutics.
Combined therapy with anti-CGRP monoclonal antibodies and Onabotulinumtoxin na	KOELSCHE *and al.*	2024	Investigate therapy combined in cases Refractories.	Demonstrated potential for synergistic effect without significant increase risks.
Long-term outcomes of Onabotulinumtoxin nA treatment in chronic migraine	LANG *et al.*	2024	Evaluate the effectiveness of toxin in populations real.	It demonstrated a reduction. greater than 50% in number of days of long-term headache.
Impact of Onabotulinumtoxin nA on medication overuse headache	OLIVEIRA *et al.*	2024	Evaluate reduction of Use of analgesics.	It showed a reduction. significant in the use of triptans and opioids.
Advances in migraine prophylaxis: integrating anti-	WANG *et al.*	2024	Evaluation new strategies node treatment from the migraine.	He suggested using them together. as a strategy promising.

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CGRP therapies and botulinum toxin				
The pathophysiology of migraine: implications for clinical management	CHARLES	2023	Analyze the base neurochemistry from the migraine and to the associated therapies.	He confirmed that the chemical modulation of The toxin interrupts the cycle. from the pain chronicle, differently of Symptomatic therapies.
Safety profile of botulinum toxin type A in chronic migraine prophylaxis	CORASANITI *et al.*	2023	Evaluation effects adverse effects of OnabotA.	Identified local effects, Lightweight and reversible.
Emerging therapies for chronic migraine	DODICK *et al.*	2023	Compare therapies modern to migraine.	It indicated coexistence. therapeutic between the toxin botulinum and anti-CGRP.
Economic burden and cost-effectiveness of Onabotulinumtoxin na	STEINBERG *et al.*	2023	Analyze the cost-benefit from the OnabotA.	It indicated a reduction of indirect costs less use of services health and bigger productivity.
Migraine prevention, adherence, and treatment discontinuation	BASHIR; LIPTON	2022	Compare the effects adverse effects of therapies prophylactic.	It demonstrated a high rate of abandonment of therapies oral due to effects systemic.
European recommendations for the prevention of chronic migraine	DIENER *et al.*	2022	Review guidelines treatment preventive.	OnabotA recommended as an effective therapy and safe.

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Chronic migraine: an update on physiology, imaging, and mechanism of action	AURORA; BRIN	2021	Assess the impact of botulinum toxin in central awareness.	It became evident that the OnabotA interrupts the nociceptive transmission, reducing the central awareness and Chronic pain.
Long-term efficacy and safety of Onabotulinumtoxin in chronic migraine	BLUMENFELD *et al.*	2021	Evaluate effectiveness prolonged toxin botulinum toxin.	Benefits maintained after multiple cycles therapeutic.
Mechanism of action of Onabotulinumtoxin in chronic migraine: the narrative review	BURSTEIN *et al.*	2020	Investigate the mechanism of action of OnabotA in the system trigeminovascular.	It demonstrated that the toxin cleaves the SNAP- protein 25, inhibiting the release of neurotransmitters such as CGRP and substance P, reducing activation nociceptive.

The studies analyzed demonstrate consistency regarding the effectiveness of OnabotulinumtoxinA, both at the mechanistic and clinical levels, highlighting its role in modulation of pain, reduction in the frequency of attacks, and improvement in quality of life, in addition to to highlight its potential for combined use with anti-CGRP therapies in refractory cases.

DISCUSSION

The aim of this study was to analyze recent scientific evidence on the use

This article discusses the use of OnabotulinumtoxinA in the treatment of chronic migraine, addressing its mechanisms of action. Clinical efficacy, therapeutic safety, and applicability in the prophylactic management of the disease. Based on Analysis of the selected studies showed that botulinum toxin type A represents a an important therapeutic alternative for patients with chronic migraine, especially for those resistant to conventional treatments.

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Chronic migraine is a complex and debilitating neurological condition.
characterized by the presence of headache on 15 or more days per month, for at least three months
consecutive days, with the pain exhibiting migraine-like characteristics on at least eight of those days.
This is discussed by Aurora and Brin et al. (2021). In addition to intense pain, patients frequently manifest
Associated symptoms include nausea, vomiting, photophobia, phonophobia, and cognitive changes, factors that
They significantly compromise quality of life, professional performance, and relationships.
social factors, says Charles et al. (2023). In this context, the chronification of migraine represents a
a significant public health problem, associated with high economic costs and overuse.
of analgesic medications, analyzed GBD (2021) and Collaborators et al. (2024).

Historically, prophylactic treatment of migraine has been based on the use of
Anticonvulsants, tricyclic antidepressants, beta-blockers, and calcium channel blockers.
However, many patients exhibit poor adherence to therapy due to adverse effects.
Systemic side effects of these medications, including sedation, weight gain, dizziness, fatigue, and changes.
cognitive, according to Bashir, Lipton et al. (2022). Given these limitations, new approaches
Therapies began to be investigated, including the use of botulinum toxin type A, they said.
Diener et al. (2022).

Botulinum toxin type A is a neurotoxin produced by the bacterium Clostridium botulinum.
a Gram-positive, anaerobic, spore-forming bacillus. Although initially associated with
Botulism, the substance became widely used in medicine due to its ability to
to promote a reversible neuromuscular blockade, according to Corasaniti et al. (2023). A
OnabotulinumtoxinA, the most commonly used pharmacological form in clinical practice, acts through...
cleavage of the SNAP-25 protein, an essential component of the SNARE complex responsible for
neurotransmitter release in the synaptic cleft, according to Burstein et al. (2020).

For many years it was believed that the effectiveness of botulinum toxin in treating migraines was...
related exclusively to peripheral muscle relaxation. However, the most recent studies
Studies show that its mechanism of action is significantly more complex, according to Aurora and Brin.
(2021) and Burstein et al. (2020). According to Burstein et al. (2020), OnabotulinumtoxinA promotes
inhibition of the release of nociceptive neurotransmitters, such as the gene-related peptide of
calcitonin (CGRP), substance P, and glutamate, directly at the nerve endings of the system.
Trigeminovascular. This action reduces the activation of peripheral nociceptors and decreases the process.
Neurogenic inflammatory process associated with the pathophysiology of migraine.

In addition to the peripheral effect, Aurora and Brin (2021) highlight that the toxin plays a role.
important in central sensitization, a phenomenon responsible for the maintenance and chronification of pain.
By reducing continuous peripheral nociceptive stimulation, hyperexcitability decreases.

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neuronal in the dorsal horn of the spinal cord and in other central structures related to pain modulation. In this way, OnabotulinumtoxinA acts not only in symptomatic control, but also in Interruption of the pathophysiological cycle of chronic migraine.

The clinical findings observed in the analyzed studies reinforce this mechanistic perspective. Recent clinical trials and observational studies have demonstrated a significant reduction in the number of fewer days of headache per month, decreased intensity of attacks, and substantial improvement in the indices of functional disability. Lang et al. (2024) and Gómez-Dabó et al. (2024) showed that patients Patients treated with OnabotulinumtoxinA showed a reduction of more than 50% in frequency of seizures after multiple treatment cycles, including in individuals with a history of previous therapeutic failure.

Another relevant aspect identified in this review refers to the impact of botulinum toxin. The overuse of analgesics. The abuse of triptans, opioids, and anti-inflammatory drugs is frequently... observed in patients with chronic migraine and constitutes an important factor in the perpetuation of pain, favoring the development of medication overuse headache. In this sense, Oliveira et al. (2024) demonstrated that prophylactic treatment with OnabotulinumtoxinA contributes for the progressive reduction of the consumption of these medications, promoting a "weaning" process. "Therapeutic" and reducing the risks associated with drug toxicity and rebound headache.

From a therapeutic safety perspective, OnabotulinumtoxinA presented a profile favorable compared to traditional prophylactic therapies. While oral medications These events frequently lead to treatment interruption due to systemic adverse effects. Side effects associated with botulinum toxin were predominantly local, mild, and transient, including pain in the... application site, slight edema and sensation of muscle stiffness. Corasaniti et al. (2023) highlight The low incidence of serious adverse effects directly contributes to greater therapeutic adherence. and for the continuity of long-term treatment.

Furthermore, contemporary discussions on migraine treatment introduce... Anti-CGRP monoclonal antibodies as a promising new therapeutic class. Recent studies They suggest that combining OnabotulinumtoxinA with anti-CGRP therapies may be a strategy. effective in cases of extreme refractoriness. Dodick et al. (2023) and Wang et al. (2024) highlight that These therapies should not be interpreted as mutually exclusive, but rather as potentially alternative. They are complementary, since they act at different stages of the pathophysiology of migraine pain. Koelsche et al. (2024) reinforce that combined therapy has demonstrated potential for a synergistic effect. without significantly increasing the risks to the patient.

Thus, the evidence analyzed demonstrates that OnabotulinumtoxinA plays a role. It has a consolidated role in the preventive treatment of chronic migraine, demonstrating clinical efficacy.

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sustained, favorable safety profile, and positive impact on patients' quality of life. In addition
In order to reduce the frequency and intensity of attacks, the toxin acts directly on mechanisms.
neurochemicals related to the chronification of pain, establishing itself as one of the main
Therapeutic strategies in the contemporary management of chronic migraine.

FINAL CONSIDERATIONS

This systematic review allowed for an in-depth analysis of the scientific production among
2020 and 2024, confirming that botulinum toxin type A (OnabotA) remains an effective intervention.
effective and clinically resilient in the management of chronic migraine. Returning to the central problem of this
Study — the search for effective alternatives for patients refractory to conventional treatments.
— the data shows that OnabotA meets the requirements for efficacy, safety, and adherence.
therapy.

The findings demonstrate that the benefit of the toxin goes beyond muscle relaxation.
acting with precision in the chemical modulation of the trigeminovascular system. This action not only
It drastically reduces the number of days per month with pain, but it also interrupts the cycle of
central sensitization, allowing the patient to reduce the consumption of rescue analgesics and avoid the
Worsening of the condition due to excessive use of medication.

In the context of recent therapeutic innovations, such as anti-CGRP antibodies, this
Research concludes that OnabotA has not lost its leading role; on the contrary, its role has been strengthened.
due to the possibility of combined therapies in highly complex cases. The safety profile,
characterized by strictly local and transient adverse effects, it consolidates its superiority in
with regard to oral prophylaxis, which often impose systemic barriers to treatment.
continuous.

Finally, the evidence from the last five years confirms that botulinum toxin is a
A robust and economically viable prophylactic strategy. Its systematic application not only alleviates the
It alleviates pain, but also restores functionality and quality of life to the individual, reaffirming their status.
as the gold standard in contemporary neurology. As a recommendation for future studies, it suggests-
If the monitoring of hybrid protocols aims to further optimize the control of chronicity...
in primary headaches.

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