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## Treatment of Notalgia Paresthetica with botulinum toxin A: a review

*A importância da toxina botulínica no tratamento da notalgia parestésica: uma revisão*

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### ABSTRACT

Notalgia Paresthetica (NP) is a sensory neuropathy characterized by itching, with or without a macule. The Botulinum Toxin A treatment may have beneficial effects on pruritus, possibly by inhibiting the substance P. This study aims to evaluate the benefits/limitations of Botulinum Toxin in NP treatment. The methodology consisted of the selection of publications in PubMed, filtered by predefined criteria. Five articles were compiled, and the results were favorable in four of them. The study concluded the effectiveness of Botulinum Toxin A treatment in most of the articles, especially in the pruritus improvement.

**Keywords:** Pruritus; Botulinum toxins type A; Hyperesthesia; Hyperpigmentation.

### RESUMO

A notalgia parestésica (NP) é uma neuropatia sensorial caracterizada por prurido, com ou sem a presença de uma mácula. O tratamento com toxina botulínica A pode ter efeitos benéficos no prurido, possivelmente por inibição da substância P. O objetivo deste estudo é avaliar os benefícios/limitações da toxina botulínica no tratamento da NP. A metodologia consistiu na seleção das publicações por meio do PubMed e na filtragem dessas publicações por critérios predefinidos. Cinco artigos foram compilados, e os resultados foram favoráveis em quatro deles. Conclui-se que há eficácia do tratamento com toxina botulínica A na maioria dos artigos, principalmente na melhora do prurido.

**Palavras-chave:** Prurido; Toxinas botulínicas tipo A; Hiperestesia; Hiperpigmentação.

## Review Article

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## INTRODUCTION

Notalgia paresthetica (NP) consists of a chronic sensory neuropathy, more frequent in middle-aged women, characterized by pruritus in the scapular region, usually unilateral, with or without the presence of a hyper or hypochromic macula. Other symptoms may also be present, such as pain, paresthesia, hypoesthesia, or hyperesthesia.<sup>1</sup> The etiology of this condition is still unclear. However, several studies propose multifactorial causes such as muscle compression of spinal nerves, especially in the dermatome region of T2 to T6.<sup>1</sup> Other possible causes are the involvement of thoracic nerves due to degeneration and herniation of the intervertebral disc, osteoarticular lesions that course with hyperostosis, among others.<sup>2</sup> The diagnosis of NP is performed mainly through detailed clinical history and physical examination.<sup>2</sup>

Regarding the treatment of notalgia paresthetica, there are several options, with different levels of success, including oral medications, topical agents, injection of botulinum toxin A, transcutaneous electrical nerve stimulation (TENS), and physiotherapy.<sup>2</sup> Treatment with botulinum toxin A may have beneficial effects concerning pruritus, possibly by inhibiting the release of substance P by the presynaptic neuron.<sup>1,2</sup> However, there are divergent results regarding the cost-effectiveness of using this therapeutic modality.<sup>1</sup>

This study aims to assess the benefits of using botulinum toxin A to treat notalgia paresthetica.

## METHODS

We selected publications in May 2022 to identify all clinical studies on botulinum toxin type A to treat NP. Through the PubMed databases, we conducted a bibliographic search in the last 20 years using the keywords: 'Botulinum Toxin', 'Notalgia Paresthetica', 'Treatment', 'Hyperesthesia', 'Itching', 'Hyperpigmented patch pruritus'.

Three researchers independently collected and compared data, considering the inclusion criteria: randomized clinical trial articles, case series, prospective studies, and case reports, published in Portuguese, English, or Spanish. Review articles were excluded. In total, seven articles were compiled for full reading and text analysis.

## RESULTS

This literature review included five articles for analysis. The results were favorable to the use of botulinum toxin A in four manuscripts.<sup>3,4,5,6</sup>

The case series by Weinfield P. et al.<sup>3</sup> administered 16 U of botulinum toxin type A to one of the patients and 24 U to the other. Both experienced symptomatic improvement maintained after 18 months, as assessed by self-reports. The one who used the lowest dosage also experienced reduced hyperpigmented area.

Wallengren J. et al.<sup>4</sup> conducted a prospective study with six patients performing an intradermal injection of botulinum toxin A, with doses of 18–100U. Five of the six patients repor-

ted improved itching one week after the procedure. Six weeks after treatment, there was a 28% reduction in itch intensity on the visual analog scale (VAS). The two patients who reported an improvement in pruritus after six weeks of treatment were followed up for 18 months; one remained pruritus-free, and the other reported a 45% decrease in pruritus according to the VAS.

Pérez-Pérez L.<sup>5</sup> case series included five patients refractory to topical and systemic therapies, yielding variable results. The application of botulinum toxin type A ranged from 50 U to 56 U. Three of these patients experienced improvement in pruritus after one month but didn't maintain it for the following semester. The other two showed minor symptoms after six months of treatment, but only one kept the result for up to 18 months.

According to the case report by Datta S. et al.<sup>6</sup> botulinum toxin was favorable in a 58-year-old patient who suffered from refractory pruritus and functional impairment caused by NP. The study used 2–5U of botulinum toxin type A in 3 ml of saline solution (0.9%) intradermally at a distance of 1–2cm from the affected area.

There was no statistical significance in the findings in only one of the articles. The double blind randomized clinical trial by Maari C. et al.<sup>7</sup> included 20 patients with NP resistant to previous topical treatments. The study randomized patients into two groups: one group treated with botulinum toxin A and the other control group that received isolated saline solution (placebo group). After 12 weeks of treatment, there was no significant difference between groups in terms of improvement in pruritus and hyperpigmentation.

## DISCUSSION

The present literature review demonstrates that the use of botulinum toxin in patients with NP has been conducted for at least 15 years since the date of publication of this dissertation.

Botulinum toxin type A still does not have its therapeutic dose defined for NP. Thus, this review compiled dosages from 2 U to 200 U. The variability of the affected surface areas justifies the dose variation. Despite this justification, not all studies have established a dose-by-area ratio.

The analysis of the therapeutic effect was based, for the most part, on the improvement of itching, the main symptom of the disease, and the area of hyperpigmentation. The tools used to quantify this improvement were also discrepant, ranging from qualitative patient reports to the use of VAS by health professionals or by the patient himself.

The follow-up of the studies included verifying the duration of the therapeutic effect, which ranged from six to 18 months. One of the case reports did not specify the follow-up duration or the effect assessment.

Only one of the included studies assessed the adverse events of the use of botulinum toxin and found them to be absent, except for the burning sensation during the injection, present in 100% of the patients.<sup>4</sup>

Table 1: Results of included articles

First author [Ref.], year	Study design	n	Botulinum toxin type A dose	Follow-up	Results
Weinfeld <sup>3</sup> , 2007	Case report	2	16-24U	18 months	Improvement in symptoms (declared by patients)
Wallengren <sup>4</sup> , 2010	Prospective	6	18-100U	18 months	Five patients showed a significant reduction in VAS after six weeks, with one maintaining the absence of pruritus for up to 18 months
Pérez-Pérez <sup>5</sup> , 2014	Case series - retrospective	5	48-56U	18 months	Three patients experienced improvement in pruritus after one month (not maintained). The other two showed symptomatic improvement after six months and only one maintained this improvement after 18 months.
Datta <sup>6</sup> , 2020	Case report	1	2-5U	Not specified	Improvement (unspecified)
Maari <sup>7</sup> , 2014	Randomized double-blind clinical trial	20	Maximum of 200U	Total of 24 weeks	No significant difference in itching (according to VAS) or hyperpigmentation

Source: The authors, 2023

The main limitation of the present study refers to the inclusion of different types of study, with consequent different levels of evidence.

## CONCLUSION

The use of botulinum toxin A in the treatment of NP proved to be effective in most of the articles included in this literature review, especially regarding pruritus improvement.

However, despite the benefits demonstrated in four articles, the duration of symptom improvement was variable in the different studies analyzed, limiting the analysis of the effectiveness of this therapy (Table 1).

Further studies are needed to define the effect of botulinum toxin type A on NP, as the only randomized clinical case included did not demonstrate favorable results. Another justification for such a statement is the discrepancy between the doses used and the tools for evaluating the results. ●

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