EFFECTIVENESS OF BOTULINUM TOXIN IN THE TREATMENT OF CHRONIC MIGRAINE: A SYSTEMATIC REVIEW

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INTRODUCTION

Migraine is a neurological syndrome of long duration characterized by the frequency of episodes of severe pain correlated with debilitating accompaniments. It is considered one of the most disabling diseases today. that disrupt the quality of life. (MARTINELLI et al., 2020; BUSE; LIPTON, 2013)The pathogenesis of migraine revolves around the sensory pathways of trigeminal pain. Nowadays, new therapeutic modalities have been sought and developed as alternatives for the treatment of migraine in relation to conventional drug therapy, for its control and prevention, such as botulinum toxin (BoNT). (TIWARI; AGRAWAL, 2022)In the 1990s, exploratory studies of the use of BoNT for the control of headaches and chronic migraines began. In 1998, the first open study found efficacy in the use of the toxin in patients with frontal and periorbital headaches. (WHITCUP et al., 2014)Botulinum toxin is popularly known for its cosmetic effects. However, treatment with BoNT for medical conditions goes beyond cosmetic use. Its medical use includes several indications, such as cervical dystonia, axillary hyperhidrosis, blepharospasm, strabismus, overactive bladder, urinary incontinence due to neurogenic detrusor overactivity and chronic migraine. (WITHCUP et al., 2014)

METHODS & MATERIAL

The bibliographic survey of the research was carried out through searches in the following databases: Embase, Web of Science and Pubmed. To aid information management, all related works found during searches have been added to the Zotero software. In the search for scientific works related to the research theme, descriptors present in the controlled vocabulary base of the Virtual Health Library (VHL) and keywords found in the works already researched were used. The descriptors used were: botulinum toxin type A (Botulinum Toxins, Type A;), chronic migraine (Chronic migraine) and randomized clinical trial.

RESULTS

The initial literature search in the databases resulted in 430 articles. After excluding duplicate articles, 106 remained, which were examined by title, abstract and publication date, leaving 25. Manually, 04 new articles were selected in Google Scholar.

Table 01. Patient data and study characteristics.

Authors	Location	Number of patients	Sex	Age	Type of study
DIENER et al., 2010	North America and	1384	Female and Male	18-65	Randomized trial
ELKIND et al., 2005	U.S	418	Female and Male	18-65	Randomized trial
FREITAG et al., 2008	U.S	60	Female and Male	18-65	Randomized trial
SANDRINI et al., 2011	Italy	68	Female and Male	18-65	Randomized trial

Table 01 represents the patients' data and the characteristics of the studies. The four articles chosen were all randomized studies, where a comparison was made between BoNT and placebo. The studies were published between 2005 and 2011.

Table 2. Description of the methodologies of the articles analyzed

Authors	application regions	commerial product	Amount	Period
DIENER et al., 2010	M. corrugator, M. procerus, M. frontal, M. temporal, M. occipital, M. supraspinatus M. cervical and M.	BOTOX, Allergan	155-195U	24 weeks 32 weeks
ELKIND et al., 2005	M. frontal, M. procerus and temporal m.	BOTOX, Allergan	7,5U - 25U-50U	4 months
FREITAG et al., 2008	M. corrugator, M. temporal, M. frontal, M. suboccipital and m. trapezius	BOTOX, Allergan	100U	4 months
SANDRINI et al., 2011	M. frontal, M. corrugator, M. temporal, M. supraspinatus and M. trapezius	BOTOX, Allergan	100U	12 weeks

Table 2 shows the selected studies that used botulinum toxin, BOTOX (Allergan Inc., Irvine, CA, USA), the amount of product used varied between them ranging from 7.5U to 195U. Two studies continued their research for a period of 4 months and the other two ranged from 12 to 32 weeks.

Table 3. Results

Authors	Results
DIENER et al., 2010	• BoNT was statistically significantly superior to placebo, frequency of headache days per 28 days from baseline (-9.0 onabotulinumtoxinA/-6.7 placebos, p<.001). • BoNT was safe and well tolerated, with few treatment-related adverse effects.
ELKIND et al., 2005	• No consistent, statistically significant differences were observed in any efficacy variable; • Adverse events were similar between the control and placebo groups; • BoNT has not been shown to be more effective than placebo.
FREITAG et al., 2008	• BoNT was statistically superior to placebo; Six patients with BoNT patients, compared to • 3 placebo patients had a 50% reduction in their migraine episodes. • Treatment with the toxin was superior to placebo for constant medication use; • Adverse events were rare and similar between groups.
SANDRINI et al., 2011	• There was a significant reduction in mean acute pain medication consumption at 12 weeks; • Patients who initially reported muscle sensitivity showed a significant improvement in the average number of days with headache and a reduction in average drug use and pain intensity. • Statistically significant improvement in patient-reported measures of quality of life, such as scores HIT-6 and MIDAS, observed in patients treated with BoNT.

Table 3 shows the effectiveness of the use of the toxin in migraine control, only one of them did not report significant differences in terms of product effectiveness and similarity between the control and placebo groups. Certain studies point to a significant reduction in days with a headache and in the use of medication for migraine relief. Adverse effects were rarely reported.

DISCUSSION

According to Martinelli et al. (2020) migraine is one of the most disabling diseases we have today. For this reason, it is necessary to search for new prophylactic and therapeutic methods to control the disease.In a study carried out by Diener et al. (2010) with a total of 1384 patients, the research was divided into two phases, PREEMPT 1 and PREEMPT 2. This PREEMP 2 study was carried out to evaluate the effectiveness of BoNT as a prophylaxis for cases of migraine. In this study, we have reports of significant improvements in relation to the BoNT group to placebo, with a decrease in days with pain and moderate/severe migraine, we observed a better quality of life for these patients.Sandrini et al. (2011) found similar results to Diener et al. They demonstrated a mean decrease in days and intensity of pain and medication consumption. Freitag et al. (2008) as well as the other authors mentioned above, their results were favorable regarding the toxin being superior to the use of placebo, with a reduction in migraine episodes and days with pain, in addition to an improvement in quality of life.However Elkind et al. (2005), portrayed the toxin not being significantly more effective than placebo, but in their study, patients received dosages of 25U or 50U, which was lower than when compared with previous authors who had a minimum dosage of 100U .

CONCLUSION

Evidence that botulinum toxin leads to a reduction in monthly days with headaches and in the use of conventional medications and even reports of quality of life based on clinical trials, but further studies are still needed to be able to arrive at a consensus on the dosage of the product and possible period of application.

REFERENCES

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Presented at the 99th Annual Session of the Greater New York Dental Meeting in 2023.