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**Chronic Migraine Prophylaxis: A comparison between Botox and Topiramate**

By

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## INTRODUCTION

Migraine is a debilitating disorder, characterized by severe headaches contributing to a poor quality of life. Approximately 14% of Americans are afflicted with migraine headaches. Migraine headache is described as unilateral pulsating pain with or without aura; it can have associated photophobia, phonophobia, nausea, vomiting, and inability to carry on with daily activities during an acute attack. People with migraine headaches often miss days from work and important family events. It is the fifth most common reason for emergency department visits and contributes to significant economic burden. Patients with episodic migraine often convert to chronic migraine, which is defined as greater than 15 migraine days per month for three consecutive months.<sup>1</sup> In addition to current acute relief medications such as triptans and non-steroidal anti-inflammatory drug (NSAIDS), it is imperative to start prophylactic medication early.

Chronic migraine is a complex disorder that is difficult to manage and would benefit from a multimodal approach. Lifestyle modifications and concomitant use of prophylactic medications are key in migraine prevention. Patients should keep a headache diary to help identify migraine triggers. Avoiding triggers and adapting the following recommendations are crucial: adequate sleep, stress relaxation techniques, adequate hydration, regular exercise, timely eating regular meals, limiting caffeine and other foods that trigger acute migraines. In addition to lifestyle modifications the careful consideration of prophylactic medication is warranted under the following circumstances: greater than 15 headache days per month, acute medication overuse (greater than 8 days), and failure of acute medications to resolve the headache. Current recommendations for chronic migraine prophylaxis are to start patients on a low dose non-selective beta blocker such as propranolol. Even though beta blockers are the preferred treatment

other medications such as tricyclic anti-depressants, anti-epileptic drugs, and onabotulinum toxin (Botox) are commonly used due to a high number of patients who that are refractory to first line treatment.<sup>1</sup> The following is a review of medical literature on patients with chronic migraine and the comparison of topiramate with Botox for migraine prophylaxis, and the effect on the number of headaches per month, over a 12-week period.

This is a review of two prophylactic medications for chronic migraine prophylaxis, Botox and topiramate. Three articles were selected that reviewed the efficacy of topiramate and regarding the effectiveness of Botox. These articles measured quality of life through a Migraine Specific Quality of Life Questionnaire. Inclusion criteria for choosing these articles is as follows; articles must be published within the last 15 years, focus must be adults excluding pediatric populations, primary focus of the articles is chronic migraines, research studies must follow patients for at least 12 weeks.

#### TOPIRMATE EFFECTIVENESS

Topiramate is an Anti-epileptic medication that has been proven to show improvement in chronic migraine symptoms. The following research studies evaluated topiramate efficacy in chronic migraine prophylaxis, both studies found that it significantly reduced the severity and number of headaches per month.

In a randomized double-blind trial conducted by Silberstein et al, topiramate was shown to be an efficacious prophylactic agent for chronic migraine prevention when compared to placebo. The study evaluated the efficacy of topiramate, in a trial that extended over the course of 16 weeks and had a total of 306 patients. Participants were divided into two groups treatment and placebo. The treatment group was titrated up to topiramate 100mg daily. The study

concluded that topiramate 100mg daily significantly reduced the number of migraine days when compared to the placebo group.<sup>2</sup> In the treatment group patients reported mild to moderate side effects ranging from paresthesia, upper respiratory infection, and fatigue. The placebo group also reported similar side effects, the most common were fatigue, nausea, and upper respiratory infection. The following study had similar findings in a slightly different chronic migraine population group, one that overused abortive treatments such as triptans and NSAIDS.

Similarly, in the following study topiramate was found to be efficacious in the treatment of those with an average of 20 migraine days per month. The study was a small 59 person randomized double-blind placebo-controlled trial. At baseline 78% of the participants were overusing acute medication. Medication overuse is defined as the use of abortive treatment such as triptans or NSAIDS greater than eight days per month. Medication overuse is a major contributor to rebound headaches thus, adding to the number of headache days per month in these patients.<sup>3</sup> All ongoing migraine prophylactic medications in the antiepileptic medication class were discontinued. Other prophylactic medications were continued if the patient continued to have greater than 15 migraine days per month.

Topiramate reduced the number of migraines in those with acute medication overuse. Topiramate was titrated up to a dose of 100mg over the course of several weeks. At the completion of the 16-week trial, topiramate statistically significantly reduced the number of migraines per month when compared to the placebo, which increased by one. The most common side effect noted in both the treatment and control group was paresthesia which occurred in about half of the topiramate group and less than 10% in the placebo group. The Migraine Disability Assessment (MIDAS) showed an improvement in quality of life with the use of topiramate; however, these results were not statistically significant, due to lack of power with a small sample

size.<sup>3</sup> Overall, topiramate is tolerated and proven to be an effective means of migraine prophylaxis, which significantly reduces the quantity and severity of migraine headaches per month.

## BOTOX EFFECTIVENESS

Botox is a medication that is injected into the muscles and leads to temporary muscle paralysis. Although the physiology behind how it prevents migraine headaches is not completely understood, the following studies demonstrate it is as an effective means of chronic migraine prophylaxis, in patients that have failed oral therapies. The first article was a review of two large phase III research studies that evaluated Botox as a prophylactic medication for chronic migraine headaches.<sup>4</sup> Both studies were randomized controlled trials that evaluated a total of 1384 participants. Patients received Botox injections every three months for a total of two years. The studies had similar findings; Botox is efficacious in decreasing the quantity of migraine headaches. The studies also assessed quality of life through several questionnaires. Botox improved quality of life in patients with chronic migraine and was generally tolerated. Patients reported the following side effects: neck pain, muscle weakness, and eye ptosis.<sup>4</sup> A similar study was done that followed patients for one year and had similar findings.

This was a long-term study that followed patients for a year and was divided into a double-blind trial then opened as a non-blinded trial. After the blinded portion of the study, researchers found that Botox decreased the number of headaches per month and the severity of symptoms when compared to placebo. During the open phase of the trial, all patients received Botox injections every three months. At one year, the study concluded that patients in the early treatment group were found to have a greater than 50% reduction in migraine days per month.<sup>4</sup> Botox also showed an improvement in quality of life as measured by the quality of life

questionnaires. Another long-term trial had similar findings such as decreased number of headache days by greater than 50% per month.

A similar trial was conducted to evaluate the effectiveness of Botox as prophylaxis for chronic migraine. This was a long-term study that followed patients for two years. This study had a total of 716 participants all of which received Botox injections every three months, for the course of the study. Upon completion of the study, patients had a statistically significant reduction of greater than 50% in migraine headaches per month.<sup>5</sup> The most common side effect reported by patients was neck pain. Quality of life was evaluated using questionnaires throughout the study. Patients had a significant improvement in quality of life with the use of Botox due to the significant reduction in pain and headaches days per month. Now that topiramate and Botox have been found to be effective it is important to compare them to determine which is the superior option. One key limitation of this study was that it was an open-label trial, researchers reported that it would be unethical to have participants on a placebo for two years.

#### COMPARISION OF BOTOX AND TOPIRAMATE

In previous studies, when Botox and topiramate were compared to placebos, they both prove to be an effective means of chronic migraine prophylaxis. A small double-blind randomized pilot study has been conducted, to determine which of these two prophylactic medications is superior. This study was conducted for 6 months and concluded that both treatment groups saw a reduction in quantity of headaches per month and improvement in quality of life. No statistical significance was found between the two medications. Both medications are equally effective, and either should be used for chronic migraine prophylaxis.<sup>6</sup>

#### DISCUSSION

In evaluation of the efficacy between Botox and topiramate for prophylaxis of chronic migraine, the conclusion was that both medications were of equal effectiveness. Individual studies with topiramate and Botox had similar findings that both medications substantially reduced the number of migraine days per month and improved quality of life. Only one trial has been conducted comparing topiramate and Botox as a treatment for prevention of chronic migraine; statistical significance was not found to favor one drug or the other due to small sample size. More research studies need to be conducted with a larger population to determine which is the best treatment option. It is important to also compare treatment options by evaluating the side effect profile, route of administration, and cost to determine the best treatment option for patients. Patients have different responses to medication, and one treatment may work better for one person and the same treatment may not work well for another patient. With chronic migraine prophylaxis it is often a process of trial and error of various prophylactic meds until the best treatment is found for that individual patient. During this time, it is also important to continue lifestyle changes in addition to pharmacological treatment.

Although, neither topiramate or Botox were found to be a superior prophylactic treatment in reducing migraine days, practitioners may soon find a better choice. An-Calcitonin gene-related peptide (CGRP) monoclonal antibodies are a new class of medication that has been found to reduce chronic migraine headaches. This new class of medication is now FDA approved for prevention of chronic migraine. CGRP antibodies medications such as Eptinezumab work by blocking Calcitonin gene related peptides that are released by the trigeminal nerve during an acute migraine. In phase three clinical trials, this class of medication was found to significantly reduce migraine days by about 15 migraine days per month. Common adverse effects noted in the trial are injection site reaction and pain.<sup>7</sup> When choosing prophylactic medication for patients

with chronic migraine, it is important to consider this new class of medication as a treatment option.

## CONCLUSION

Chronic migraine headaches are a complex disorder to manage. It is important for practitioners to consider prophylactic medication in patients with chronic migraine, those who have failed acute treatments, and those with acute medication overuse. Medication overuse as an indication for migraine prophylaxis because this can quickly progress from episodic migraine headache to chronic migraine headaches.<sup>6</sup> Patients were found to have an improvement in quality of life with the use of either topiramate or Botox as prophylactic agents. Practitioners can also consider the use of CGRP antibodies as prophylaxis for their patients. It is important to also consider side effect profiles. Careful consideration needs to be done when using a new medication with unknown long-term side effects. Overall, these are all suitable options for the prevention of chronic migraine and should be used in conjunction with lifestyle modifications.

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