

BOTULINUM TOXIN IS A NECESSARY, SAFE AND EFFECTIVE TREATMENT OF CHRONIC MIGRAINE - YES

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Chronic migraine is a complex progressive headache disorder that affects anywhere from 1 ½ to 2 ½% of the general population. It is recognized as a complication of migraine, distinct from episodic migraine, characterized by headache frequency of at least 15 days per month. Chronic migraine is associated with significant disability, and considerable costs. From a variety of sources, it is clear that patients with chronic migraine are more disabled and more dysfunctional than those with episodic migraine. One of five chronic migraine sufferers is occupationally disabled, and many have difficulty attending social functions or performing household work. The American Migraine Prevalence and Prevention Study has demonstrated that the HIT-6 score is a reliable instrument for chronic migraine characterization, and demonstrates increased disease related burden in chronic than episodic migraine. People with chronic migraine have greater odds of severe headache impact when compared with chronic migraine. In addition, MIDAS scores are also more elevated in those with chronic migraine than with episodic migraine.

Few preventive medications have been studied for chronic migraine and currently only onabotulinumtoxinA has regulatory approval. In general, preventive oral medications for episodic migraine have responder rates of approximately 50% in reducing headaches by 50%, and studies of these excluded chronic migraine sufferers. Of various medicines currently approved for episodic migraine, only topiramate has been studied to some degree for chronic migraine. Studies of this medication for chronic migraine have shown some effectiveness, even in individuals who overuse acute abortive medicines. However, systemic side effects with this medication, as with other oral medications are common. Dropout rates due to side effects in the pivotal topiramate approval trials average about 30%, reflecting tolerability issues. In addition, no large well-designed, blind placebo controlled, pivotal trials for the management of chronic migraine with this medication have been performed.

There are 7 serotypes of botulinum toxin, but only serotypes A and B are commercially available. Of several botulinum toxin A products, only onabotulinumtoxinA has undergone substantial clinical trials for headache management. Studies of onabotulinumtoxinA have been performed evaluating its effectiveness in headache prophylaxis. Prior studies of episodic migraine showed no evidence of definitive benefits, and likewise a study of chronic tension type headache did not show a significant benefit favoring Botox in the number of headache free days per month. However, other study designs, dosage, and injection paradigms, might be explored and could potentially show benefits in these conditions.

Pivotal trials have been performed of onabotulinumtoxinA for chronic migraine. These two studies included a total of 1384 patients randomized and treated. A variety of safety and effectiveness measures were captured and analyzed with a last observation carried forward methodology. The demographic baseline data of these studies was representative of the usual chronic migraine population. Patients on average were about 40 years old, and about 85% were women. At baseline they averaged approximately 20 headache days per month, of which 19 were defined as migraines. 93% had HIT-6 greater than 60. Approximately 2/3 were overusing acute headache pain medicines, which is common amongst chronic migraine sufferers.

Analysis of the studies by headache days and headache hours showed statistical benefit compared to placebo. Compared to baseline, Botox treated patients had a marked reduction in headache frequency and headache hours. The reduction of headache days compared to placebo was greater than in pivotal trials of divalproex or topiramate.

Side effects in the onabotulinumtoxinA pivotal trials were generally mild and transient, including headache, neck pain, or lid droop. Discontinuation in onabotulinumtoxinA treated patients due to adverse effects was seen in 4%, vs 1% in placebo treated patients.

Summary: Chronic migraine is a disruptive and complex condition, which has significant costs and consequences, and for which more effective management strategies are needed. OnabotulinumtoxinA has been studied for the management of chronic migraine, and has been shown to be safe, generally well tolerated, and with good effectiveness. Thus, botulinum toxin is a necessary, safe and effective treatment of chronic migraine.