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EFFICACY OF ONABOTULINUM TOXIN IN THE TREATMENT OF CHRONIC MIGRAINE

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ABSTRACT

Chronic migraine (CM) is a disabling headache characterized by characteristic throbbing quality, moderate to severe intensity, unilateral headache associated with photophobia, phonophobia, and gastrointestinal distress. Episodic migraine occurs less than 15 days per month, while chronic migraines occur more or equal to 15 days per month. Treatment includes acetaminophen, aspirin, and NSAIDs for mild attacks and triptans for severe attacks. Preventive daily treatment of migraine is recommended when migraine episodes exceed 6–8 days per month, or what is tolerable to the patient and includes beta-blockers, topiramate, amitriptyline, and divalproex sodium. The United States Food and Drug Administration (FDA) approved onabotulinumtoxinA (Botox®) for the prophylactic treatment of CM in 2010 as onabotulinumtoxinA is effective in reducing the frequency and severity of chronic migraine. This article reports on the efficacy of onabotulinumtoxinA in treatment of CM.

KEYWORDS: Botulinum neurotoxin, chronic migraine, onabotulinum toxin A, chronic headache.

INTRODUCTION

Migraine is the third most common neurological disorder featuring recurrent attacks of unilateral headache lasting for 4–72 hrs, of pulsating quality, moderate or severe intensity and aggravated by routine physical activity. Attacks can be accompanied with nausea, vomiting, photophobia and phonophobia.[1] As stated by the International Headache Society (IHS) classification, migraine has two types: migraine without aura and migraine with aura. Aura symptoms are focal, fully reversible neurological symptoms usually occurring prior to or sometimes during a migraine attack and last for 5–60 min. CM is defined as a headache occurring on at least 15 days per month for more than 3 months, including typical features of migraine on at least 8 days per month.[1] Diagnosis of CM includes the patient's history (including a headache diary) and neurological examination. The main goal of the treatment of CM is to improve the quality of life of the patients and to reduce the duration and impact of migraine attacks. Treatment includes pharmacological and nonpharmacological methods. The nonpharmacological methods include prevention of migraine attacks with trigger avoidance (caffeine, alcohol, stress) and dealing with risk factors (losing weight, modify response to stressors, sufficient sleep).[2] Pharmacological methods include nonsteroidal anti-inflammatory drugs (NSAIDs) and triptans to treat acute migraine attacks but can lead to medication overuse headaches. This observation highlights the importance of prophylactic treatment in CM. The drugs which have been studied in patients with CM are valproate, amitriptyline, gabapentin, topiramate and onabotulinumtoxin A.[3,4,5,6,7,8] The onabotulinumtoxin A is the only substance approved by the United States Food and Drug Administration (FDA) for prophylactic treatment of CM. American Academy of Neurology states that onabotulinumtoxin A is effective in the treatment of patients with CM.[9] The National Institute for Health and Care Excellence (NICE) recommends prophylactic use of onabotulinumtoxin A in CM patients who did not respond to at least three prior pharmacological prophylaxis or patients of medication overuse. According to NICE criteria, treatment with onabotulinumtoxinA should be stopped when patients do not respond to treatment adequately (defined as a reduction of monthly headache days of <30%) or when the patient's condition changes to EM (defined as a headache on <15 days per month in three consecutive months).[10]

OnabotulinumtoxinA is a protein found in gram-positive, anaerobic bacteria *Clostridium botulinum*. There are at least seven serotypes of onabotulinumtoxinA of which only two are in clinical use: serotype A and serotype B.[11] After intramuscular or subcutaneous injection, onabotulinumtoxinA moves into the cell with the help of peripheral motor neurons *via* SV2 binding protein.[12] In the cytoplasm, it enzymatically cleaves the synaptosomal-associated protein (SNAP-25), a protein, which mediates the fusion of neurotransmitter-containing

vesicles with the cell membrane. Hence, it inhibits the release of neurotransmitters from presynaptic nerve endings.[13] This effect helps in suppressing the release of acetylcholine at the neuromuscular junction. However, onabotulinumtoxin A also modifies the release of neurotransmitters responsible for transmission of pain such as substance P or calcitonin gene-related peptide (GCRP).[14,15,16] Therefore, it inhibits the peripheral sensitization that leads to an indirect inhibition of central sensitization, hence, OnabotulinumtoxinA is also efficacious in treatment of chronic pain.[17] But there are few research models supporting the efficacy of onabotulinumtoxinA. Hence, we describe the efficacy of OnabotulinumtoxinA in the treatment of our case of 45 year old male patient with CM.

CASE REPORT

A 45 year old male patient who was a known case of migraine headache was referred to the pain clinic after no reduction in the severity of headache on NSAIDs and triptans. The patient had a history of migraine since 5 years but it has aggravated in last 6 months. Hence, patient was taken to operation theatre and was asked to sit comfortably. An intravenous cannula of 20 gauge was placed in the right hand and monitors like sPO2 and NIBP were attached. Then, the 200 units of botulinum injection was diluted in 4 cc of Normal Saline. The botulinum injection was injected in 31 sites blocking 7 specific head and neck muscle areas with a total dose of 175 Units. Firstly, the procerus muscle was blocked using 0.1 ml of the dose in insulin syringe. Then, the finger was placed against the supraorbital rim above the right eyebrow and the corrugator muscle was blocked and similarly the left corrugator was blocked. Then the frontalis muscle was blocked on both the sides using 0.1 ml each by inserting the injection botulinum at the bilateral lateral canthus of the eyes and at mid pupillary lines above bilateral eyebrows. After that, the temporalis muscle was blocked bilaterally by inserting the injection at 4 sites i.e. 3 sites across the breadth of temporal fossa and 1 site above the root of zygomatic arch. The splenius capitis muscle was injected by asking the patient to flex his neck and sliding the finger from occipital tubercle upto the midline raphe and then pinching the bilateral splenius capitis muscle and 0.1ml was injected in between the raphe and muscle at 6 sites. The occipitalis muscle was injected by making a claw of the 3 fingers and placing behind the mastoid tip and the claw was dragged upwards over the nuchal ridge and 0.1 ml was injected in the place of each 3 fingers. This process was also done bilaterally. Lastly, the trapezius muscle was injected by impinging the trapezius and 0.1 ml was injected at 3 sites bilaterally, thereby completing the 31 sites. Then the patient was followed up for next month and the migraine attacks decreased to only 2 days out of 30 days.

DISCUSSION

The results of this study showed that OnabotulinumtoxinA is an option with high potential for treating migraine as an inflammatory neurological disease. It reduces the frequency of migraine attacks per month, the severity of pain, use of other drugs, emergency visits, disabilities associated with migraine headaches.

The effectiveness of OnabotulinumtoxinA has been studied from various perspectives and by different groups.[18,19,20] Mimeh et al compared the safety and efficacy of OnabotulinumtoxinA with placebo in the prophylactic treatment of CM. They reported that OnabotulinumtoxinA can be considered as an effective treatment but has side effects and there is still uncertainty about the effectiveness of OnabotulinumtoxinA in comparison with placebo.[21] A systematic review and meta-analysis by Herd et al. evaluated the effect of botulinum toxin on migraine prevention among adults, and the results showed that botulinum toxin treatment alleviated the severity of CM and EM. Besides, in CM, botulinum toxin reduced the migraine frequency by two days a month and had an acceptable safety profile.[22] Another review by Shen et al. investigated the effect of botulinum toxin A(BoNT-A) in the prevention of adult migraine disorders. It was proved that BoNT-A did not decrease the frequency of migraine attacks per month compared with placebo but improved the quality of life of patients.[23] Loeb et al. conducted a randomized controlled trial (RCT) to evaluate CM patients treated with botulinum toxin A (BT-A). After comparing BT-A with low-level laser therapy (LLLT), it was shown that both treatments reduced the frequency of headaches, acute drug use, pain intensity and hence, both treatments could be used to treat CM.[24] A study by Cheng and Ahmed showed that BoNT-A is a very good option for migraine prophylaxis in adults.[25] Moreover, in a prospective, real-life analysis by Ahmed et al. positive data from long-term treatment and follow-up of at least two years of patients with CM showed that they still appropriately responded even after two years.[26] A systematic review by Argyriou et al. showed the effectiveness of BoNT-A in primary headaches (PHs) other than CM as it can be used as treatment option for patients who do not respond to common migraine prophylaxis.[27] Hence, in line with our study, the above studies also conclude that botulinum toxin is potentially effective in the treatment and prevention of migraine attacks.

CONCLUSION

Our study states that OnabotulinumtoxinA is an effective and cost-effective option for the treatment of chronic migraine. It can significantly improve the quality of life of the patients as well as decrease the frequency of migraine attacks.

REFERENCES

1. Headache Classification Committee of the International Headache Society. The international classification of headache disorders, 3rd edition (beta version). Cephalalgia, 2013; 33: 629–808.

2. Schwedt T. Chronic migraine. Brit Med J., 2014; 348: g1416.
3. Yurekli V, Akhan G, Kutluhan S et al, The effect of sodium valproate on chronic daily headache and its subgroups. J Headache Pain,v; 9: 37–41.
4. Couch J. and Amitriptyline versus Placebo Study Group Amitriptyline in the prophylactic treatment of migraine and chronic daily headache. Headache, 2011; 51: 33–51.
5. Spira P, Beran R and Australian Gabapentin Chronic Daily Headache Group. Gabapentin in the prophylaxis of chronic daily headache: a randomized, placebo-controlled study. Neurology, 2003; 61: 1753–9.
6. Diener H, Bussone G, Van Oene J et al, Topiramate reduces headache days in chronic migraine: a randomized, double-blind, placebo-controlled study. Cephalalgia, 2007; 27: 814–23.
7. Silberstein S, Lipton R, Dodick D et al. Efficacy and safety of topiramate for the treatment of chronic migraine: a randomized, double-blind, placebo-controlled trial. Headache, 2007; 47: 170–80.
8. Silvestrini M, Bartolini M, Coccia M et al, Topiramate in the treatment of chronic migraine. Cephalalgia, 2003; 23: 820–4.
9. Simpson D, Hallett M, Ashman E et al. Practice guideline update summary: botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache: report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology, 2016; 86: 1818–26.
10. NICE Technology appraisal guidance [TA260]. Botulinum Toxin Type A for the Prevention of Headaches in Adults with Chronic Migraine, 2012.
11. Bigalke H. Botulinum toxin: application, safety, and limitations. Curr Top Microbiol Immunol, 2013; 364: 307–17.
12. Mahrhold S, Rummel A, Bigalke H et al. The synaptic vesicle protein 2C mediates the uptake of botulinum neurotoxin A into phrenic nerves. FEBS Lett., 2006; 580: 2011–4.
13. Rummel A. The long journey of botulinum neurotoxins into the synapse. Toxicon, 2015; 107: 9–24.
14. Purkiss J, Welch M, Doward S et al. Capsaicin-stimulated release of substance P from cultured dorsal root ganglion neurons: involvement of two distinct mechanisms. Biochem Pharmacol, 2000; 59: 1403–6.
15. Welch M, Purkiss J, Foster K. Sensitivity of embryonic rat dorsal root ganglia neurons to Clostridium botulinum neurotoxins. Toxicon, 2000; 38: 245–58.
16. Durham P, Cady R, Cady R. Regulation of calcitonin gene-related peptide secretion from trigeminal nerve cells by botulinum toxin type A: implications for migraine therapy. Headache, 2004; 35–44.
17. Aoki K. Evidence for antinociceptive activity of botulinum toxin type A in pain management. Headache, 2003; 43: 9–15.
18. Sycha T, Kranz G, Auff E et al. "Botulinum toxin in the treatment of rare head and neck pain syndromes: a systematic review of the literature," Journal of Neurology, 2004; 251(1): 1.
19. Gupta VK, "Botulinum toxin-A treatment for migraine? A systematic review," Pain Medicine, 2006; 7(5): 386–94.
20. Linde M, Hagen K, and Stovner LJ, "Botulinum toxin treatment of secondary headaches and cranial neuralgias: a review of evidence," Acta Neurologica Scandinavica, 2011; 124(s191): 50–5.
21. Mimeh H, Fenech AM, Myers S et al, "A critical review of botulinum toxin type A in the prophylactic treatment of chronic migraine in adults," Aesthetic Surgery Journal, 2019; 39(8): 898–907.
22. Herd CP, Tomlinson CL, Rick C et al., "Cochrane systematic review and meta-analysis of botulinum toxin for the prevention of migraine," BMJ Open, 2019; 9: 7.
23. Shen B and Wang L, "Impact of the botulinum-A toxin on prevention of adult migraine disorders," Journal of Integrative Neuroscience, 2020; 19(1): 201–8.
24. Loeb LM, Amorim RP, Mazzacoratti GN et al, "Botulinum toxin A (BT-A) versus low-level laser therapy (LLLT) in chronic migraine treatment: a comparison," Arquivos de neuro-psiquiatria, 2018; 76(10): 663–7.
25. Cheng F and Ahmed F, "OnabotulinumtoxinA for the prophylactic treatment of headaches in adult patients with chronic migraine: a safety evaluation," Expert Opinion on Drug Safety, 2021; 20(11): 1–15.
26. Ahmed F, Buture A, Tanvir T et al, "Long term outcome for onabotulinumtoxinA (Botox) therapy in chronic migraine: a 2-year prospective follow-up audit of patients attending the Hull (UK) migraine clinic," Cephalalgia Reports, 2021; 4.
27. Argyriou A, Mitsikostas D, Mantovani E et al, "Beyond chronic migraine: a systematic review and expert opinion on the off-label use of botulinum neurotoxin type-A in other primary headache disorders," Expert Review of Neurotherapeutics, 2021; 21(8): 923–44.