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OnabotulinumtoxinA (Botox) in chronic migraine with and without medication overuse

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Abstract

Objective: To review the evidence of efficacy of OnabotulinumtoxinA (Botox) in chronic migraine (CM) with and without medication overuse, its limitations and key findings from prospective data from a tertiary headache clinic.

Development: CM is a disabling neurological condition, affecting around 2% of the general population with significant impact on quality of life and ability to work and perform activities of daily living. Botox is the only medication licenced for CM prevention. Its safety and efficacy has been shown in randomized controlled trial PREEMPT. However, it remains debatable as to whether patients with CM and analgesic overuse be subjected to withdrawal of overused medication before commencing preventive treatment.

Methods: Patients that attended the Hull Migraine Clinic and received Onabotulinumtoxin A for chronic migraine were included. The patients were dived in those with and without medication overuse based on the International Headache Criteria. The data was collected through a dedicated headache diary.

Conclusion: The Hull Migraine Clinic provides prospective real-life data on patients with CM treated with OnabotulinumtoxinA (Botox). The data showed OnabotulinumtoxinA (Botox) to be equally effective in CM patients with and without medication overuse.

Keywords: Chronic migraine, medication overuse, OnabotulinumtoxinA

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Introduction

Chronic Migraine (CM) is one of the most disabling primary headache disorders affecting 2% of general population. CM is defined as headaches on ≥15 days per month for ≥3 months of which ≥8 days fulfill the criteria for migraine with or without aura or relieved by migraine-specific treatment [1].CM has an important economic and social impact compared with episodic migraine [2]. CM patients require preventative treatment taken on a daily basis and acute treatment during migraine attacks. Some of the current preventative drugs (beta-blockers and antidepressants) are low-priced and generic and do not have randomized controlled trial to support their efficacy in CM. The only oral medication with some evidence of efficacy in CM is Topiramate [3,4]. Other treatments such as greater occipital nerve block and occipital nerve stimulator are invasive and have limitations [5].

Analgesics used excessively may lead to the development of medication overuse headache. Around 50-80% of patients with CM overuse medication [6]. It is unclear whether preventative migraine treatment should be started before or after the withdrawal of analgesics. However two randomized controlled trial with Topiramate have shown that detoxification from medication overuse is not necessary [7].

The efficacy of OnabotulinumtoxinA for the prevention of CM has been shown in the phase III Research Evaluating Migraine Prophylaxis Therapy (PREEMPT) clinical program [8]. OnabotulinumtoxinA was effective and well tolerated in patients with CM and a sub-group analysis in those with medication overuse found the treatment to be equally effective in those with medication overuse [9]. The Hull prospective study is the first from a real-life clinical practice to confirm findings from the PREEMPT trial [12].

Real life data from clinical practice

The PREEMPT study results lead to licensing of OnabotulinumtoxinA in prevention of CM by the Medicine and Healthcare produce Regulatory Agency (MHRA) in the UK and Food and Drug Administration (FDA) in the USA [10,11]. This was approved further by the National

Institute for health and Clinical Excellence (NICE) to be made available in the UK on the National Health Service (NHS) [10]. However, experts had mixed feelings on whether findings from the PREEMPT Study would be seen in actual real-life clinical practice. The data from Hull prospective study reported the outcome on a large cohort of patients treated in real-life clinical practice from a tertiary care headache centre [12]. Patients with medication overuse were included as per the International Headache Society recommendations [1].

The Hull Migraine Clinic (Hull Royal Infirmary and Spire Hospital Hull and East Riding) is a large tertiary center in the UK that serves a large area in the North of England. Patients were seen on the NHS and received Botox treatment as per NICE recommendations i.e. after they failed at least three oral preventative agents. The data on headache, migraine, headache free (crystal clear) and analgesic consumption days were collected through a dedicated headache diary [13]. Quality of life data was collected through the Headache Impact Test (HIT-6). Patients were classified into those with or without medication overuse based on the International Headache Society criteria [1]. Responders were defined as per NICE criteria i.e. those with at least 30% reduction in headache days although the authors used their own criteria (Hull Criteria) that uses reduction in severity (migraine days) and increment in headache free (crystal clear) days in addition to headache days [10,12]. A 50% and 75% responder rates were also measured. The treatment outcome for all parameters i.e. headache, migraine and headache free days was compared in the two groups.

The Hull prospective study found OnabotulinumtoxinA to be effective in all patients irrespective of their use of analgesic consumption before treatment.

There was no difference in reduction of headache or migraine day in the two groups. Both groups showed reduction on analgesic consumption more so in those with previous medication overuse. Responder rates of 50% and 75% were also similar. Similarly there was no difference in the outcome on quality of life (measured through HIT-6) in the two groups.

The Hull Study provided data from a large cohort of patients treated in a tertiary care headache centre and replicated findings from the PREEMPT study. The authors felt their patient population reflected what is typically seen in any other headache centre and their results could be generalized to a similar population. The authors acknowledged the fact that their study was open-label and hence a placebo response could not be estimated. A high-placebo response has been described especially with injectable treatments [14] although this would have influenced the results in both groups.

The patient population in Hull study was different in some aspects to PREEMPT patients. The patients in Hull study were more refractory as 94% had previously failed three treatments compared to 35% in the PREEMPT study. Furthermore, the number of headache days before treatment in Hull patients was much higher (27) than PREEMPT (19.9) although only 50% of the cohort in Hull study was found to be misusing painkillers compared to 67% in the PREEMPT.

Conclusion

The prospective data from a large cohort of real-life patients showed preventative treatment with OnabotulinumtoxinA to be equally effective in CM patients with and without medication overuse. Onabotulinumtoxin A reduces the number of headache days, migraine days and increases the number of headache-free days similarly in patients with or without analgesic overuse. The results challenge the view that detoxification of analgesic is required before preventive treatment is introduced.

Disclosure

Fayyaz Ahmed has received honorarium to deliver training workshops for Allergan paid to the British Association for the Study of Headache (BASH) and has received honorarium to attend Allergan Advisory Board meetings. He is on the standing committee of the Headache Guidelines (CG150 Revision) for the National Institute of Clinical Excellence, he is trustee for the Migraine Trust, and is an educational officer for BASH. The authors report no other conflicts of interest in this work.

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