New and Emerging Treatments for Migraine

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Rec date: Nov 26, 2014; **Acc date:** Dec 15, 2014; **Pub date:**

migraine as well as how a profound neurophysiological event such as CSD sometimes causes only slight or no neurological symptoms, need to be addressed.

Greater Occipital Nerve Blockade

Peripheral nerve blocks have been practised over the past few years for the management of headache disorders. The greater occipital nerve has sensory fibres originating mainly form the C2 segment of the spinal cord [14]. The effectiveness of GONBs probably arises as a result of its close proximity to the trigeminal afferents [15]. Several techniques to perform occipital nerve blocks exist, and they all appear effective [15]. However, there is a lack of controlled trials to assess its therapeutic benefits in treating migraines; most of them being small and uncontrolled [16,17]. For example, a study of 97 patients with migraine and 87 with post-traumatic headache who had GONB with a combination of lidocaine and methylprednisolone showed a significant improvement in 54% of migraineurs for up to 6 months [17]. Those who display occipital tenderness are more likely to respond [14]. Over the past few years, there has been renewed interest in GNOB. However, despite the fact that it is generally safe, potential side effects such as dizziness, light-headedness and nausea, and rarely cardiac arrhythmias and hypersensitivity reactions, are some limitations to its use [15]. Also, the invasive nature of the procedure makes it less acceptable to patients as a first-line treatment. We nevertheless believe that GNOB is an effective option in a subset of patients with refractive migraine.

OnabotulinumtoxinA

The anti-migraine properties of OnabotulinumtoxinA (Botox®) were incidentally noted in patients who were cosmetically treated for wrinkles, and its efficacy was first shown in an open-label study.[18] Several other trials confirmed these benefits in migraine prophylaxis at the beginning of the 21st century [19,20]. OnabotulinumtoxinA has been around for years and is not a new treatment per se. The phase III Research Evaluating Migraine Prophylaxis Therapy (PREEMPT) trial [21] established the role of OnabotulinumtoxinA, as well as its efficacy, in the treatment of chronic migraine (CM) which is defined as a headache on ≥15 days per month for ≥3 months, of which ≥8 days meet the criteria for migraine without aura or responds to migraine-specific treatment [22]. This was the largest clinical program to evaluate the use of OnabotilinumtoxinA in CM. 1384 patients were randomised to either OnabotilinumtoxinA or placebo in the double-blind phase and 1236 patients continued into the open-label phase. Treatment with OnabotulinumtoxinA significantly reduced measures that impact on the patient's ability to function such as headache days, migraine days, headache episodes, and migraine episodes [21]. It eventually gained approval from the Medicine and Healthcare Regulatory Agency (MHRA) in the UK, and the Drugs and Food Administration (FDA) in the USA in 2010. It was recommended for use in the National Health Service (NHS) in the UK by the National Institute of for Health and Care Excellence (NICE) in 2012.-

trigeminal neurostimulation with a supraorbital transcutaneous stimulator (STS) [35]. 67 patients were assigned to either verum or sham stimulation with the stimulator applied for 20 minutes daily for 3 months. The primary outcome of 50% responder rate was significantly higher (38.1%) in the verum group than in the sham group (12.1%). In a patients' satisfaction survey involving 2313 participants, the Cefaly® device was found to be safe and was well-tolerated with 53.4% of patients willing to purchase the device [36]. In March 2014, the U.S Food and Drug Administration (FDA) granted approval for the marketing of Cephaly®. The device is small and reasonably priced [37]. This is currently being appraised by NICE although funding through the NHS remains doubtful.

Non-Invasive Vagal Nerve Stimulation

The benefits of vagal nerve stimulation (VNS) in treating migraine attacks were incidentally noted while treating patients with intractable epilepsy [38,39]. However, the invasive nature and potential complications of this procedure has significantly limited its use. Gammacore® is a portable non-invasive VNS (nVNS) that transmits a small electrical signal to the vagus nerve through the skin when held against the neck [40]. In an open-label pilot study including 27 patients using nVNS to treat acute migraine, 21% were pain-free at 2 hours while 42% reported an improvement [41]. Raneiro et al. treated

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