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Repetitive transcranial magnetic stimulation in cluster headache

Dear Sir,

Cluster headache is a primary headache belonging to the trigeminal autonomic cephalgias. The International Classification of Headache Disorder-3 (ICHD-3) describes cluster headache as attacks of severe unilateral pain which may be orbital, supraorbital, temporal or in any combination of these sites lasting for 15–180 minutes and occurring for once every day to 8 times in a day. Pain is associated with ipsilateral conjunctival injection, lacrimation, nasal congestion, rhinorrhoea, forehead and facial sweating, miosis, ptosis or eyelid edema. Attacks characteristically come in clusters, last for weeks to months separated by remission period of months to years [1].

Treatment of cluster headache includes oxygen or triptans for abortion of acute attacks. For prophylaxis, high dose verapamil or corticosteroids are considered as first line medication, and lithium, valproate or topiramate is used as second line drugs. First line abortive treatment for cluster headache provides 15 min pain relief in 50% of patients while first line prophylaxis reduce attack frequency by at least 50% in 70% of patients; thereby a fairly large number of patients are refractory to current medications [2]. Several invasive and non-invasive methods of neurostimulation are now being used as a second line treatment of cluster headache. High rate repetitive transcranial magnetic stimulation (rTMS) has been reported as effective nonpharmacological treatment in migraine [3,4]. Cluster headache has somewhat similar etio-pathogenesis to migraine, therefore rTMS may also be effective in cluster headache, but there is paucity of such study. We report long term efficacy of high rate rTMS in a patient with cluster headache.

Case summary

A 35 year old male presented with 10 years history of recurrent episodes of short lasting unilateral severe pain predominantly involving left half of face over eye and temple. Duration of pain was about 60 minutes and was associated with tearing, redness and swelling of the ipsilateral eye (Fig. 1). Attacks came almost 3–4 times in a day and predominantly came in the evening or after dinner. Cluster headache initially came during early summer, lasted for about 2 months followed by pain free period for about a year. He was diagnosed as a case of cluster headache and received non-steroid anti-inflammatory drugs or triptans for acute attacks, and prescribed verapamil (120mg/day) in the first and sodium valproate (400mg-600mg) was replaced with verapamil in the subsequent two episodes for prophylaxis. There was however no effect on the frequency and duration of the cluster attacks following these treatments for initial 3 years, and he had yearly cluster attacks. On failure of medical management for 3 years, during 4th episode of cluster headache, he was given a trial of 10 Hz rTMS, 600 pulses in 412.4 seconds delivered on the left frontal cortex corresponding to the hot spot of right abductor digiti minimi [3,4]. This protocol of magnetic stimulation was approved by our Institute Ethics Committee in migraine (PGI/BE/256/2011) and patient consented for the magnetic stimulation. At the beginning of each cluster headache, three sessions of magnetic stimulation was given on alternate day; May 2015, February 2017 and July 2018. Prophylactic medication was not prescribed when he was on rTMS therapy. The details are presented in the supplementary Table 1. He took ibuprofen and paracetamol combination for headache as and when necessary. Following rTMS, the total duration of cluster attack reduced from 2 months to 1 month, daily headache episodes reduced from 4 to 1 or 2 attacks, and the remission period increased from 12 months to 21 months. rTMS was effective in him both as an abortive and prophylactic treatments.

Our patient with cluster headache responded to high rate rTMS in terms of frequency and duration of clusters compared to his medical treatment. Treatment of cluster headache primarily includes triptans and high flow oxygen therapy for abortion of acute attack and verapamil, lithium, valproate and topiramate for chronic prophylaxis. A large subset of patients, however are refractory to medical therapy. Neuro-stimulation as an alternative to pharmacotherapy, and has now been used in cluster headache. These include hypothalamic deep brain stimulation and stimulation of occipital nerve, vagus nerve and sphenopalatine ganglion. These treatments are invasive and cumbersome. Transcutaneous vagal nerve stimulation, even though safe has a wide treatment related adverse effect such as neck and shoulder pain, frequent urination, stimulation site redness which leads to poor tolerability [5]. As an abortive treatment of migraine, vagus nerve stimulation device gamma Core, supra-orbital nerve stimulation by Cefaly and single pulse TMS have approved by FDA [6]. High frequency rTMS has been reported effective in migraine prophylaxis both in episodic and chronic. We have chosen 10Hz rTMS on the left frontal area corresponding to hot spot of abductor digiti mini because of efficacy of this protocol in both episodic and chronic migraine [3,4]. The role of rTMS has not been evaluated systematically in cluster headache. In one study, patient with drug resistant cluster headache (minimum pharmacotherapy given for 1 year) were given high frequency rTMS and 68% patients had moderate to very good response with respect to number of attacks/day, paroxysmal and permanent pain by day 15 of stimulation. 26% patients had persistent analgesia even at 180 days of stimulation [7]. Possible mechanisms of rTMS induced analgesia include decreased cortical excitability, release of beta endorphins, changes in glutamine/glutamate levels and effects on hypothalamus. Hypothalamus has been considered to play an important role in producing cluster headache [5]. Stereotactic

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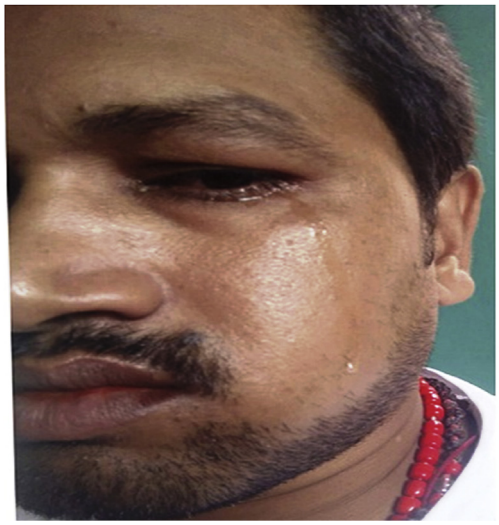

Fig. 1. Photograph of the patients during headache showing left eyelid edema and tearing.

stimulation of hypothalamus has shown to abort acute cluster headache [8]. Melatonin has been found to be low in patients of cluster headache, and lack of melatonin related hypothalamic pituitary axis suppression may be an aggravating factor for headache [9]. Magnetic stimulation has been recommended in various psychiatric disorders (depression, attention deficit and hyperkinetic disorder) and fibromyalgia [10]. Our patient showed acute and long term improvement with rTMS as evidenced by decreased number of attacks/day (4–2), decreased duration of cluster attack (2 month–1 month) and an increased remission period (1 year–1.5 years) compared to pharmacotherapy over 7 years follow up. He had poor response to triptans, high flow oxygen and high dose sodium valproate prophylaxis.

Magnetic stimulation being a noninvasive procedure and having excellent side effect/tolerability profile may be an alternative modalities to pharmacological treatment in cluster headache.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.brs.2018.12.004.

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None.

Conflicts of interest

There is no conflict of interest to declare.

Ethical approval

The high rate repetitive magnetic stimulation in migraine and chronic daily headache was approved by the Institutional Ethics Committee, SGPGIMS, Lucknow INDIA (PGI/BE/256/2011).

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