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Letter to the Editor

Use of multi-site neuromodulation transcranial magnetic stimulation in management of tinnitus: A case study with review of literature

Tinnitus is a worrisome health concern in many patients receiving ototoxic agents (Baguley et al., 2013). Evidences support that even tricyclic antidepressants like imipramine may produce tinnitus (Tandon et al., 1987). Factors like head injury and psychiatric disorders like depression may increase the risk of tinnitus. Tinnitus can be reversible as well as irreversible. Patients with irreversible tinnitus often experience significant distress. Till date there is no definitive drug treatment for management of tinnitus. Some psychological interventions (cognitive behaviour therapy, counselling) have been found to have some supplemental role (Baguley et al., 2013). In the recent years, brain stimulations, sound therapies as well as certain surgical interventions have been tried in the management of tinnitus (Baguley et al., 2013). Some early evidences support the role of electroconvulsive therapy, in reducing intensity of tinnitus and distress associated with it (Salah et al., 1995). Tinnitus may or may not be associated with hearing loss; though hearing loss is most commonly associated with it. Evidences support that tinnitus results from damage to specific type of cochlear damage (Schaette, 2014).

An adult science graduate male was admitted with chief complaints of ringing sensation in ears for past three years. About three years back he was diagnosed as Multi-Drug Resistant (MDR) pulmonary tuberculosis and treated for the same. After one month of initiation of antitubercular drug regime (which included injection streptomycin too), he developed ringing sensation in both ears. Onset of the symptom was acute. Initially, patient tried to get rid of such sound by placing fingers or cotton over external auditory meatus, without any improvement. Intensity of this noise did not show any diurnal variation. There was no impairment in hearing. There was no tenderness or redness over local area and no ear discharge associated with it. There was no past history of otitis media, hearing difficulties or head trauma. The patient perceived the ringing noise to be disturbing and distracting; hence reported anxiety and distress due to it. He had difficulty in focusing on daily chores and studies due to continuing ringing noise.

Over next two months, he developed symptoms of low mood, decreased interest in previously pleasurable activities, disturbed sleep, hopelessness, impaired concentration in work and studies. The ringing noise continued with same intensity and severity during this period. He sought psychiatric consultations for the same and was prescribed sertraline 50 mg/day, which was subsequently increased to 100 mg/day. During routine investigations, he was found to have raised thyroid stimulating hormone (TSH) level, for which opinion was sought from endocrinologist and he was prescribed thyroxine supplementation (50 µg/day, later increased to 75 µg/day). With this dose his subsequent thyroid function tests remained within normal limits.

Over a period of three months, there was significant improvement of depressive symptoms; however, the ringing noise persisted, which used to interfere in his day to day activities (focusing on work and studies). The patient continued his treatment for MDR pulmonary tuberculosis and depression as earlier. Multiple opinions were taken from neurologists and otorhinologists for persistent symptoms of ringing noise in the ears. No hearing impairment was found in audiometry. His neuroimaging was also normal. He was diagnosed with tinnitus (antitubercular drug streptomycin -induced) and was advised multivitamins, antioxidants as well as Valsalva maneuver along with steam inhalation. There was no improvement in his tinnitus despite all these measures. He was even treated with risperidone (upto 3 mg/day) and carbamazepine (upto 400 mg/day) in separate occasions lasting for 3 to 6 months, without noticeable improvement. Mindfulness based cognitive behaviour therapy was done over a period of three months (initially weekly sessions and subsequently biweekly sessions, for a total of 8 sessions), but he did not report any improvement. After one year of resolution of depressive symptoms, antidepressant was stopped, gradually tapering over a period of two months. In March 2019, patient visited neuropsychiatry OPD and was planned for transcranial magnetic stimulation (TMS) therapy due to failed pharmacological and psychological interventions.

Multisite neuromodulation was planned by using repetitive transcranial magnetic stimulation (rTMS) (Lefaucheur et al., 2014). The resting motor threshold (RMT) was identified by using the five-centimetre technique. A total of 10 sessions of rTMS given over a period of two weeks. Each session consisted of delivering high frequency (10 Hz) rTMS over left dorso-lateral pre-frontal cortex (DLPFC) at 110% of RMT, followed by low frequency (1 Hz) rTMS at 110% RMT over temporo-parietal junction. In the first five sessions, stimuli were delivered at the left temporo-parietal junction (T3-P3 junction as per 10–20 system of electrode placement in electroencephalogram). In the subsequent five sessions, stimuli were delivered at the right temporo-parietal junction (T4-P4 junction). The DLPFC target remained same (left side), throughout the therapeutic process. A total of 600 pulses at 10 Hz frequency, with 60 pulses per train and 24 s inter-train interval were delivered over left DLPFC, followed by 1200 pulses at 1 Hz frequency, with 60 pulses per train and 5 s inter-train interval, delivered over temporo-parietal junction, during each daily session. The patient tolerated well to TMS, except after the sixth session, when the patient reported after shifting from left temporo-parietal to right temporo-parietal junction, there was worsening in the loudness of tinnitus for an hour, which normalized spontaneously to the level of improved severity after the last session (*i.e* fifth session).

After 10 sessions of rTMS, the patient's symptoms of tinnitus persisted almost all day, decreased in loudness to about 30–40 percent, impairment and subjective distress improved by 70–80 percent. Patient's symptoms were assessed on a self-designed Likert scale (Table 1). The scale contains four items (frequency of tinnitus, loudness, distress and impairment) and each item can be scored between 1–5, with a maximum rating of 20 and a minimum rating of 5.

The patient had a baseline score of 18, which was reduced to 11 at the end of 10 sessions. The patient was evaluated in follow up after 3 weeks and his tinnitus severity score was 10 out of 20, indicating persistence of beneficial effect of TMS.

There are certain unique clinical characteristics in our case, like –

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Table 1
Tinnitus severity rating scale.

Items / Scores	1	2	3	4	5
Frequency of tinnitus	Less than or equal to once per day	More than once per day	More than once every hour	More than once every minute	Continuously present all the day, absent only while asleep
Loudness	Audible less than whisper	Equivalent to whispering sound	More than whispering sound	Less than normal conversation	Audible equal to normal conversation
Distress	None	Mild	Moderate	Severe	Extreme
Impairment	Minimal	Mild (slight interference, but overall performance not impaired)	Moderate (definite interference with functioning)	Severe (substantial impairment in functioning)	Extreme (incapacitating)

development of tinnitus (ototoxicity) one month after initiation of streptomycin, presence of tinnitus in the absence of hearing loss; persistence of tinnitus in the same severity despite discontinuation of streptomycin; non-response of tinnitus to antidepressant (sertraline), antipsychotic medication (risperidone), mood stabilizer (carbamazepine), antioxidants (vitamin B12, E and levocarnitine) and thyroxine. Evidence supports some beneficial role of serotonergic agents, dopamine antagonists, GABAergic agents, anti-glutamatergic agents, zinc, melatonin, Trazodone, tricyclic antidepressants, surgical interventions, neuromodulation as well as cognitive behaviour therapy in the management of tinnitus (Baldo et al., 2012; Langguth et al., 2009; Lefaucheur et al., 2014; Shin et al., 2017). The Cochrane database systematic review concludes the evidence of antidepressants in the management of tinnitus to be insufficient (Baldo et al., 2012). A case study reports improvement of tinnitus with trifluoperazine treatment in a patient with psychosis and ear disease (Jain et al., 2017).

Evidence supports that tinnitus of shorter duration and less severity responds well to TMS treatment (Ahmed, 2016). In contrast, our patient had tinnitus of higher severity and longer duration and the patient had reported approximately 40% improvement after 10 sessions of TMS. Kleinjung et al. (2005) had reported that the therapeutic effects of TMS in chronic tinnitus are sustained for longer period (six months and beyond) (Kleinjung et al., 2005). In patients of chronic tinnitus, Kreuzer et al. (2017) attempted various TMS protocols and recommended that selection of TMS protocols are more individualized than general (Kreuzer et al., 2017). It was found that combined (multi-site neuromodulation) protocols targeting prefrontal cortex (high frequency TMS over dorso-lateral prefrontal cortex) and temporo-parietal cortex (low frequency TMS at temporo-parietal junction) simultaneously, are effective in reducing the severity of tinnitus (Kreuzer et al., 2017).

Muller et al., (2013) in their study reported about the usefulness of TMS in chronic tinnitus and mentioned that the reduction in loudness of tinnitus in response to TMS is related to increase in alpha activity in the stimulated auditory cortex (Müller et al., 2013). Targeting multiple sites during neuromodulation using rTMS may be beneficial in the management of tinnitus. Commonly, stimulation of DLPFC and simultaneous inhibition of temporo-parietal junction are used for treating tinnitus (Lefaucheur et al., 2014). The response to TMS in our case was solely attributable to TMS as the patient had received TMS as standalone modality of treatment. The clinicians need to discuss the option of TMS treatment with the patients and their caregivers with tinnitus, as evidences support that the knowledge and prior experience of TMS are likely to decide acceptability of TMS as a treatment modality (Singh et al., 2018). The clinicians may consider TMS as an augmenting modality of treatment or as a standalone treatment modality in the management of tinnitus.

Conflict of interest

Nil.

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