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Effect of transcranial direct current stimulation on short-term and long-term treatment of chronic tinnitus

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ABSTRACT

Objective: This study was conducted to investigate the effectiveness of anodal and cathodal methods in reducing the intensity of tinnitus and to compare them with the control.
Methodology: This randomized double-blind clinical trial with case and control groups was conducted in Al-Zahra Hospital in Isfahan between 2015 and 2016. In this trial, 51 patients with tinnitus, for at least one year, were selected among those outpatients visiting the throat, nose and ear clinic within this period. Inclusion criteria were patients on electrical stimulation prohibition, with Ménière's disease, otosclerosis, chronic headache, and pulsatile tinnitus. Patients were randomly divided in three equal-sized groups: anodal stimulation group, cathodal stimulation group, and control group. The subjects received 20-min current stimulation (2 mA). Five subjects were selected from those with a significant difference between the stimulated states (anodal or cathodal) and/or control. They received weekly transcranial electrical stimulation for two months, and their long-term recovery from tinnitus was investigated. Data analysis was done with SPSS20.
Results: Findings showed no significant between-groups difference in mean scores of tinnitus before the intervention ($p = .68$); whereas, this difference was significant immediately after the intervention ($p = .02$) and 1 h after it ($p = .03$). The mean score of tinnitus in the anodal stimulation group was significantly lower than the control; whereas, no significant difference was observed between the anodal and cathodal stimulation groups, and between the cathodal and control groups ($p < .05$). Findings also showed that the mean scores of tinnitus in two cathodal stimulation groups ($p = .24$) and control group ($p = .62$) were not significantly different at three different points of time; whereas, this score was significantly different in the anodal group at these time points ($p = .01$).
Conclusion: In conclusion, anodal stimulation was more effective than the cathodal and control stimulation in reducing the intensity of tinnitus in the short term.

1. Introduction

Tinnitus with the prevalence of between 3% and 30% can be caused by the outer, middle, inner ear diseases and sometimes by brain disorders from the eighth nerve to the brain cortex. Most tinnitus comes from damage to the microscopic endings of the hearing nerve in the inner ear.

Approximately, 5–10% of population suffers from tinnitus, which is the perception of sound without external acoustic stimulation. This rate reaches 30% among the elderly [1, 2], and often becomes chronic, and may lead to sleep disorders, depression, life quality drop, and anxiety in some cases [3–6]. Some types of tinnitus are normal and typically cannot be heard, unless the external sounds are masked. Anything like earwax or foreign body in the outer ear may mask external sounds and result in this type of tinnitus. Subjective tinnitus can only be heard by the patient; whereas, the objective tinnitus can also be heard by the physician by means of some medical techniques [7]. In several cases, tinnitus is not a serious problem, except that it is often very unpleasant. Tinnitus can be persistent, intermittent, and/or pulsatile. It can be caused by diseases of the outer, middle and inner ear diseases and sometimes by brain disorders from the eighth nerve to the brain cortex.

It seems that sensorineural hearing loss [7–12] and/or defects in noise removal system [13–14] cause tinnitus. According to the proposed mechanisms, it is possible that transcranial electrical stimulation (TES) changes the underlying mechanism of tinnitus. Among these electrical methods are transcranial altering current stimulation (tACS), repetitive transcranial magnetic stimulation (rTMS), and transcranial direct current stimulation (tDCS). The tDCS is a safe, painless, and non-aggressive technique for the correction of the neuron structure and function. The therapeutic effects of this method on depression, migraine, stroke, pain, craving for substance abuse, etc., have been already investigated [15–19].

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tDCS is applied by one anodal and one cathodal surface electrodes. They are located over the scalp and a considerable portion of the current of them reaches the brain [20]. It has been revealed that anodal direct current stimulation induces depolarization of the underlying neurons but cathodal stimulation by influencing the resting membrane potential leads to hyperpolarization [21].

Previous studies have investigated the effect of anodal and cathodal tDCS in left temporal and dorsolateral prefrontal regions on the intensity of tinnitus [22–24]. Factors, such as current intensity, electrical stimulation site, and stimulation type determine the effectiveness of this therapeutic method. Attempts are made to find the most optimal state for obtaining the best results. The long-term effects (for few days) of TES on tinnitus intensity have been reported [25]. As a result, this study was conducted to investigate the effect of anodal and cathodal stimulation methods on the intensity of tinnitus, and to compare the results with the control.

2. Methodology

This double-blinded clinical trial was conducted in Al-Zahra Hospital between 2015 and 2016. The statistical population included tinnitus patients, visiting the throat, nose, and ear clinic.

Inclusion criteria were as follows: Patients suffering from tinnitus for at least 1 year, aged between 18 and 80 years, not on electrical stimulation prohibition (due to the self or family history of epilepsy, pregnancy, implantation, brain surgery, and poor cardiac conditions), and without such diseases as Ménière, otosclerosis, chronic headache, and pulsatile tinnitus. The only exclusion criterion was the patient's unwillingness to continue the study.

After the approval of the proposal and obtaining permission from the Ethical Committee of the University, 51 eligible patients were included in the study. First, an audiogram test was administered. Then, subjects were randomly divided in three equal-sized groups. The first, second, and third (control) groups received anodal stimulation, cathodal stimulation, and electrical stimulation. The stimulation was done with Active Dose II device, a single-channel amplifier with the power of 80 V and maximum electric current of 4 mA. To perform stimulation, the electrodes (length: 235 cm) were moistened with NaCl solution (140–150 mmol) to make a proper connection between the electrode and the skull. The location of scalp electrodes on T3 or T4 was recognized according to the International 10–20 system. Twenty minutes current stimulation (2 mA) was applied. The reference electrode was fixed on the opposite arm. Before the stimulation, the intensity of tinnitus was scored between 0 and 4 by the participants. Immediately and 1 h after the intervention, the participants were asked to score tinnitus intensity variations on a scale between −4 and +4. In this scale, −4 indicated worsening conditions, +4 meant full recovery, and zero conveyed no change in the tinnitus intensity.

For data analysis, the one-way ANOVA, ANOVA with replication of observations, and chi-square test were used in SPSS20. In this study, $p < .05$ was considered significant.

3. Results (Tables 1, 2 and 4)

Table 1
Mean age in three groups.

Variable	Anodal stimulation group		Cathodal stimulation group		Control group		p-Value
	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation	
Age (year)	47.4	15.8	46.9	14.6	45.4	13.2	.89

The one-way ANOVA showed no significant between-groups difference in terms of the mean age ($p = .89$).

Table 2
Gender frequency distribution in three groups.

Gender	Anodal stimulation group		Cathodal stimulation group		Control group		p-Value
	Number	Percentage	Number	Percentage	Number	Percentage	
Male	16	69.6	15	65.2	15	65.2	65.2
Female	7	30.4	8	34.8	8	34.8	
Sum	34.8	100	23	100	23	100	

The chi-square test showed no significant between-groups difference in terms of the distribution frequency of gender ($p = .94$).

Table 3
Mean tinnitus score at different points of time in all three groups.

Time	Anodal stimulation group		Cathodal stimulation group		Control group		p-value
	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation	
Pre-intervention	3.3	0.5	3.2	0.5	3.4	0.4	.68
Immediately after the intervention	2.3	1.5	2.9	1.3	3.2	0.7	.02
One-hour after the intervention	2.4	1.6	2.8	1.3	3.3	0.8	.03
p-Value	.01		.24		.62		

The one-way ANOVA showed no significant between-groups difference in terms of the mean tinnitus score before the intervention ($p = .68$); whereas, the difference became significant immediately ($p = .02$) and 1 h ($p = .03$) after the intervention. The LSD test showed that the mean tinnitus score in the anodal stimulation group was significantly lower than the control group immediately after the intervention ($p = .01$) and 1 h after the intervention ($p = .02$); whereas, there was no significant difference between the anodal and cathodal groups and between the cathodal and control groups ($p < .05$). Findings of ANOVA with replication of observations showed that the mean scores of tinnitus in cathodal groups ($p = .24$) and control group ($p = .62$) were not significantly different at the three different points of time; whereas, this score was significantly different in the anodal group at the same points of time ($p = .01$). The LSD test also showed that the mean tinnitus score of the anodal group was significantly higher before the intervention than immediately after ($p = .003$) and one-hour ($p = .008$) after the intervention; whereas, there was no significant difference in this score between immediately after and one-hour after the intervention ($p = .57$).

4. Discussion

This study showed that the mean score of tinnitus before tDCS was not statistically significant different between three groups, but immediately after and 1 h after tDCS there were statistically significant differences between three groups. There are likely similar studies that compare anodal and cathodal tDCS. One similar study evaluated the effect of anodal, cathodal and sham tDCS on treating patients with chronic untreatable tinnitus showed that immediately and 1 h after tDCS, the alteration in VAS scale for intensity was not statistically different between anodal, cathodal, and sham tDCS groups [25]. Another study evaluated anodal, cathodal and sham tDCS on patients with chronic stroke revealed that there were no statistical differences in improving motor improvement between three groups at different times of evaluation [17].

In this study the mean score of tinnitus in anodal group was significantly lower than control groups, and there were no significant differences between anodal and cathodal groups and also cathodal and control groups. Indeed, the mean score of tinnitus in cathode and control stimulation groups was not significantly different between the three times of evaluation but in the anode stimulation significant difference was found between these three times. There was significant difference between mean score of tinnitus before and 1 h after intervention, and there was no significant difference in this variable between immediately and 1 h after intervention. Jood et al. comparing the effects of anodal and cathodal tDCS on treating tinnitus in patients with chronic

Table 4
Complication frequency distribution in three groups.

Complications	Anodal stimulation group		Cathodal stimulation group		Control group		p-Value
	Number	Percentage	Number	Percentage	Number	Percentage	
Without complication	22	95.7	22	95.7	23	100	.35
Headache	1	4.3	0	0	0	0	
Insomnia	0	0	1	4.3	0	0	
Sum	23	100	23	100	23	100	

The likelihood ratio chi-square test showed no significant between-groups difference in terms of the distribution frequency of complications ($p = .35$). According to Table 3, one subject in the anodal stimulation group and one subject in the cathodal stimulation group developed headache and insomnia, respectively.

tinnitus and reported that anodal tDCS has more pronounced effect on tinnitus annoyance [24]. In the study of Teismann and his colleagues concluded that cathodal tDCS over auditory cortex could possibly reduce tinnitus-related hyperactivity, while anodal tDCS might either boost adaptive changes triggered by treatment agents [26].

Fregni et al. evaluated the effect of five daily sessions of tDCS on patients with chronic neuropathic central pain due to traumatic spinal cord injury and suggested that active tDCS can significantly reduce pain in comparison to sham tDCS [17]. Song and his colleagues studied about transcranial direct current stimulation in tinnitus patients. They revealed that tDCS may be a promising tool for tinnitus management. Also they believed that future RCTs in a large series of patients regarding the efficacy of tDCS as well as the comparison between LTA-tDCS is recommended and to set up a standard treatment protocol [27]. In addition, Langguth and De Ridder studied about therapeutic use of superficial brain stimulation. Results of this study showed that both auditory and frontal tDCS have shown tinnitus reduction in a subgroup of patients [28].

There are more studies that evaluated active tDCS overall and compare it with sham tDCS. Also Frank and his colleagues investigated the treatment of chronic tinnitus with repeated sessions of prefrontal transcranial direct current stimulation. According to their results they suggested that some beneficial effect of bifrontal tDCS (anode right and cathode left) in the treatment of severe tinnitus [29].

In Shekhawat study, there were used HD-tDCS of dorsolateral prefrontal cortex (DLPFC) for tinnitus relief in chronic cases. Results shown tinnitus annoyance was significantly reduced after treatment sessions with this technique [30].

Recently, Lee and colleagues found combined bifrontal tDCS and Tailor-Made Notched Music Training had positive effect (over 50%) on chronic tinnitus which used both electrical and acoustical interventions [31].

In this study there were no statistical differences between three groups of intervention in age and gender as the strength of this study which showed there is no effect of age or gender as confounding variables. In addition, the mean score of tinnitus was likely similar in three groups before intervention. One of the limitations of this study was its small sample size that is too small for generating these findings to general population. Further studies with greater sample size are needed to evaluate and compare the exact effects of anodal and cathodal tDCS on treating tinnitus in patients.

In conclusion, anodal stimulation was more effective than the cathodal and control stimulation in reducing the intensity of tinnitus in the short term without showing any significant side effects.

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