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Effectiveness of Transcranial Direct Current Stimulation [tDCS] on Headache Sign and Sleep Quality in Migraine Patients

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ABSTRACT

Aims: Migraine is a common, painful and, in severe and chronic cases, debilitating disease characterized by frequent, unilateral and pulsating attacks with moderate to severe intensity, sensitivity to light, nausea or vomiting. The aim of this study was to investigate the effectiveness of Transcranial Direct Current Stimulation [tDCS] on headache sign and sleep quality in migraine patients.

Method and Materials: The current research design was a semi-experimental type of pre-test, post-test with 2-week follow-up. The statistical population of this study was all patients suffering from migraine in Yazd city, a sample of 30 people was selected using the available sampling method and they were placed in two experimental and control groups by random sampling. The tools used in this research were Ahvaz Migraine Questionnaire and Pittsburgh Sleep Quality Questionnaire. The tDCS treatment method included 5 sessions of 20 minutes with a current of 2 mA .The data were analyzed using the analysis of covariance method.

Findings: The results showed that there is a significant difference between the experimental and control groups in the scores of headache sign and sleep quality in the post-test and follow-up [p<0/01].

Conclusion: The study showed that tDCS treatment has an effective role in improving headache sign and sleep quality.

Keywords: Transcranial Direct Current Stimulation, tDCS, Headache, Sleep Quality, Migraine

Introduction

Migraine is a common, painful and, in severe and chronic cases, debilitating disease that is characterized by frequent, unilateral and pulsating action. This problem is frequent among 10 to 20% of people all over the world [1-3]. According to the global disease report, migraine is the sixth disease worldwide and the first disease among neurological diseases [4]. It can be defined as a problem of primary headache with the intensity of intermittent headache for 4 to 72 hours [5]. The rate of migraine in the male population is 1 to 4% and in the female population is 3 to 10%, which is about three to one in women compared to men [6]. The rate of this problem in Iran is estimated at 14% or even higher than the global average percentage [7].

A migraine attack can be divided into different phases, based on the headache, into the prognostic temporal relationship with the phase, the aura phase, in cases where it is accompanied by the aura, the headache phase , and the post-headache phase are divided [8]. Clinical features of episodic migraine include unilateral, throbbing pain that is aggravated by physical activity. Headache may be associated with a variety of emotional, cognitive, sensory and autonomic nervous system symptoms [9].

The exact etiology of migraine is still unknown and may involve both central and peripheral nervous systems. Recent studies show that the calcitonin gene-related peptide plays an important role in the activation of the tripartite pathway [10]. In addition to these cases, the abnormal motor role of the visual cortex or occipital lobe has been accepted in the pathophysiology of migraine [11-13]. Therefore, useful treatments that control this movement can be used to

reduce migraine headache sign.

There is a migraine target that can be refered to people's sleep. It is an active process that is regulated by the central nervous system, neuro-endocrine and behavioral factors [14]. A few studies have shown that the target of migraines may occur due to sleep. In addition, sleep is considered as one of the relieving factors of migraine pain [15]. Moreover, sleep problem is a common problem among migraine sufferers such as children or adults, which affects 30 to 50% of migraine patients. In addition, sleep can trigger migraine activity that improves with enough restful sleep[4, 16]. In people with migraine, sleep deprivation and simple sleep pattern change has been reported as an accelerating factor in the occurrence of headache reports [17]. Low sleep quality may increase pain and severe sleep disorders may increase headache [18].

Several treatment methods are used to treat migraines by different specialists. Other treatments including drug and non-drug treatments are considered. Due to the fact that people do not recover with drug treatments and non-drug treatments are of little help, non-drug treatments have been given attention [19]. For this reason, non-pharmacological and non-invasive treatments are needed and necessary for the treatment and prevention of migraine recurrence. A non-invasive and non-pharmacological intervention method that has received much attention over the years and has been studied a lot is Transcranial electric stimulation[tES], which is performed by The Effectiveness of Transcranial Direct Current Stimulation.[20, 21].

In tDCS, a device is used to transmit a direct and weak electric current [about 1 to 2 mA] on the scalp and underlying cortical tissue. It has two electrodes, a positive pole [anode] and a negative pole [cathode] [22, 23]. tDCS of neurons increases the target, which defines this target as positive stimulation, while stimulation causes the neuron to decrease or release neural activity in the target region [20].

The therapeutic applications of tDCS have been investigated in a wide range of studies. In a systematic review and meta-analysis. Kai et al showed that tDCS every few days for 4 weeks or more is effective in migraine pain intensity and migraine duration [24]. In a research aimed at the effect of cathodal tDCS guided by thermography as an adjunctive treatment for chronic migraine patients, Dallavolta et al. stated that tDCS is an adjunctive technique in migraine, provided that the electrodes are placed in the correct place [25]. Also, Antal et al. conducted a study with the aim of determining whether tDCS can be a therapeutic preventive treatment for migraine and related migraines or not. This non-invasive method was performed for 6 weeks on the visual cortex three times a week, which showed that cathode stimulation over V1[primary visual cortex] and may be a critical treatment in migraine, less with regard to pain control [26].

Considering the high prevalence of migraine and the significant relationship between migraine and headache and sleep disorder, as well as the lack of a study on the improvement of the sleep status of these patients with tDCS, the present study aims to investigate the effectiveness of Transcranial Direct Current Stimulation [tDCS] on headache sign and Sleep Quality in migraine patients.

Method and Materials

The present study was conducted as a semi-experimental type of pre-test, post-test with two-week follow-up in which one experimental group and one control group were took part. The statistical population of the study was all patients with migraine in Yazd city in 2023 who were diagnosed by neurologists based on the criteria of the International Headache Society. The sample size, including possible attrition, was considered to be 30 people, who were selected by the available method from neurology clinics in Yazd city. Finally, through random assignment, 15 patients were placed in the experimental group and 15 patients were placed in the control group. The inclusion criteria were migraine patients aged 14 to 54 years, at least 1 month has passed since migraine diagnose by a neurologist, a score of 62.5 or higher in the Ahvaz Migraine Headache Questionnaire, not receiving psychological treatments or medication during the study, non-participation in

treatment with stimulation, including tDCS, neurofeedback etc. at least 6 months before the study. The exclusion criteria were not being satisfied to attend and non-cooperation in the research [with a maximum of two absences from the research], the presence of co-existing psychological disorders, history of seizures and epilepsy, head trauma, acute psychiatric disorders, observation of any severe side effects tDCS sessions, receiving other psychological treatments during the study.

The questionnaires which were as follows:

1- Ahvaz Migraine Questionnaire [AMQ]: This questionnaire was created in 1996 by Najarian to measure migraine headaches. This questionnaire has 25 questions. In a research conducted by the questionnaire makers in Iran, the reliability of the questionnaire was reported as 0.80 by the test-retest method and 0.80 through internal consistency, respectively. The Hospital Anxiety and Depression Questionnaire [HADS], the short form of the Minnesota Multidimensional Questionnaire [MMPI] and the Ahvaz Aggression Inventory [AAI] were used that their reliabilities were obtained as 0.49, 0.46 and 0.40, respectively [27]. In the present study, the Cronbach's alpha value of Headache Sign Scale was equal to 0.83.

2- Pittsburgh Sleep Quality Questionnaire [PSQI]: This questionnaire was compiled in previous study[28]. As the name suggests, the Pittsburgh Sleep Quality Questionnaire measures the quality of people's sleep because sleep is one of the main elements in the circadian cycle of humans and helps to restore the physical and mental strength of people. The higher the score, the lower the sleep quality. The reliability of this tool was estimated by Cronbach's alpha method as 0.83 and its validity was reported with 89.6% sensitivity and 86.5% specificity in subjects with sleep problems. In the present study, the total score of this questionnaire was 0.78.

All patients with migraine aged 18 to 50 years in Yazd city in 2023 were considered as the statistical population. 30 people were selected using the available sampling method. The participants were randomly assigned into 2 groups of 15 patients in each group of the experimental and the control group. Before the beginning of the intervention sessions, explanations about how to treat, the number and duration of the sessions were presented to the participants. The implementation of the treatment was only on the experimental groups. In order to pre-test, the participants answered the Ahvaz Migraine and Pittsburgh Sleep Quality Questionnaires. In the intervention phase, tDCS of the experimental group was performed in 5 sessions of 20 minutes with an interval of 48 hours, with a current of 2 mili-Amper using the Neurostim2 device. The cathode electrode with dimensions of 4x4 cm was placed in the central region of the occipital lobe [visual cortex] [Oz] in the 10-20 system, and the anode electrode with dimensions of 4x8 cm was placed over the Cz[Central lobe]. Cz was placed in the 10-20 system as a reference point [15]. In the sham group, the participants received sham stimulation with a current of 2 mA in 5 sessions of 20 minutes with an interval of 48 hours according to the mentioned protocol. In order to create the initial itching sensation, the current was applied in the first 30 seconds and then stopped during the test. Sham stimulation does not alter brain excitability. After completing the intervention sessions for the post-test, the participants of the experimental and control groups answered the Ahvaz Migraine and Pittsburgh Sleep Quality questionnaires again. It should be noted that the follow-up phase was done after two weeks.

Findings

The age range of all participants in this research was 18 to 50 years and each group included 15 patients. The average age for the experimental group was 40.8±7.79 and the control group was 38.70±8.71 years. In the experimental group, 11 patients (73.3%) were women and 4 patients (26.7%) were men, and in the control group, 9 patients (60%) were women and 6 patients (40%) were men. In terms of education level, in the experimental group 5 patients [33.3%] had a diploma, 2 patients) 13.3%) had an associate degree, 4 patients [26.7%] had a bachelor's degree, and

4 patients (26.7%) had a master's degree. In the control group, 5 patients (33.3%) had a diploma, 1 patient (6.7%) had an associate degree, 6 patients (40%) had a bachelor's degree, and 3 patients (20%) had a master's degree.

In order to analyze the obtained data, first of all, descriptive statistics were used and presented in Table 1.

The results of Table 3 showed that tDCS was effective on the total score of sleep quality and five components of subjective sleep quality, sleep delay, sleep duration, sleep adequacy and sleep disturbance and headache sign [p<0.05]. According to the results of the intervention, the use of sleeping pills and daily dysfunction improved, but this difference was not statistically significant [p<0.05]. The results showed that by controlling the pre-test scores, the post-test scores of sleep quality and headache sign were significantly reduced in the experimental group.

The analysis of the adjusted averages is shown in Table 4. The results of the ANCOVA test are shown in order to check the persistence of the intervention effect, and the average follow-up time of the variables in the two groups was compared with the control of the pre-test scores.

Table 1) Descriptive indices of migraine sign and sleep quality and its components by group and time

Variable	Time	Experimental group		Control group	
		Mean	Standard Deviation	Mean	Standard Deviation
Mental sleep quality	Pre-test	1.27	0.46	1.27	0.70
	Post-test	0.53	0.52	1.33	0.72
	Follow-up	0.80	0.56	1.13	0.64
	P-value				
Sleep delay	Pre-test	1.73	1.28	1.47	0.92
	Post-test	0.80	0.68	1.40	0.99
	Follow-up	0.93	0.70	1.27	0.88
	P value				
sleep duration	Pre-test	1.07	0.70	1.20	1.01
	Post-test	0.47	0.52	1.13	0.83
	Follow-up	0.47	0.52	1.20	0.78
	P value				
enough sleep	Pre-test	1.33	0.90	1.60	1.18
	Post-test	0.53	0.52	1.33	1.05
	Follow-up	0.60	0.51	1.47	0.92
	P value				
sleep disturbance	Pre-test	1.60	0.51	1.53	0.74
	Post-test	0.93	0.70	1.73	1.03
	Follow-up	1.07	0/59	1.73	0.88
	P value				
Use of sleeping pills	Pre-test	1.33	1.11	1.40	1.45
	Post-test	0.73	0.46	1.40	1.06
	Follow-up	0.80	0.56	1.53	0.83
	P value				
Daily dysfunction	Pre-test	1.00	1.00	1.27	0.70
	Post-test	0.53	0.52	1.07	0.80
	Follow-up	0.60	0.51	1.27	0.59

	P value				
sleep quality [total]	Pre-test	9.33	3.60	9.73	4.51
	Post-test	4.53	1.60	9.40	4.07
	Follow-up	5.27	1.79	9.60	3.27
	P value				
Headache sign	Pre-test	62.53	7.74	64.60	7.20
	Post-test	42.58	4.97	63.80	6.28
	Follow-up	44.00	4.90	63.33	6.47
	P value				

After reviewing the descriptive findings, inferential statistics were analyzed. First, the presence of single variable outlier data was checked using a box plot and the results showed that there is no outlier data in the variables. Also, before applying the analysis of covariance test, Shapiro-Wilk test was used to check the default for the data distribution, which indicated the normal distribution of the data [p<0.05].

Levine's test was also used to check the homogeneity of variances, and the results indicating compliance with these assumptions are shown in Table 2.

Table 2) Homogeneity test of variance of sleep quality and its components among groups [Levin's test]

variables	F	P
Mental sleep quality	0.067	0.798
Sleep delay	0.107	0.746
Sleep duration	2.75	0.109
enough sleep	1.49	0.231
sleep disturbance	0.83	0.369
Use of sleeping pills	1.67	0.207
Daily dysfunction	1.01	0.325
sleep quality [total]	0.73	0.399
Headache sign	2.04	0.165

The data from Table 2 showed that the significance level for the total score of sleep quality and all components of sleep quality and headache sign was higher than the criterion of 0.05, which showed that the assumption of homogeneity of variances was valid [p<0.05].

Table 3 shows the results of univariate analysis of covariance [ANCOVA] in order to investigate the effectiveness of the intervention on the variables (comparing the post-test scores of the two groups with the control of the pre-test scores).

Table 3) Covariance analysis test to measure tdcs on sleep quality and its components

Dependent variables	Weighted mean		Sum square	Mean square	df	F	p	Effect size
	Intervention	Control						
Mental sleep quality	0.55	1.32	4.06	4.06	1	10.26	0.004	0.328
Sleep delay	0.72	1.48	4.03	4.03	1	6.67	0.017	0.241
Sleep duration	0.47	1.13	2.93	2.96	1	6.22	0.021	0.229
Enough sleep	0.65	1.22	2.25	2.25	1	5.11	0.034	0.196
Sleep disturbance	0.92	1.75	4.75	4.75	1	6.54	0.018	0.235
Use of sleeping pills	0.76	1.37	2.55	2.55	1	4.10	0.056	0.163
Daily dysfunction	0.62	0.98	0.93	0.93	1	2.84	0.107	0.119
Sleep quality [total]	4.63	9.31	163.65	163.65	1	27.17	<0.001	0.502
Headache sign	43.38	63.28	2910.75	2910.75	1	154.68	<0.001	0.851

The results of Table 3 showed that tDCS was effective on the total score of sleep quality and five components of subjective sleep quality, sleep delay, sleep duration, sleep adequacy and sleep disturbance and headache sign [p<0.05]. According to the results of the intervention, the use of sleeping pills and daily dysfunction improved, but this difference was not statistically significant [p<0.05]. The results showed that by controlling the pre-test scores, the post-test scores of sleep quality and headache sign were significantly reduced in the experimental group.

The analysis of the adjusted averages is shown in Table 4. The results of the ANCOVA test are shown in order to check the persistence of the intervention effect, and the average follow-up time of the variables in the two groups was compared with the control of the pre-test scores.

Table 4) Paired t-test in order to compare the mean sleep quality in the two post-test and follow-up periods by separating the two groups.

Group	Variable	Mean		Between groups	df	t	p
		Post-test	Follow-up				
Intervention	Mental sleep quality	0.53	0.80	-0.27	14	1.29	0.217
	Sleep delay	0.80	0.93	-0.13	14	0.62	0.546
	Sleep duration	0.47	0.47	0.00	14	0.00	1
	Enough sleep sleep	0.53	0.60	-0.07	14	0.44	0.670
	Sleep disturbance	0.93	1.07	-0.13	14	0.62	0.546
	Use of sleeping pills	0.73	0.80	-0.07	14	0.56	0.582
	Daily dysfunction	0.53	0.60	-0.07	14	0.37	0.719
	Sleep quality [total]	4.53	5.27	-0.73	14	1.21	0.246
	Headache sign	42.87	44.00	1.13	14	1.21	0.246
Control	Mental sleep quality	1.33	1.13	0.20	14	1.15	0.271
	Sleep delay	1.40	1.27	0.13	14	1.47	0.164
	Sleep duration	1.13	1.20	-0.07	14	1.00	0.334
	Enough sleep	1.33	1.47	-0.13	14	1.47	0.164
	Sleep disturbance	1.73	1.73	0.00	14	0.00	1
	Use of sleeping pills	1.40	1.53	-0.13	14	0.81	0.433
	Daily dysfunction	1.07	1.27	-0.20	14	1.87	0.082
	sleep quality [total]	9.40	9.60	-0.20	14	0.54	0.595
	Headache sign	63.80	63.33	0.47	14	0.83	0.418

The results of Table 4 showed that by controlling the pre-test scores of the two groups, a significant difference was observed in the average follow-up time, and the average sleep quality and its' five components as well as headache sign in the experimental group which were significantly lower than the control group The intervention had an effect over time and in the follow-up phase [P<0.05].

Discussion

The aim of this study was to determine the effectiveness of Transcranial Direct Current Stimulation [tDCS] on headache sign and sleep quality in migraine patients. The results of the present study showed that tDCS led to a reduction in headache sign in people with migraine in the experimental group compared to the control group. Moreover, the effectiveness of tDCS on headache sign was sustained up to 2 weeks after the end of the intervention. The most effective tDCS was on the score of headache sign This finding is in line with the results of previous studies[26, 29--32] It has been shown in research that people with migraines have subtle functional and morphological abnormalities that manifest themselves as attacks. Electrical stimulation of the brain is a method that can balance the spontaneous firing rate of neurons by changing the resting membrane potential and

can reduce the excitability of the cerebral cortex [26]. Among other cases in the etiology of migraine is the abnormal processing of the visual cortex or the occipital cortex, since the primary center of the visual cortex is also located in the occipital lobe, and the sensory input originates from the eyes, passes through the lateral occipital lobe, and then reaches the visual cortex. The area of the visual cortex that receives sensory input from the lateral geniculate lobe is the primary visual cortex, which is considered as the visual area [V1]. Therefore, the extreme sensitivity to light that is reported in people suffering from migraine can be considered as a result of this issue, and since several studies show that Repetitive Transcranial Magnetic Stimulation [rTMS] on the visual cortex [V1] reduces headache, then it can be one of the causes of migraine. considered a disorder in the occipital lip. Therefore, according to what was said, inhibitory tDCS in the occipital lobe can be effective in preventing migraines and have therapeutic effects by reducing the excitability of the cerebral cortex and also the effect on the brain stem [26].

The results of the present study showed that tDCS improved the total score of sleep quality and the five components of mental sleep quality, sleep delay, sleep duration, sleep adequacy and sleep disturbance in people with migraine in the experimental group compared to the control group. The effectiveness of tDCS on sleep quality was sustained up to 2 weeks after the end of the intervention. The results of the present study are consistent with the researches of previous researches [15, 33]. The frequency of migraine attacks has a significant relationship with the duration of sleep and the low quality of sleep [34]. Reducing pain and improving headache in tDCS treatment can lead to deep sleep at night and improve sleep efficiency and quality in this group. Also, sleep efficiency increased with tDCS treatment [35]. Cathodal stimulation has nothing to do with increasing the total sleep time and reduces the total sleep time in people and causes contradictory effects. Another component of sleep that can be mentioned in addition to total sleep time is sleep efficiency. Cathodal stimulation can increase sleep efficiency [36]. In general, it can be said that both stimulation [cathodic and anode stimulation] can have beneficial effects on people's sleep quality. Cathodic stimulation on the occipital cortex or visual cortex or anodic stimulation on the two frontal lobes can be effective on the sleep quality of people with migraine. There is still no result about the combination of stimulation of the frontal lobes and the caudal of the occipital cortex. The simultaneous stimulation of the occipital cortex of the occipital cortex and the anodal of the central region of the brain has been investigated, which has been effective in the quality of sleep [15]. In the present study, the combination of cathodal stimulation on the occipital lip and anodal stimulation on the central region was used. It seems that the effect of these areas has caused the quality of sleep to be affected.

This research included some limitations including the use of available sampling method. This issue limits the possibility of generalizations to other populations. Since the target areas are not intervened locally, as desired by the researcher, but these stimulations cover the brain areas in an inclusive manner and in addition to the target area, they also overshadow a wide range of surrounding areas. According to the mentioned cases, it is suggested to increase the generalization of the results by increasing the sample size and non-random sampling method, using different protocols, increasing sample size and longer follow-up period. Since self-report evaluation and questionnaire completion can be associated with subjective bias, it is suggested to use specialized and more accurate tools such as brain imaging such as Quantitative electroencephalography[QEEG] and various methods of examining brain electrical activity and cognitive tasks in future studies. Also, the use of actigraphy and sleep test through polysomnography are suggested as valid and objective methods of evaluating sleep parameters and sleep disorders. However, it is suggested that in psychological service and counseling centers, specialized psychological clinics and all mental health service providers use tDCS to help people with migraines.

Conclusions

This study reported tDCS has an effective role on headache sign and sleep quality of people with migraine. In such a way that it not only led to the reduction of headache sign, but also played a role in improving the quality of sleep; Therefore, this treatment can be used to improve people with migraine in neurology clinics and other clinical environments.

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Authors' Contribution

YA was the main investigator and conduct all stages of the study. SZ advised the different stages and SGh supervised the different stages of the studies.

Conflict of Interests

The authors declare no conflict of interest.

Ethical Permission

All ethical principals were considered in the study and written consent form was signed by the participants.

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