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Original Article

Transcranial Direct Current Stimulation Efficacy on Pain and Quality of Life of Patients with Fibromyalgia Syndrome

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Keywords
Transcranial direct current stimulation; Fibromyalgia; Chronic pain; Quality of life

Abstract

Background: Fibromyalgia (FM) is a chronic pain disorder which is determined by pain and accompanying symptoms such as emotional distress, fatigue, and sleep inconvenience. One opinion is that it may be associated with changes in pain and sensory processing in the central nervous system (CNS), especially nociceptive pathways. The purpose of this study is to assess the efficacy of transcranial direct current stimulation (tDCS) on pain and quality of life (QOL) of patients with FM syndrome (FMS) by affecting the level of neurotransmitters and changing the functional connectivity of the stimulated region.

Methods: This study was a randomized double-blinded sham-control clinical trial. The groups were matched in terms of gender, age, education, pain duration, and premenstrual syndrome. In the case group, patients received M1 anodal stimulation with 2 mA constant current for 20 minutes for ten sessions (3 times a week). QOL and pain improvement were measured with Fibromyalgia Impact Questionnaire (FIQ) and Visual Analog Scale (VAS) forms before and 2 weeks (short-term) and 10 weeks (long-term) after the 10-session treatments.

Results: 80 patients with inclusion criteria were enrolled, out of which 12 were excluded due to lack of cooperation. The remaining 68 patients [46 (68%) women] had an average age of 46 years. Pain intensity was significantly lower in the case group compared to the sham group 2 weeks and 10 weeks after the treatment ($P < 0.001$). The QOL in patients 2 weeks after the treatment showed no significant improvement compared to the baseline, but 10 weeks after the treatment, QOL was higher than the sham group ($P < 0.001$).

Conclusion: Our results imply that tDCS is a safe and effective method in treating patients with FMS by reducing the pain and QOL improvement.

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Introduction

Fibromyalgia (FM) is a chronic pain disorder which is determined by pain and accompanying symptoms such as emotional distress, fatigue, and sleep inconvenience. One opinion is that it may be associated with changes in pain and sensory processing in the central nervous system (CNS), especially nociceptive pathways. These changes may be the result of maladaptive plasticity in pain-associated neural circuits.[1-4] In addition, disorganized neurotransmitters in patients with FM can result in exaggerated central sensitization to pain.[5]

The pain perception is strongly controlled by interactions of ascending and descending pathways at supraspinal levels with collaboration of dopaminergic and nicotinic transmissions. Different neural responses in the brain play different roles in translation of sensory information and depiction and inflection of the pain experience which can contribute to inter-individual variability in pain response, particularly in chronic pain conditions like FM syndrome (FMS).[6,7]

The current treatments for FMS include anti-inflammatory, pain control medications and CNS stimulation. Clinical trials have revealed no significant difference between prednisolone, ibuprofen, and naproxen compared to placebo. Glucocorticoids not only do not play a role in FMS treatment, but also they have serious long-term side effects.[8] Pain control medications such as acetaminophen and tramadol, alone or combined, could be effective for patients with FMS.[9] Clinical trials have displayed that CNS stimulants such as tricyclic antidepressants (TCAs) and cyclobenzaprine are considered the first choices of FMS treatments.[10,11] However, use of these treatments has been limited due to numerous side effects, mostly in the elderly. Furthermore, the effect of TCA medications in some patients decreases over time.[12] Selective serotonin reuptake inhibitors (SSRIs) are among other CNS stimulants consumed in FMS treatment.[13]

According to previous studies, beneficial non-medical treatments for FMS include cardiovascular exercise, hyperbaric oxygen therapy (HBOT), increasing muscle tone, physiotherapy, biofeedback, hypnotherapy, and cognitive behavioral treatments. Goldenberg et al.[8] confirmed that these methods led to noticeable results compared to massage, chiropractic, electrotherapy, and ultrasound treatments. Currently, we do not have sufficient data regarding efficacy of acupuncture.[14,15] Since most of the patients with FMS cannot benefit from the current treatments, necessity of novel methods is upraised.[16]

Recent studies have shown a direct association between FMS and altering the brain integrity. Tomography studies on brains of patients with FM showed a lower brain blood current in the thalamus, caudate nucleus, and pontine tegmentum compared to healthy individuals.[17] Several reports revealed that stimulation of the brain cortex by epidural electrodes could be beneficial for reducing the pain in patients suffering from defiant central pains.[18-22]

The mechanism of transcranial direct current stimulation (tDCS) on treatment remains unclear. According to functional magnetic resonance imaging (fMRI), an increased level of gamma-aminobutyric acid (GABA) in the anterior insula and decreased levels of glutamate and glutamine (Glx) in the anterior cingulate were found in patients with FM after tDCS treatment compared with baseline.[23] In addition, other studies have shown that tDCS may influence excitability by modulating the resting membrane potential based on fMRI data during and after stimulation. Based on fMRI data from 12 patients with FM, repetitive M1 tDCS stimulation can change the functional connectivity of regions under the electrode and structurally-connected regions such as the thalamus.[24,25] In regard to this mechanism, it is possible that changes in functional connectivity between the thalamus and brain regions are involved in pain perception.

Therefore, tDCS may alter the level of neurotransmitters and convert the functional connectivity of the stimulated region.

Although there are several studies regarding the efficacy of tDCS on other diseases,[26] there have been limited investigations on the action of tDCS on FMS, especially in Iran. One of the most important factors of a treatment efficacy is the patients' quality of life (QOL) before and following the treatment. The purpose of this study is the evaluation of the efficacy of tDCS on pain intensity level and QOL of patients with FMS by influencing the level of neurotransmitters and changing the functional connectivity of the stimulated region.

Methods

This randomized double-blinded sham-control clinical trial was conducted on all the patients diagnosed with FM at Imam Reza Hospital, Tehran, Iran, from 2012 to 2013. After receiving the study approval by the Institutional Review Board at the AJA University of Medical Sciences, Tehran, and obtaining informed consent from all participants, the patients' files were reviewed for pertinent demographic and clinical data and the outcomes.

Inclusion criteria: All diagnosed patients based on New Clinical Fibromyalgia Diagnostic Criteria 2010 within the age range of 18-65 years who had not benefited from current medications for FM were included. All included individuals reported no change in their medication four weeks prior to the study and continued with their medication throughout the study.

Exclusion criteria: All patients with underlying diseases such as cardiovascular, pulmonary, renal, hematologic, and psychiatric diseases, history of drug and alcohol abuse, history of seizure, oral contraceptive pill consumers, and pregnant and nursing women were excluded from the study.

The eligible individuals were assigned to either the case or the control groups by a double-blinded method. In this study, we prescribed for the case group 10 sessions (20 minutes, three days a week) of anodal tDCS at a constant current of 2 mA over primary motor cortex. TDCS was performed with a Neuromuscular Elecrostimulation Device designed by Enraf-Nonius, Netherlands.

To assess QOL and pain improvement, the Fibromyalgia Impact Questionnaire (FIQ) and Visual Analog Scale (VAS) forms were completed before, 2 weeks (short-term) and 2 months (long-term) after receiving 10 sessions of treatment. Afterward, physical evaluation was completed for all patients.

Data Analysis: Data analysis was completed using SPSS software (version 18, SPSS Inc., Chicago, IL, USA). For each measured variable, descriptive values are expressed as the mean and standard deviation (SD). Analysis of quantitative variables was performed using t-test, paired t-test, repeated measures analysis of variance (ANOVA), and Kolmogorov-Smirnov test. Categorical variables were compared using the chi-square test. Reported P-values were 2-tailed and $P < 0.05$ was considered statistically significant.

Results

A total of 80 individuals were enrolled, out of which 12 were excluded due to lack of cooperation. The remaining 68 patients [46 women (68%)] had the same basic demographic data provided in Table 1. The tDCS was well tolerated by the patients, and no major adverse effects were reported.

At the baseline, the mean of pain intensity scores was similar in the two groups. After receiving the treatments, there was a significant improvement in the tDCS group compared to the sham group 2 weeks and 10 weeks after the treatment ($P < 0.001$). The tDCS group (case) showed a statistically significant change in the mean of pain improvement from the baseline to 2 weeks after treatment ($P < 0.001$), while there was no obvious change from 2 weeks to 10 weeks after receiving the tDCS treatment (Figure 1).

Table 1. Patients' demographic data

	Sham	tDCS	P
Age (year) (mean ± SD)	47.60 ± 8.60	44.50 ± 8.70	> 0.05
Education (year) (mean ± SD)	9.70 ± 2.30	10.80 ± 3.10	> 0.05
Pain duration (year) (mean ± SD)	3.05 ± 1.40	2.70 ± 1.40	> 0.05
VAS at baseline (mean ± SD)	7.47 ± 1.60	6.59 ± 2.10	> 0.05

tDCS: Transcranial direct current stimulation; VAS: Visual Analog Scale; SD: Standard deviation

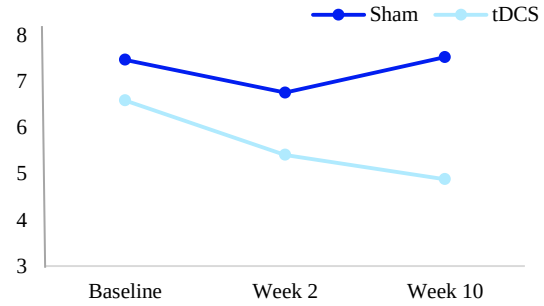

Figure 1. The means of pain intensity scores in the sham and the transcranial direct current stimulation (tDCS) groups before and 2 weeks and 10 weeks following the treatment

In the control (sham) group, there was a statistically considerable difference in pain improvement means between the baseline and after the 2-week treatment. Also, there was a statistically significant difference between the 2-week treatment and the 10-week treatment (P < 0.001), but at week 10 after receiving treatment, the mean pain improvement came back to the previous level. Therefore, there was not any difference between the baseline and week 10 after receiving the suitable treatment in the sham group (Figure 2).

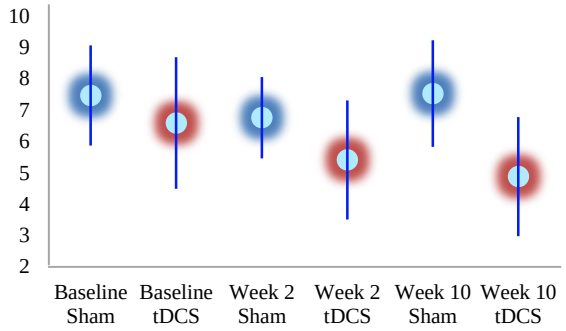

Figure 2. The means of pain improvement scores in the sham and the transcranial direct current stimulation (tDCS) groups before and 2 weeks and 10 weeks following the treatment

At the baseline, QOL was similar for the two groups. The tDCS group showed a significant improvement 2 weeks and 10 weeks following the treatment (P < 0.001). The mean of QOL improvement in the tDCS group showed a statistically significant change from the baseline to 2 weeks and 10 weeks after treatment (P < 0.001), while no significant change was seen in the means of QOL improvement between 2 weeks and 10 weeks after treatment (Figure 3).

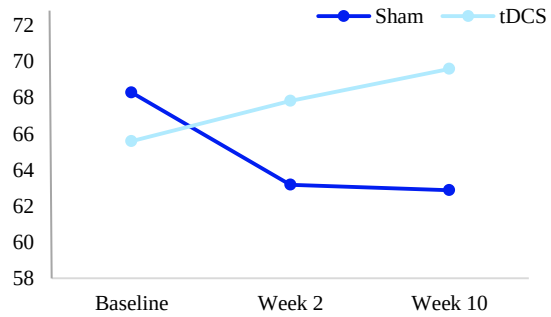

Figure 3. The means of quality of life (QOL) scores in the sham and the transcranial direct current stimulation (tDCS) groups before and 2 weeks and 10 weeks following the treatment

In the sham group, there was a statistically significant difference in the mean of QOL improvement from the baseline to 2 weeks and 10 weeks after the treatment (P < 0.001), where there was also a statistically significant difference between 2 weeks and 10 weeks after the treatment (P = 0.0001) (Figure 4).

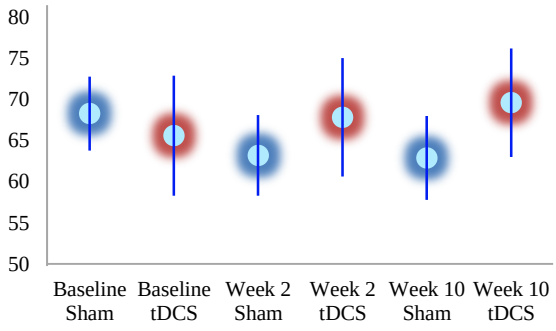

Figure 4. The means of quality of life (QOL) scores in the sham and the transcranial direct current stimulation (tDCS) groups before and 2 weeks and 10 weeks following the treatment

Discussion

FMS is a major cause of the widespread pain in the countries with diverse ethnicities and climates. Different general population studies, all over the world, reported 0.5-5 percent for prevalence of FMS.[27,28]

Pain experience is multidimensional which means each individual can have a different pain perception from the same stimuli. Since accurate measurement of these pain experiences is not possible, alike previous studies, we applied FIQ and VAS to assess QOL and pain improvement. Both forms have been operating as measurement instruments to demonstrate the wide-ranging spectrum of lifetime difficulties related to FM and response to therapy.[29,30]

We investigated anodal tDCS effects over the primary motor cortex and concluded the same results similar to previous studies. In several studies, the highest efficacy was shown when the M1 brain area was stimulated.[31] The stimulation of the M1 area resulted in a more lasting effect in pain reduction compared to the dorsolateral prefrontal cortex (DLPFC) stimulation.[32-36] In another study operating with a similar study design, the same results were concluded: a clinically significant improvement in pain (50% reduction) ($P = 0.035$) as well as improved QOL ($P = 0.001$) over time.[37]

Fregni et al. reported 50% pain reduction generated by tDCS in FMS cases by employing VAS.[38] In this study, we numerated the intensity of pain from baseline and 2 and 10 weeks after treatment and there was a great change in the mean of pain improvement from baseline to 2 weeks after treatment, while there was no considerable change from 2 weeks to 10 weeks after receiving the tDCS treatment.

Roizenblatt et al. stated that the stimulation of primary motor cortex improved sleep quality and successively, diminished symptoms of patients with FM as well.[39] Valle et al. showed that M1 stimulation had an affirmative outcome on patients' sleep quality where there was a significant correlation between sleep improvement and patients' pain reduction.[32] On the other hand, in our study, no significant change was seen in the means of QOL improvement between 2 weeks and 10 weeks after treatment. This shows that more data should be collected to evaluate this item in the future.

Conclusion

In this study, we showed that tDCS was a safe, non-invasive, and side effect-free treatment method for patients with FMS which helped to improve QOL by reducing the chronic pain. The tDCS should be considered as an adjuvant therapy for patients who are resistant to the routine treatments.

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Conflict of Interest

Authors have no conflict of interest.

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