Migraine Prophylaxis by Anodal Transcranial Direct Current Stimulation, A Randomized, Placebo-Controlled Trial

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Background: *Migraine is a common headache syndrome in adult populations. Prophylaxis is necessary to improve the quality of life but some patients with migraine have contraindication or suffer from side effects of medication, and therefore, establishing non-medical, neuromodulatory approaches is necessary. Past evidence had shown that consecutive motor cortex (M1) stimulation with anodal transcranial direct current stimulation (tDCS) was effective to relieve central pain.*
Objective: *To determine whether 20 consecutive days of the left M1 can be an effective prophylactic treatment for migraine.*
Material and Method: *Forty-two episodic migraine patients who had never received any prophylactic treatment, failed prophylactic treatment, or discontinued treatment due to adverse events were recruited in the present study. Patients were randomized to receive either active tDCS or sham tDCS 1mA, 20 m for 20 consecutive days and followed up for 12 weeks. Differences between and within groups were determined using repeated measures ANOVA. The level of significance was set at* $p < 0.05$.
Results: *Thirty-seven patients participated in the final analyses (active: n = 20, sham: n = 17). Between-groups comparison of attack frequency, pain intensity, and abortive medications used were performed at 4, 8, and 12 weeks after treatment. The results showed statistically significant reduction in attack frequency and abortive medications at week 4 and 8 after treatment. The pain intensity was statistically significant reduced at week 4, 8, and 12. All patients tolerated the tDCS well without any serious adverse events.*
Conclusion: *The present study suggests that anodal M1 tDCS may be a safe and useful clinical tool in migraine prophylaxis. The mechanism of action of anodal tDCS on neuromodulation in migraine patients needs further investigation.*

Keywords: *Noninvasive brain stimulation, Transcranial direct current stimulation, Migraine, Pain, Chronic headache*

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Migraine is a common episodic headache syndrome with estimated prevalence 11% in adult populations worldwide[1], and is commonly associated with a reduced quality of life[2]. For many patients, particularly those with frequent migraine episodes, prophylaxis is necessary to improve the quality of life[3]. However, some patients with migraine have contraindication or suffer from side effects[4]. Therefore, establishing non-medical, neuro-modulatory approaches are promising.

Transcranial magnetic stimulation (TMS) is a noninvasive technique and capable of easily inducing painless cerebral stimulation through application of a magnetic field on the scalp. Repeated magnetic pulses (repetitive TMS, rTMS) are able to induce long-lasting

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plastic effects that also last after the end of the stimulation frequency employed: Low frequencies (≤ 1 Hz) reduce, while high frequencies (> 1 Hz) increase cortical excitability[5]. Only a few clinical studies had investigated about migraine prophylaxis using noninvasive brain stimulation. Brighina et al 2004, delivered high-frequency rTMS on alternate days on the left dorsolateral prefrontal cortex (DLPFC) for 12 sessions. They found that headache attacks, headache index, and number of abortive medications were significantly reduced. In addition, the effect of treatment was stable for a month[6]. Teepker et al, 2009 applied two trains of 1-Hz TMS 500 monophasic pulses separated by a 1-min interval over the vertex on five consecutive days. Twenty-seven patients with migraine were randomly treated with either rTMS (n = 14) or the sham treatment (n = 13). Measures of attack frequency, migraine days, migraine hours, mean pain intensity, and use of analgesics were recorded before and eight weeks post-treatment. It was found that migraine attack frequency, migraine days, and migraine hours were significantly reduced in the active group. Furthermore, the migraine days were also significantly reduced in the sham group. However, there was no significant difference in all the outcomes between the two groups. They hypothesized that one of the pathophysiological factors involved in migraine might be owing to the reduction in cortical preactivation, rather than cortical hypoexcitability. However, the authors reported that the limitation of their study might be the feature difference between active and sham coil leading to subject bias[7].

Analogous to TMS, transcranial direct current stimulation (tDCS) is a safe non-invasive neuromodulatory technique where low amplitude electrical current is conducted to the cortex via scalp electrodes. However, in contrast to most neuro-stimulation modalities, the current strength in tDCS is not the intensities used and does not evoke action potentials, and modulate cortical excitability by altering cell membrane potential. The precise mechanisms that underlie tDCS are poorly understood, but overall the effect on the human cortex is reliable such that anodal tDCS facilitates cortical activity and cathodal tDCS depresses cortical activity[8]. Antal et al, 2011 published the first study using tDCS as a prophylactic treatment in migraine. They applied a constant current of 1 mA of tDCS to migraine patients over the visual cortex (V1) for 15 min, three days a week for six weeks. Twenty-six patients participated in the final analyses (cathodal: n = 13, sham: n = 13). The attack frequency, primary outcome, was assessed at two months before and after treatment. The results showed no reduction in attack frequency. They proposed that cathodal stimulation over V1 might not be able to ameliorate cortical hyperexitability in migraine patients[9].

Since migraine shares some causative, genetic, biochemical, or environmental factors with depression[10]. Therefore, the authors stimulated 20 consecutive days as in the treatment of medication-refractory depression[11,12]. For the site of stimulation, Machii et al, 2006 reported adverse events of high frequency rTMS at DLPFC. They found 25% of headache in healthy participants and 6.8% in patients with depression[13]. Fregni et al, 2006 studied about the stimulation site of anodal tDCS in treatment of pain in fibromyalgia. They found that anodal tDCS of M1 induced significantly greater pain improvement compared with DLPFC[14]. Other experiments also revealed the positive effect of pain reduction and safe in patients when treated by anodal tDCS over M1[15,16]. In the year 2010, the authors performed an open label pilot study on prophylactic treatment in 11 migraine patients. They received 1 mA, 20 m anodal tDCS for 20 consecutive days and followed-up for 12 weeks. The authors found the statistically significant reduction in the attack frequency at week four and eight. All patients could tolerate the tDCS well without any serious adverse events; however, the authors' sample size might not be large enough to detect a positive effect until 12 week-post treatment[17]. The open-label study might lead to subject evaluation bias. Therefore, the aim of this phase II study was to perform randomized double blind controlled study for determining whether 20 consecutive days of anodal tDCS on the left M1 can be an effective prophylactic treatment of migraine.

Material and Method

Migraine patients were defined according to criteria of the International Classification of Headache Disorder, 2nd Edition[18] and recruited by advertisement in Srinagarind Hospital, Faculty of Medicine and Physical therapist clinic, Faculty of Associated Medical Science, Khon Kaen University, Khon Kaen, Thailand. The volunteers received an information letter and a migraine headache diary and instructed to record every migraine attack in a set 4-week period prior to the eligibility assessment. On the enrollment visit, the diagnosis of migraine was confirmed by a practicing physician, and each patient

received a thorough neurological examination. Inclusion criteria were as follows: 1) ages between 18 and 65 years; 2) migraine with or without aura; 3) migraine, diagnosed by a physician, present for at least one year before enrollment; 4) headache was characterized by the presence of 0 to 14 days of headache per month; 5) had never received any prophylactic treatment, failure of the previous prophylactic treatment, or discontinuation of treatment due to adverse events for at least three months prior to the start of the experiment; 6) agreement not to take concurrent prophylactic treatment for headaches by pharmacological and non-pharmacological treatments; and 7) agreement to be available for a follow-up of at least three months. Exclusion criteria were psychiatric conditions, schizophrenia, major depression, mania, pregnancy, lactations, skull defect, and other serious neurological diseases. Participants who used herbal remedies and other alternative therapies such as massage were excluded from the present study.

All patients gave their written informed consent. The present study conformed to the declaration of Helsinki and was approved by the Ethics Committee of Khon Kaen University (Identifier number is HE 521331).

Experimental design

The present study contained the following three phases: 1) a pre-treatment 4-week baseline evaluation where attack frequency, pain intensity, and dosages of abortive medications were recorded; 2) 20-day double-blind treatment sessions; 3) a post-treatment 12-week period of observation.

After the baseline period, the patients were randomized in a 1:1 ratio in blocks of four randomizations to receive either sham or active tDCS. All the patients were informed about all possible adverse events, including headache exacerbation. Participants were advised to continue their routine abortive or analgesic medication regimen for the duration of trial. All changes in dosages were recorded in the patient's medication diary.

Direct current stimulation

Direct current was transferred using a saline-soaked pair of surface sponge electrodes (35 cm^2) and delivered through battery-driven power supply. Constant current stimulator with a maximum output of 2 mA was developed by Pattawit Electronic, JP advance LTD, Thailand. The current density delivered was between 0.029 and 0.08 mA/cm^2. The anodal electrode was placed at the M1 and the cathodal electrode was placed over the contralateral supraorbital area. We identified M1 at the C3 10/20 international system of EEG electrode placement.

The tDCS device was designed to mask sham or real stimulation. The control switch was on the side of the instrument, which was covered by opaque adhesive during stimulation. The power indicator was on the front of the machine, which lit up during the time of stimulation both in real and sham. However, in sham stimulation, the current was discontinued after 30 seconds while the power indicator remained.

The staff who analyzed the data were unaware of device setting (active mode or sham mode), and thus were blinded to the treatment condition.

Frequency of attacks

Frequency of attacks, the primary outcome, was recorded by patients four weeks before the treatment to assess the baseline. They were also requested to record their attack every four weeks after treatment. The self-recording terminated at week 12.

Pain measurement

Pain intensity, the secondary outcome, in a form of visual analog scale (VAS) was evaluated by the patients. This self-evaluation scale ranges from 0 to 10 as visually described in centimeter units: 0 cm indicates no pain and 10 cm denotes the most possible pain.

Abortive and analgesic medications

Abortive medications were recorded as the total dosage per drug, per four week observation block. For the abortive and analgesic medications, we prescribed acetaminophen 1,000 mg every 6 hours for mild headache; ibuprofen 200 mg, two tablets every 4 hours for moderate pain; ergotamine 1 mg with 100 mg of caffeine, two tablets at the onset, and then one tablet every half an hour until the symptom relief (maximum six tablets per day, or ten tablets per week) for moderate pain; and sumatriptan 50 to 100 mg at the onset and repeated after 2 hours (maximum 200 mg per day) in severe cases. These medications were prescribed as standard of care[19].

Statistical analysis

Analyses were done with Stata software, version 10.0 (StataCorp, College Station, TX). Since dropouts could indicate either treatment failure or absent improvement that discouraged them to continue

in this trial, the authors analyzed the endpoints using the intention-to-treat principle. The authors used the last evaluation carried out to the session before the missed session, assuming no further improvement after the dropout.

Factorial ANOVA was used to analyze the difference between the groups. The differences over time in either active or sham group were carried out using Bonferroni correction repeated measures ANOVA. Finally the overall mean differences of outcomes between active and sham group were calculated by generalized estimating equations implemented under generalized linear model frameworks. The level for establishing significant differences was set at $p < 0.05$.

Results

Fifty-nine patients were included in the present study between October 2010 and January 2012. The patients were assessed for four weeks, and 17 did not meet the inclusion criteria. Table 1 shows the demographic profile of the included patients. The mean age of the subjects in the sham group was higher than those in active group, but no other significant difference was observed. Two patients in the active group and three patients in the sham group dropped out at the treatment period. These were excluded before the follow-up period. Two subjects in the sham group dropped out at week eight and 12 due to lack of improvement. The authors analyzed data from all the available participants (35/37) who completed the present study as an intention-to-treat analysis.

Frequency of attacks

The mean frequency of attack between the active and sham groups was significantly reduced at week four and week eight, there was no statistical reduction between groups by week 12.

Within the active tDCS group, there was a statistically significant reduction in attack frequency at week four (1.05, 95% CI: 0.87 to 1.23, $p < 0.01$) and week eight (0.85, 95% CI: 0.58 to 1.12, $p < 0.01$) but

Table 1. Demographic data and baseline characteristics

	Active group	Sham group
No. of subjects	20	17
Sex (female/male)	14/6	12/5
Age (mean ± SD)	28.60 ± 6.83	35.06 ± 13.54
Diagnosis		
Migraine with aura	9	5
Migraine without aura	11	12
Family history	12	9
Baseline pain intensity (VAS score) (mean ± SD)	4.45 ± 1.00	4.17 ± 1.07
Migraine attack frequency/ 4 weeks (mean ± SD)	3.85 ± 0.88	3.76 ± 0.90
Mean age at onset of migraine (mean ± SD)	23.70 ± 5.70	28.58 ± 10.45
Number of abortive medication/4 weeks (tablets) (mean ± SD)	19.40 ± 2.62	20.65 ± 3.59
Abortive medications		
Ergotamine	11*	7
Ibuprofen	8	7
Acetaminophen	2*	1
Triptans	-	2
History of prophylactic medications		
Failed tricyclic antidepressant	4	2
Failed beta-blockers	1	3
Never take prophylactic medications	15	12

Subjects matched for characteristics; no statistical difference between groups by student's test ($p < 0.05$)
* One patient took both ergotamine and acetaminophen

there was no statistically significant reduction in attack frequency at week 12 (0.10, 95% CI: -0.04 to 0.24, p = 0.16). Within the sham group, there was no statistically significant reduction in attack frequency at week four (0.05, 95% CI: -0.06 to 0.18, p = 0.33); week eight (-0.06, 95% CI: -0.28 to 0.16, p = 0.58); and week 12 (-0.12, 95% CI: -0.37 to 0.13, p = 0.33) respectively.

Pain intensity

There was a significantly reduction in mean pain intensity in the active relative to sham group at the 4-week and 8-week follow-up points, while there was no statistically significant reduction at week 12.

Within the active tDCS group, there was a statistically significant reduction in pain intensity at week four (1.50, 95% CI: 1.18 to1.82, p < 0.01) and week eight (1.30, 95% CI: 1.03 to 1.57, p < 0.01) but no statistically significant reduction was observed at week 12 (0.35, 95% CI: -0.07 to 0.62, p = 0.06). Notably, in the sham group, there was also statistically significant reduction in the pain intensity at week four (0.53, 95% CI: 0.26 to 0.79, p < 0.01). However, no statistically significant reduction was found at week eight (0.18, 95% CI: -0.03 to 0.38, p = 0.08); and week 12 (-0.12, 95% CI: -0.29 to 0.05, p = 0.16) respectively.

Abortive medications

All patients stook abortive medications until the symptom disappeared. The overdose or more than one medication was not advised. Three patients exceeded the prescribed ergotamine dose and took 8 to 10 tablets/day. In addition, one patient took both ergotamine and acetaminophen for relieving her pain. However, all other patients used the medications as recommended at the start of the trial.

On comparing between the groups, the abortive medications used were statistically reduced in the active relative to sham at week four and eight.

Within the active tDCS group, there was a statistically significant reduction in mean abortive medications at week four (5.40, 95% CI: 4.42 to 8.89, p < 0.01) week eight (2.58, 95% CI: 2.22 to 7.18, p < 0.01), and week 12 (1.70, 95% CI: 0.31 to 5.59, p = 0.03). With regard to the sham group, there were also statistically significant reduction in abortive medications at week four (3.85, 95% CI: 2.73 to 4.92, p < 0.01) and week eight (1.83, 95% CI: 1.05 to 2.60, p = 0.04). However, no statistically significant reduction was observed at week 12 (1.0, 95% CI: -0.29 to 0.05, p = 0.16). The summary of the outcome data is shown in Table 2.

Adverse events

Thirty-five out of 37 patients completed open-end adverse event questionnaires; two patients who dropped out did not report their symptoms in the last week. Most of them had mild tingling sensation during the beginning of stimulation, but the symptom had no long-lasting effect. All the patients could well tolerate to tDCS and no serious adverse event was found in the present study. However, nine patients reported mild adverse events: five during active tDCS and four during sham.

Of the five patients in the active group who reported adverse events, two had headache, one had transient mild first-degree burn that completely healed within five days, one had drowsiness and rash under electrode, which disappeared in two hours, and one patient had three adverse events, namely, headache, decreased appetite, and rash. In the sham group, there were four patients who had adverse events, rash under the electrode, itching, headache with decreased appetite, headache with dizziness.

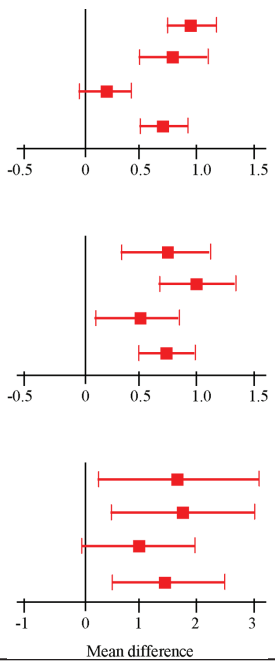
Discussion

The present study is the first randomized, double-blind, sham-controlled anodal tDCS of M1 study on migraine prophylaxis. The authors found that the frequency of attack in the active group was significantly lower than that in the sham group at week four and eight after treatment, but did not last long up to week 12. The present outcomes support the authors pilot study[17] and the results of high-frequency rTMS on the left DLPFC studied by Brighina et al, 2004[6]. Moreover, other studies showed the TMS effect in pain abortion. Clarke et al, 2006 used two stimulus pulses over the area of perceived pain or over the area of the brain, generating the aura at the beginning of the attack[20]. Lipton et al, 2010 employed hand-held devices operated by patients. The stimulator was placed over the visual area and administered three attacks over three months while experiencing aura[21].

The effect of non-invasive brain stimulation studied by several research centers is still controversial. There are at least three different hypotheses regarding migraine. The first shows primary cortical hyperexcitability[22-24], the second reveals reduced cortical inhibition[24-27], and finally, the third presents reduced cortical excitability[29,30].

Table 2. The summary of outcomes in the active and sham group

Outcomes	Active	Sham	Mean difference*	95% CI*
A. Frequency of migraine attacks				
Weeks 4	2.80 ± 0.69	3.71 ± 0.92	0.91	0.76 to 1.20
Weeks 8	3.00 ± 0.73	3.82 ± 0.88	0.82	0.48 to 1.16
Weeks 12	3.75 ± 0.79	3.88 ± 0.86	0.13	-0.06 to 0.47
Overall			0.67	0.50 to 0.84
B. Pain intensity				
Weeks 4	2.95 ± 0.76	3.59 ± 1.12	0.64	0.31 to 1.09
Weeks 8	3.15 ± 0.75	4.00 ± 1.06	0.85	0.70 to 1.35
Weeks 12	4.10 ± 0.97	4.29 ± 1.10	0.19	1.14 to 0.84
Overall			0.74	0.48 to 1.00
C. Abortive medications				
Weeks 4	14.00 ± 3.60	16.80 ± 3.90	2.80	0.16 to 3.07
Weeks 8	16.82 ± 3.94	18.82 ± 3.68	2.00	0.53 to 3.00
Weeks 12	17.70 ± 2.92	19.65 ± 3.18	1.95	-0.03 to 1.96
Overall			1.43	0.49 to 2.38



* Mean difference (sham-active) of the endpoint of outcomes at week 4, 8, and 12 using analysis of variance (ANOVA) and for overall using generalized estimating equations implemented under generalized linear model frameworks

With regard to the evidence of reduced cortical inhibition, many noninvasive brain stimulation studies have shown that migraine patients have lower phosphene threshold than normal controls[31,32]. Additionally, both the intracortical and cerebellar inhibition levels were also found to be significantly a lower in migraine patients, when compared with those in the controls[33]. Owing to the fact that pathophysiologic mechanism of migraine is still controversial. Outcome of clinical trials might support some mechanisms, with regard to the effects of non-invasive brain stimulation on migraine prophylaxis. Recently, Siniatchkin et al, 2011 found that glutamate/creatine ratio (Glx/Cr) was higher in migraine patients than in control in a resting state. The first photic stimulation (PS) caused a reduction in the Glx/Cr ratio. This reduced glutamatergic neurotransmission remained stable and unchanged after both 1 mA, 10 min of anodal and cathodal tDCS at Oz. Moreover, the second PS had no effect on the reduced Glx/Cr ratio. There were also minimal and non-significant changes in the VEP amplitude and habituation after their tDCS. It seems likely that the altered modifiability of cortical excitability in migraine and insufficient homeostatic plasticity are associated with altered glutamatergic function. In migraine patients, single dose tDCS decreased the Glx/Cr ratio, regardless of the polarity of tDCS. This stimulation induced reduction in the Glx/Cr was explained in terms of the Glx pool being as a result of induced neuronal currents and subsequent depolarization, an effect, which has been demonstrated in animals[34]. Siniatchkin proposed that migraine was associated with an increased consumption of glutamate, which is quickly utilized by the first sequence of stimulation and cannot be effectively used for homeostatic regulation of cortical excitability.

According to the neurophysiologic knowledge, anodal tDCS and high frequency TMS might have a role in homeostatic regulation by acting on the neuronal membranes leading to increased firing rates driven by postsynaptic membrane depolarization accompanied by enhanced presynaptic input, resulting in NMDA receptor-mediated augmentation of synaptic strength, presumably via the increase in the intracellular

calcium levels[35]. Similar to the induction of long-term neuroplasticity, a combination of glutamatergic and membrane mechanisms is necessary to induce the after-effects of anodal tDCS.

Due to the stimulation of various brain areas[6,17] had positive effects in migraine prophylaxis. Based on these studies, it might propose that an increase in the local excitability of the cortex can be associated with pain control or modulation[15,16]. Strafella et al, 2004 published the first report of TMS-induced modulation of subthalamic neuronal activity in six patients with Parkinson's disease (PD) undergoing implantation of deep brain stimulators. They found that single-pulse TMS of the motor cortex induced an excitation in 74.9% of the neurons investigated. This activation was followed by a long-lasting inhibition of the subthalamic neuronal activity, which did not correlate with PD severity[36]. Garcia-Larrea et al, 1997 proposed a model in which thalamic nuclei activation would lead to several events in other pain-related structures, such as the anterior cingulate, periaqueductal gray, and spinal cord, which could ultimately modulate the affective-emotional component of pain and inhibit pain impulses from the spinal cord[37].

The pathway of tDCS at M1 modulated synaptic plasticity in the presented migraine patients might be similar, because anodal tDCS is also associated with an increase in cortical excitability that lasts beyond the stimulation period[8]. Both TMS and tDCS techniques might lead to a similar indirect change in the activity of the connected areas and thus result in similar effects on neuronal plasticity, which may occur in the thalamus[36,37]. The authors proposed that the homeostatic regulation of cortical excitability might occur via corticothalamic loop despite of the different stimulating brain area. However, there is no evidence supported.

Limitation of this study

1. The authors could not investigate the neurotransmitter change in patients' brain after anodal tDCS so the true mechanism was not established.

2. The reduction of pain intensity in the present study might occur from abortive or analgesic medications overuse because the authors did not exclude these patients.

In summary, the authors conclude that consecutive stimulation of anodal tDCS on M1 for 20 sessions can significantly decrease the frequency of attack, pain intensity, and abortive medications in active than in the sham group for eight weeks. The effects of long-term anodal tDCS on neuromodulation and neuroimaging after tDCS in migraine patients need further investigation.

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Potential conflicts of interest

None.

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การป้องกันไมเกรนด้วยไฟฟ้ากระแสตรงขั้วบวกผ่านกะโหลก การทดลองแบบสุ่มโดยมีกลุ่มควบคุม

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ภูมิหลัง: *ไมเกรนเป็นกลุ่มอาการปวดศีรษะที่พบได้บ่อยในผู้ใหญ่ การป้องกันเป็นสิ่งจำเป็นในการเพิ่มคุณภาพชีวิต แต่ผู้ป่วยไมเกรนส่วนหนึ่งมีข้อห้ามหรือมีอาการข้างเคียงจากยาป้องกันไมเกรน ดังนั้นการป้องกันโดยวิธีไม่ใช้ยาจึงเป็นสิ่งจำเป็น ในการศึกษาที่ผ่านมาแสดงให้เห็นว่าการกระตุ้นด้วยไฟฟ้ากระแสตรงผ่านกะโหลกบริเวณเปลือกสมองส่วนมอเตอร์สามารถลดอาการปวดเรื้อรังในอาการปวดจากระบบประสาทได้*

วัตถุประสงค์: *เพื่อที่จะประเมินว่าการกระตุ้นด้วยไฟฟ้ากระแสตรงผ่านกะโหลกบริเวณเปลือกสมองส่วนมอเตอร์ต่อเนื่องกัน 20 วัน สามารถป้องกันอาการปวดในไมเกรนได้หรือไม่*

วัสดุและวิธีการ: *ผู้ป่วยไมเกรนชนิดปวดเป็นพัก ๆ จำนวน 42 ราย ที่ไม่เคยได้รับยาป้องกัน หรือ เคยได้รับยาป้องกันแต่ล้มเหลวหรือเลิกรับประทานยาเนื่องจากอาการข้างเคียง จะถูกสุ่มให้ได้รับการกระตุ้นจริงหรือกระตุ้นหลอกด้วยขั้วบวกของไฟฟ้ากระแสตรงอย่างอ่อนขนาด 1 มิลลิแอมแปร์ เป็นเวลา 20 นาทีทุกวันต่อเนื่องกัน 20 วัน และได้รับการติดตามผลการรักษาเป็นเวลา 12 สัปดาห์ ความแตกต่างระหว่างกลุ่มและภายในกลุ่มก่อนและหลังการรักษาใช้สถิติ repeated measures ANOVA โดยค่า p-value ที่น้อยกว่า 0.05 ถูกจัดเป็นระดับความแตกต่างอย่างมีนัยสำคัญทางสถิติ*

ผลการศึกษา: *มีผู้ป่วยไมเกรนจำนวน 37 ราย ที่เข้าร่วมจนสิ้นสุดการศึกษานี้ (กลุ่มกระตุ้นจริง 20 ราย กระตุ้นหลอก 17 ราย) เมื่อเปรียบเทียบความถี่ของการเกิดอาการ ระดับความเจ็บปวด และจำนวนเม็ดยาที่ใช้ระหว่างกลุ่มกระตุ้นจริงและกระตุ้นหลอกในสัปดาห์ที่ 4, 8, และ 12 พบการลดลงอย่างมีนัยสำคัญทางสถิติของความถี่ของการเกิดอาการและจำนวนเม็ดยาที่ใช้ในสัปดาห์ที่ 4 และ 8 ส่วนระดับความเจ็บปวดลดลงอย่างมีนัยสำคัญทางสถิติในสัปดาห์ที่ 4, 8, และ 12 ผู้ป่วยทุกรายทนต่อการกระตุ้นไฟฟ้ากระแสตรงได้เป็นอย่างดีโดยไม่มีอาการไม่พึงประสงค์ที่ร้ายแรง*

สรุป: *ผลการศึกษานี้แสดงให้เห็นว่าการกระตุ้นด้วยไฟฟ้ากระแสตรงอย่างอ่อนบริเวณเปลือกสมองส่วนมอเตอร์ อาจจะเป็นประโยชน์และปลอดภัยในการป้องกันอาการปวดในไมเกรน กลไกการออกฤทธิ์ของการกระตุ้นด้วยไฟฟ้ากระแสตรงอย่างอ่อนในการปรับเปลี่ยนทางระบบประสาทของผู้ป่วยไมเกรนยังต้องการการศึกษาต่อไป*