



Research Article

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ACUPUNCTURE DECREASES ATTACK FREQUENCY AND IMPROVES DISABILITY IN PATIENTS WITH MIGRAINE WITHOUT AURA: A RANDOMIZED CONTROLLED TRIAL

 **Rabia Rukiye Akinci**¹,  **Yasemin Cayir**²,  **Nuray Bilge**³

¹Department of Family Medicine, Kadınhanı Refik Saim Koyuncu State Hospital, Konya, Turkey

²Department of Family Medicine, Ataturk University, Faculty of Medicine, Erzurum, Turkey

³Department of Neurology, Ataturk University, Faculty of Medicine, Erzurum, Turkey

Correspondence:

Yasemin Cayir (e-mail: dryasemincayir@yahoo.com)

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Abstract

Objectives: This study investigated the effect of acupuncture treatment on attack frequency, pain intensity, and disability in patients with migraine without aura that received prophylaxis treatment.

Materials and Methods: Eighty-four patients with migraine without aura were randomized to the intervention group (IG; n=42) and control group (CG; n=42). IG received 12 sessions of Acupuncture in addition to prophylaxis treatment. CG received only prophylaxis treatment. The primary outcome measures were monthly attack frequency, duration of attacks and pain severity during attacks. The secondary outcome measure included a change of Migraine Disability Assessment (MIDAS) scores from baseline to endpoints. All participants were followed up for three months.

Results: A total of 80 participants completed the study. There were no statistically significant differences between the IG and CG for either socio-demographic features or the outcome measures at baseline. VAS score decreased from 8.8 ± 0.9 to 3.9 ± 1.5 in IG, while it decreased from 8.7 ± 0.8 to 4.4 ± 2.4 in CG ($p=0.001$). After three months mean monthly attack frequency decreased from 7.2 ± 3.0 to 3.3 ± 2.3 in IG, while it decreased from 6.3 ± 3.3 to 4.4 ± 2.4 in CG ($p=0.040$). The mean duration of attacks was 12.1 ± 2.6 hours before intervention; it decreased to 3.1 ± 1.7 hours in IG ($p=0.002$). There was a significantly higher proportion of participants in IG who had MIDAS Grade 2 compared to those with CG (42.50% versus 2.50%) at the end of the study ($p=0.001$).

Conclusion: Acupuncture may be suggested as a complementary treatment option to optimize the clinical management of patients with migraine without aura via decreasing attack frequency and pain severity, also improving disability.

Keywords: Acupuncture, migraine, MIDAS, pain, VAS score.

Introduction

Migraine is a primary headache disorder that occurs with attacks lasting 4-72 hours, accompanied by photophobia, phonophobia or nausea, and which is unilateral, throbbing recurrent headaches. The current global prevalence of migraine is 10-12%, and it is seen 2-3 times more in women than in men.^{1,2} Migraine is one of the important causes of disability-related day loss. Migraine negatively affects the quality of life and mostly creates a cost burden with workday losses due to attacks.³

There are several pharmacological treatment options to treat migraine attacks. Non-migraine-specific drugs such as antiemetics, analgesics, non-steroidal anti-inflammatory drugs (NSAIDs) and migraine-specific drugs such as ergot derivatives and triptans are widely used for treating acute migraine attacks. However, because of relatively few trials that compared the different pharmacological treatment options to treat migraine attacks, comprehensive treatment algorithms are not available.^{4,5}

While acute attack treatment is sufficient for some patients with migraine, approximately 40% of patients with migraine require prophylaxis treatment in order to reduce attack frequency, pain severity, and headache-related distress.⁶ There are several indications for prophylaxis treatment, such as; having four or more migraine attacks in a month, despite appropriate attack treatment having debilitating attacks, difficulty tolerating or having a contraindication for attack treatment, having a medication-overuse headache, and having attacks with the risk of serious and permanent neurological damage. β blockers such as propranolol, antidepressants and antiepileptic drugs are among the widely used prophylaxis treatment options.⁷ However, each drug has its own potential side effects such as fatigue, sleep disorders, nausea and vomiting, and long-term use causes both non-compliance due to side effects and an increase in health costs. Therefore, more and more patients are looking for effective non-pharmacological therapies for preventing migraine attacks.⁸

Acupuncture is a Traditional Chinese Medicine method that has been used for 3000 years to control symptoms, treat illnesses, and relieve pain.⁹ Acupuncture is widely used in many countries today as a complementary therapy, especially in cases of chronic pain. Acupuncture is recommended by the NIH (National Institutes of Health) in the treatment of primary headaches.¹⁰ Migraine is one of the diseases in which acupuncture treatment is commonly used. Studies conducted so far have focused more on the effect of Acupuncture on pain intensity in patients with migraine.¹¹ Data comparing the impact of Acupuncture on both the attack frequency and disability in migraine are relatively scarce. We aimed to investigate the effect of acupuncture treatment on attack frequency, pain intensity, and disability in migraine without aura patients who receive prophylaxis treatment.

Materials and Methods

Study design

This randomized-control trial was carried out between March-September 2018 at Atatürk University Research and Practice Center for Acupuncture and Complementary Therapy Modalities and Atatürk University Medicine Faculty Department of Neurology. The study was performed in adherence to Helsinki Declaration, which is a guideline for clinical trials. The acupuncture treatment was documented in accordance with Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA). The written informed consent form was obtained from all the participants. This study is registered on the website of ClinicalTrials.gov (www.clinicaltrials.gov) with the number NCT04542811.

Participants

In March 2018, a total of 115 migraine patients visited Atatürk University Neurology Outpatient Department. Inclusion criteria were being diagnosed with migraine according to IHS (International Headache Association), receiving migraine prophylaxis treatment, having more than four attacks per month/more than one attack per week, and not having received acupuncture treatment before. Exclusion criteria included being diagnosed with migraine with aura/secondary headache, having received acupuncture treatment for any reason within the last year, not giving consent for acupuncture treatment, and having a fear of needles. It was calculated that a sample of 40 patients for each group provided a statistical power of 80% for determining a difference in VAS score with an error of 5% by the G-power[®] program. After baseline evaluation by a neurologist, eligible patients (n=84) were enrolled in the study. The secretary in the Neurology Outpatient Department generated a random allocation sequence for the patients who met the inclusion criteria. Eighty-four migraine without aura patients were randomly assigned to the Intervention Group (IG) and Control Group (CG) at a 1:1 ratio. CG received only prophylaxis treatment, while the IG received acupuncture treatment for a total of 12 sessions, three sessions in a week, in addition to prophylaxis treatment. All participants were followed up for three months. The flow chart of the study is presented in Figure 1.

Intervention

Acupuncture points were used without a formal Traditional Chinese Medicine (TCM) diagnosis in the IG. All acupuncture points were selected and localized on the basis of the WHO Standardized Acupuncture Point Location. Acupuncture points selected were bilateral LI-4, LI-11, ST-8, ST-44, SP-6, GB-1, GB-14, GB-20, LR-3, and also GV-14, GV-20. Sterile and single-use stainless steel acupuncture needles measuring 0.25x25 mm were inserted to a depth of 10 mm and retained for 30 minutes without any further stimulation. Acupuncture was

performed by an acupuncturist with an acupuncture practitioner license from the Turkish Ministry of Health. Adverse events were monitored for all acupuncture sessions.

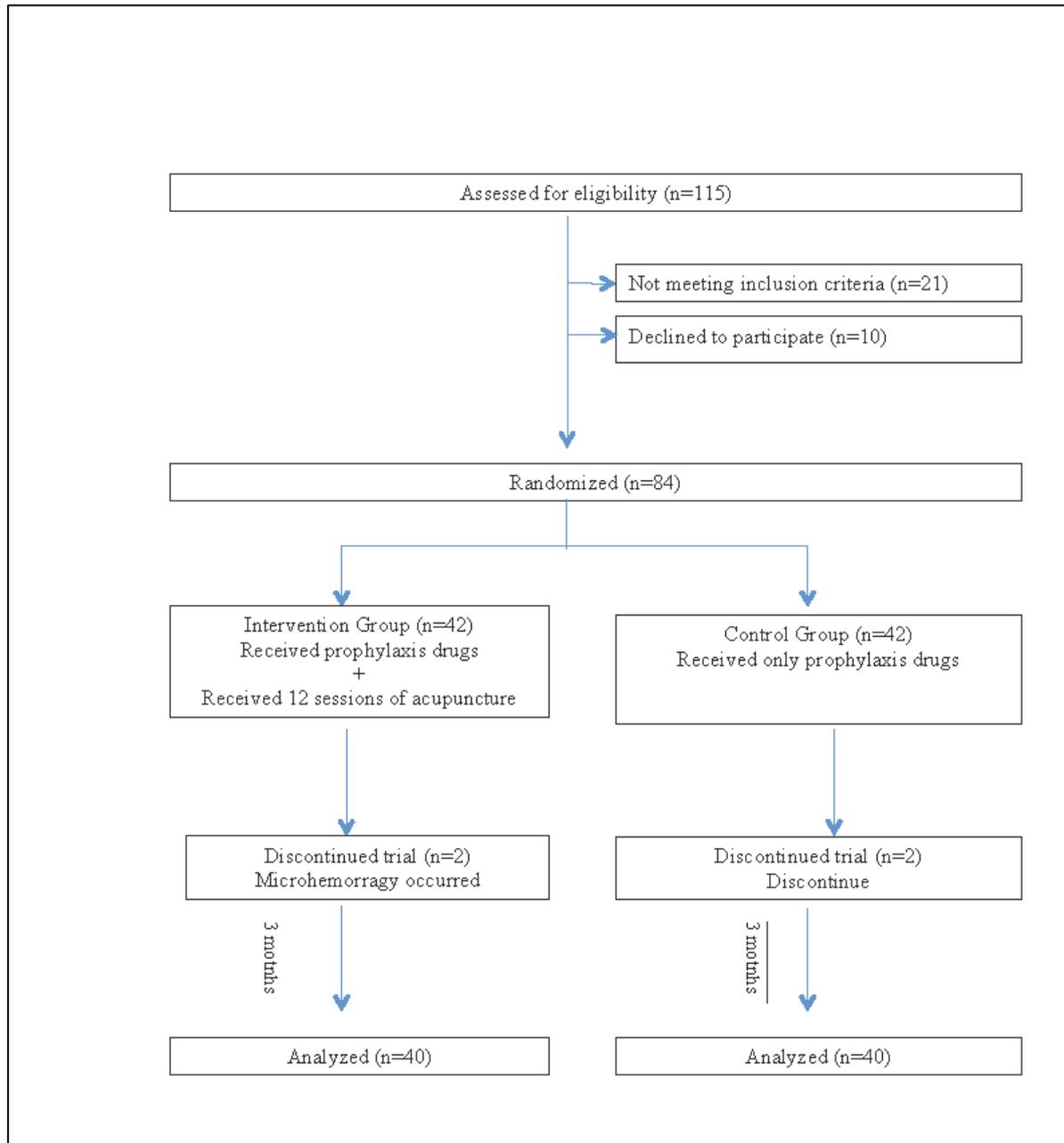


Figure 1. Flowchart of the participants

Outcome measurement

The primary outcome measures were monthly attack frequency, duration of attacks and pain severity during attacks. According to the guidelines of the IHS for Clinical Trials in Migraine, the participants documented each migraine attack day in a month at pain-free intervals of at least 48 hours and durations of the attacks in hours.¹² The pain severity during attacks was measured using a 10-point visual analog scale (VAS). While 0 indicates no pain, ten indicates the most severe pain imaginable.

The secondary outcome measure included a change of Migraine Disability Assessment (MIDAS) scores from baseline to endpoints. The MIDAS questionnaire is an ordinary rating scale to assess the migraine-related disability of a patient with migraine. It is based on responses to five questions about disabilities associated with headaches in the last three months. MIDAS questionnaire has a four-point grading system. Scores ranging from 0 to 5 indicate Grade 1 (little or no disability), scores ranging from 6 to 10 indicate Grade 2 (mild disability), scores ranging from 11 to 20 indicate Grade 3 (moderate disability), and scores 21 or greater indicates Grade 4 (severe disability). Previous studies have demonstrated that the MIDAS is a valid, effective and sensitive tool to assess the disability of migraine.¹³ Ertaş et al. performed Turkish validity and reliability of MIDAS.¹⁴ All data were collected at baseline and in the third month.

Statistical analysis

SPSS 23.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Numerical variables are expressed in mean±standard deviation and categorical variables in numbers and percentages (%). Numerical data were analyzed for normal distribution by Skewness. Independent sample t-test and χ^2 test were used to analyze the differences between the groups in terms of outcome measurements. P values <0.05 were regarded as statistically significant.

Results

A total of 115 participants entered the study screening, and 84 participants with migraine who received prophylaxis treatment were randomized. A total of 80 patients completed the study. The mean age of the participants was 37.80 ± 11.70 years. Both IG (n=40) and CG (n=40) had similar baseline characteristics in terms of age, gender, family history, monthly attacks frequency, duration of migraine, and used prophylaxis drug. The baseline characteristics of the participants are presented in Table 1.

Table 1. Baseline characteristics of the participants in each group

Characteristics	IG (n = 40)	CG (n = 40)	P value
<i>Age (year) (mean ± SD)</i>	38.1 ± 12.4	37.5 ± 11.0	0.828
<i>Gender (n,%)</i>			0.531
Male	7 (17.50%)	5 (12.50%)	
Female	33(82.50%)	35 (87.50%)	
<i>Family history (n,%)</i>			0.823
Yes	19 (47.50%)	20 (50.00%)	
No	21 (52.50%)	20 (50.00%)	
<i>Monthly attack frequency (mean ± SD)</i>	7.2 ± 3.0	6.3 ± 3.3	0.200
<i>Duration of migraine (year) (mean ± SD)</i>	7.5 ± 6.3	5.5 ± 6.1	0.165
<i>Used prophylactic drug (n,%)</i>			0.169
Amitriptyline	8 (20.00%)	10 (25.00%)	
Venlafaxine	5 (12.50%)	12 (30.00%)	
Flunarizine	12 (30.00%)	9 (22.50%)	
Others	15 (37.50%)	9 (22.50%)	

The comparison of the measurements between IG and CG is presented in Table 2. There were statistically significant differences between the groups as regards VAS score, MIDAS score, duration of attacks and monthly attack frequency at the end of the study. After three months mean monthly attack frequency decreased from 7.20 ± 3.00 to 3.30 ± 2.30 in IG, while it decreased from 6.30 ± 3.30 to 4.40 ± 2.40 in CG ($p=0.040$).

Table 2. Comparison of the measurements between groups at the beginning and the third month

	IG (n = 40)	CG (n = 40)	P value
VAS (0-10)			
Beginning	8.8 ± 0.9	8.7 ± 0.8	0.704
Third month	3.9 ± 1.5	4.4 ± 2.4	0.001*
Duration of attacks (hour)			
Beginning	12.1 ± 12.6	9.3 ± 8.1	0.235
Third month	3.1 ± 1.7	5.2 ± 3.6	0.002*
Monthly attack frequency			
Beginning	7.2 ± 3.0	6.3 ± 3.3	0.200
Third month	3.3 ± 2.3	4.4 ± 2.4	0.040*
MIDAS Score			
Beginning	39.1 ± 15.1	34.4 ± 15.1	0.173
Third month	8.3 ± 9.3	24.9 ± 9.5	0.001*

(VAS: Visual Analogue Scale; MIDAS: Migraine Disability Assessment; * $p<0.05$)

The comparison of MIDAS grades of participants is displayed in Table 3. While the proportion of the grades was similar at the beginning of the study in each group ($p=0.745$), a significantly higher proportion of participants in IG had MIDAS Grade 2 compared to those with CG (42.50% versus 2.50%) at the end of the study ($p=0.001$). Conversely, CG was more likely to be in MIDAS Grade 4 (2.50% versus 55.00%, $p=0.001$) at the end of the study.

Table 3. Distrubion of the MIDAS grades

	IG (n = 40)	CG (n = 40)	P value
MIDAS-1			
Grade 1	None	None	0.745
Grade 2	None	None	
Grade 3	35 (87.50%)	34 (85.00%)	
Grade 4	5 (12.50%)	6 (15.00%)	
MIDAS-2			
Grade 1	14 (35.00%)	None	0.001*
Grade 2	17 (42.50%)	1 (2.50%)	
Grade 3	8 (20.00%)	17 (42.50%)	
Grade 4	1 (2.50%)	22 (55.00%)	

(MIDAS: Migraine Disability Assessment; MIDAS 1: MIDAS score at the beginning of the study, MIDAS 2: MIDAS score at the end of the study; * $p<0.05$)

Discussion

The results of this randomized-controlled clinical trial demonstrated that 12 sessions of acupuncture treatment, in addition to prophylaxis treatment, decreased attack frequency in migraine without aura patients. In addition, acupuncture treatment reduces the duration of attacks and pain severity that occurs during attacks and also improves the disability of the patients.

Acupuncture is widely used for the prevention and treatment of migraine attacks not only in China but also in western countries.¹⁵ Clinical studies have shown that Acupuncture as a non-pharmacological treatment is an effective and safe therapeutic method for migraine, at least as a pharmacological treatment.¹⁶ A Cochrane meta-analysis which included 4985 people and 22 studies, indicates that Acupuncture was found to be at least as effective as medication in reducing the frequency of headaches and the number of days that patients experienced migraine attacks and increased the effectiveness of pharmacological treatment.¹⁷ In another study that investigated the long-term effect of Acupuncture applied to migraine without aura; patients determined

that there was a significant decrease in the frequency of migraine attacks.¹⁸ In the present study, while the monthly attack frequency and duration of attacks were similar between the groups before the study, there was a significant decrease in the monthly attack frequency in IG compared to CG. Furthermore, there were observed no serious side effects after acupuncture treatment. The reduction in the frequency of attacks and the duration of pain may also be affected by to decrease in drug consumption. When the side effects and costs of current drug treatments are considered, the direct and indirect cost-effectiveness of Acupuncture as a safe non-pharmacological treatment option is also important in this respect.

Acupuncture is preferred in pain management in most pain clinics today. Approximately one million patients with pain syndrome receive Acupuncture annually in the United States.¹⁹ Studies have shown that patients with migraine have a reduction in pain severity with acupuncture treatment.²⁰ Wang et al. applied real and sham Acupuncture to 150 patients during migraine attacks, and pain severity was evaluated with VAS scores. The acupuncture group was superior to the sham acupuncture group in relieving pain and reducing acute drug usage.²¹ In our study, the severity of pain was measured with a VAS score at the beginning and at the third month. It was found that acupuncture treatment, in addition to prophylaxis treatment in migraine without aura patients, significantly decreased the severity of pain compared to only prophylaxis treatment. The gate control system, nociceptive afferent system and endorphin theories have been found to pain-reducing mechanisms of acupuncture treatment. Besides, our previous study conducted in migraine without aura patients demonstrated that Matrix Metalloproteinase-2 (MMP-2) enzyme activity, which is thought have a role in the pathophysiology of migraine, decreased after acupuncture treatment.⁹ Although there are different studies on the analgesic effect of Acupuncture, this mechanism has not been fully clarified yet. The underlying mechanisms of acupuncture treatment in reducing pain severity of migraine require further research.

According to 2017 Global Disease Burden study data, migraine is ranked as the first cause of neurological disorders and the second cause of general disorders in the ranking of years spent with disability in the population of all ages.²² Migraine attacks not only negatively affect the work and school performances of the patients but also cause a decrease in the quality of life in family and social activities.²³ The Irish Migraine Association reported that migraine affects the performance of the majority of young adults negatively at work or in education, and 39% of these effects are severe.²⁴ A study conducted in Delhi compared the effects of acupuncture treatment and conventional pharmacological treatment on the psychological profile of migraine patients based on the evaluation of disability parameters. The disability was measured with the MIDAS questionnaire. At the beginning of the study, the quality of life of migraine patients was low, and disability scores were high. At the end of the treatment, it was observed that the acupuncture group showed a better response and therefore was more effective than the pharmacological treatment. Therefore, it was concluded that Acupuncture is a better treatment option than traditional pharmacological treatment not only to relieve migraine pain but also to decrease disability scores of migraine patients.²⁵ Our findings are in line with all these

researches. In our study, a decrease of close to 80% in mean disability scores was observed after 12 sessions of acupuncture treatment, while it was only 30% in CG.

The severity of migraine can be assessed by determining the grade of disability. MIDAS is reported as easy to use and corresponds to judgments physicians make about disability.¹³ MIDAS is widely used to measure disability in three domains: work (school or for pay), household chores, and non-work activities in migraine patients associated with functionality in the last three months. The high grade of MIDAS causes loss of workforce, decrease in production and increase in treatment costs. In our study, there was moderate and severe disability in both groups according to the MIDAS grading system at the beginning. At the end of the study, while most of the patients in the IG had mild disabilities, only 2.5% had severe disabilities. On the contrary, nearly half of the patients in the CG had moderate disabilities, and more than half had a severe disability in the third month. The results of our study indicated that Acupuncture improves the disability status of migraine without aura patients. Reducing disability may also prevent the loss of the workforce.

There are several potential limitations of this clinical trial. Firstly, the sample size in each group was relatively small. Secondly, there was no sham acupuncture group. However, near acupuncture points can be triggered by sham acupuncture. For this reason, adding a sham group is not recommended by some authors.²⁶ On the other hand, this study demonstrated the effect of our acupuncture prescription on decreased migraine attack frequency and improved disability. Further research is needed to demonstrate how Acupuncture affects migraine attacks frequency and disability.

This study highlights the use of Acupuncture in addition to prophylaxis drugs for migraine without aura patients may optimize the clinical management of the patients. To further confirm this conclusion, additional larger and multicenter randomized-controlled trials with long-term follow-up would be appropriate to address the effectiveness of the acupuncture treatment and the validity of these findings.

Ethical Considerations: The study protocol was approved by the ethics committee of Atatürk University Faculty of Medicine (Date: 29.03.2018, Number: 3/31).

Conflict of Interest: The authors declare no conflict of interest. No financial assistance was obtained for this study.

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