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The effect of acupuncture in reducing the severity of migraine headaches: a randomized controlled clinical trial

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Abstract
Objective: The present study investigates the effect of acupuncture in reducing the severity of migraine headaches compared to the control group.
Methods: In this study, 121 people were selected by convenience sampling and randomly placed in two groups of acupuncture and control. Using a visual analog scale (VAS), data were collected in the pre-test, post-test, and follow-up stages and were analyzed using repeated analysis of variance statistical method.
Results: The results showed a significant difference between the two groups of acupuncture and control in the post-test and follow-up stages, compared to the pre-test, regarding the severity of headaches (P<0.05). However, no significant difference was found between the post-test and follow-up stages (P>0.05).
Conclusion: Based on the results of the present, acupuncture can reduce migraine headaches. However, more trials are needed, especially with long-term follow-up in the area.

Introduction

Migraine is considered a common disorder characterized by frequent headache attacks (1). It can be chronic or episodic (2, 3). Due to its adverse effects on the daily life and work of patients with migraine, it can disrupt people's work performance and reduce their quality of life, and impose much cost on the person and society (4, 5). In a study conducted to investigate the prevalence of migraine in Canada, France, Germany, Japan, England, and the United States, results showed that the prevalence of migraine was about 16% and the mean number of headaches in terms of days per month varied from 2.33 to 3.33 in different countries (6). The prevalence of this disease is higher in females and people with lower social and economic class (7). The mechanisms that cause migraine have not been clarified yet. However, it seems that genetic factors, epigenetic factors, inflammatory processes, and central sensitization can play a significant role in this regard (8). Acupuncture is a treatment that has become very popular in recent years due to the side effects of chemical drugs. Acupuncture has become more popular in Iran to reduce migraine headaches (9).

This method was derived from traditional medicine in China and has been used by traditional and complementary medicine physicians and specialists for more than 2500 years (10). Acupuncture entered Korea and Japan in the 6th century, entered Vietnam in the 8th to 10th centuries, was used in France in the 16th century, and was widely used in America and Britain in the 19th century (11). It can reduce acute and chronic pain in different parts of the body such as acute and chronic back pain (12-14), postoperative pain (15-17), dysmenorrhea (18-20), knee pain (21, 22), pain neck (23, 24), shoulder pain (25, 26), and headache (27, 28). Traditionally, 365 points are considered for acupuncture. In this method, the flow of Qi energy is modified by inserting needles into these points and manipulating them (29). Nowadays, this approach is challenged in the West and neural mechanisms are replacing it (11, 30).

The results of a systematic review in 2021 indicated that Precuneus, the right precentral gyrus, the left postcentral gyrus and the right parahippocampal gyrus, Precuneus, the right precentral gyrus, the left postcentral gyrus and the right parahippocampal gyrus, which are primarily located in the path of pain guidance and somatosensory cortex and are closely related to pain, were changed after acupuncture (31). However, studies have identified different brain areas for the effectiveness of acupuncture. This difference could be due to not using the same points for acupuncture, using different brain imaging methods, differences in the time of receiving neural images, and different treatment protocols for acupuncture. Chang et al. (2021) also recommended that researchers should emphasize the relationships between the functional connection networks of brain areas instead of focusing on one area of the brain (32).

Other mechanisms of acupuncture's analgesic effects include the release of adenosine triphosphate (ATP) (33) and increased degranulation of mast cells (34) in acupuncture points, regulation of neurotransmitters such as serotonin, norepinephrine, opioids, orexin, and endocannabinoids in the central nervous system (CNS) (35-37), reducing the levels of prostaglandin E2 (PGE2) and cyclooxygenase-2 (COX-2) through affecting the hypothalamic-pituitary-adrenal (HPA) axis at the peripheral level (38), inhibiting the sympathetic system (39), and modulating dopamine release in the nucleus accumbens (40) (41).

The results of animal studies indicate the effectiveness of acupuncture for migraines so a meta-analysis in 2023 that investigated 13 animal studies showed that acupuncture can improve the behavioral function of migraine rates and its mechanism. Its mechanism is probably through the inhibition of meningeal vasodilation and reduction of neuro-inflammation (42). A study conducted on human samples revealed that acupuncture can reduce migraine symptoms in patients and reduce the use of drugs in the short term and the long term (43). Another study revealed that acupuncture can play a role in reducing migraines through changes in people's lifestyles (44). Several systematic reviews and meta-analyses have indicated that acupuncture plays a role in improving migraine headaches (27, 31, 45-48). A study revealed that acupuncture is a cost-effective treatment in the UK and Germany for migraine headaches (49). Studies comparing acupuncture and Reich drugs have reported conflicting results. Some studies have indicated that acupuncture is more effective than conventional drugs (48, 50), while a systematic review revealed that these two treatments are equally effective (47). Several studies have reported the side effects of acupuncture for migraine at a low level (47, 48, and 51). There is no difference between different acupuncture methods in reducing migraine headaches (52). Also, there is no difference between 5-session and 10-session acupuncture treatment in preventing migraines, reducing headache severity, and improving quality of life (53). There is much evidence on the effectiveness of acupuncture in reducing migraine headaches. However, the results of some studies suggest that acupuncture is not different from sham acupuncture (54) and acupuncture could not reduce migraine headaches (55, 56).

Due to a lack of paying attention to the severity of the pain of people suffering from migraine headaches and its extensive effects on the personal, social, and professional life of these people and since it harms the family and social life of the person, it is necessary to take appropriate measures to reduce the severity of pain in these people. Due to conflicting different results reported by the studies conducted in this area and a few studies, especially in Iran, the present study investigated the effect of acupuncture in reducing migraine headaches.

Methods

Participants

The participants of the present study included all the people with migraines who were referred to the ... Clinic. Among them, 121 people were selected using convenience sampling and randomly placed in two groups acupuncture and waiting list. Diagram 1 shows the process of allocating them to experimental and control groups. The visual analog scale (VAS) was completed to measure headache intensity in the pre-test, post-test (4 weeks), and follow-up (4 months after the post-test) stages.

The inclusion criteria of this study were having reading and writing skills, a history of episodic or chronic migraine headaches diagnosed by a neurologist, reporting migraines at least 3 times a month, having an age between 20 and 50 years, no history of chronic psychological disorders such as anxiety and depression and acute and chronic physical diseases, no history of using acupuncture, no use of antipsychotic drugs, no participation in another clinical trial in the last six months, and informed consent to participate in the research. The exclusion criteria of the study were non-cooperation, unwillingness to continue participating in the study, and pregnancy during the study. Except for the use of sedative drugs, the use of any other drugs was not allowed during the study.

Tools

Visual Analog Scale (VAS)

This tool is a 100 mm ruler on which the participants determined the severity of their headaches. A score of 0 to 10 mm indicates no pain, a score of 10-20 mm indicates mild pain, a score of 20-50 mm indicates moderate pain, a score of 50-80 mm indicates severe pain and a score of 80-100 mm

indicates very severe pain (57). The summary intra-class correlation coefficient (ICC) for all paired VAS
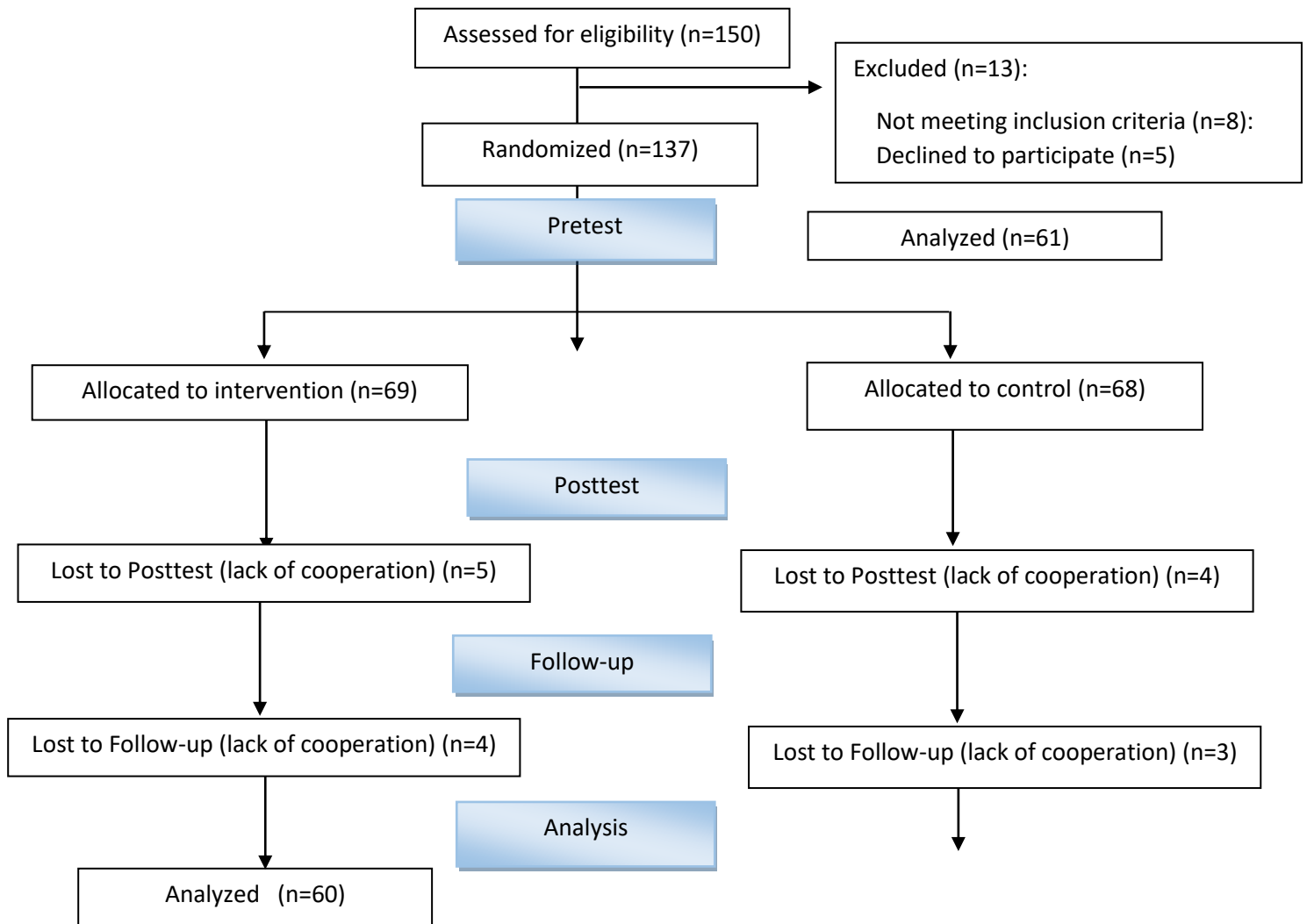
scores was 0.97 (58).

Assessed for eligibility (n=150)

Excluded (n=13):

  Not meeting inclusion criteria (n=8):
  Declined to participate (n=5)

Randomized (n=137)

Pretest

Analyzed (n=61)

Allocated to intervention (n=69)

Allocated to control (n=68)

Posttest

Lost to Posttest (lack of cooperation) (n=5)

Lost to Posttest (lack of cooperation) (n=4)

Follow-up

Lost to Follow-up (lack of cooperation) (n=4)

Lost to Follow-up (lack of cooperation) (n=3)

Analysis

Analyzed   (n=60)

Diagram 1: Randomly allocation of samples into experimental and control groups

Interventions
Acupuncture
To achieve a uniform protocol in studies to compare data, the treatment method of Jia et al.'s study (59) was used. This method is based on TCM theory. Accordingly, a headache point was selected according to the differentiation of meridians in the headache areas, which is as follows:

For temporary headaches or Shaoyang headaches, Zuqiaoyin (GB44) acupoint was selected. For posterior headache or Taiyang headache, Zhiyin (BL67) acupoint was selected. For the region of the forehead and the brow bone or Yangming headache, the Lidui (ST45) acupoint was selected. Table 1 shows a summary of them. Similar to Jia et al.'s

study, the needles used in this study were sterilized, disposable, and had a size of 25 mm x 0.25 mm, which were inserted 2 to 3 mm deep in the desired point, and it was twisted for about 5 seconds. Acupuncture treatment lasted 12 sessions (4 weeks, 3 sessions per week, and 30 minutes per session).

Control group
Sham acupuncture was not used as a placebo in the present study. Studies suggest that sham acupuncture can affect the results more than other controls (60, 61). Also, sham acupuncture can have physiological effects (60) and cause higher effects compared to non-treatment (62).

Table 1: Details of Acupoints of Acupuncture

	The headache region	Acupoint Selection	Location	Depth
acupuncture	Temporal headache (Shaoyang headache)	Zuqiaoyin (GB44)	On the lateral side of the fourth toe, about 0.1cun away from the corner of the nail	2–3mm
	Occipital headache (Taiyang headache)	Zhiyin (BL67)	On the lateral side of the little toe, 0.1cun lateral to the corner of the nail	
	Forehead headache (Yangming headache)	Lidui (ST45)	On the lateral side of the second toe, 0.1cun lateral to the corner of the nail	

To avoid the nocebo effect, the control group included migraine patients on the waiting list who could receive the desired treatment after completing the study.

Data analysis

Descriptive statistics including mean and standard deviation were used in this study. The Kolmogorov-Smirnov test was used to examine the normality of data distribution. After examining the normality of the data distribution, repeated analysis of variance. A significance level of $P<0.05$ was considered and these statistical methods were performed in SPSS-26 software.

Results

Based on the data shown in Tables 2 and 3, there is no statistically significant difference between the studied groups in the variables of sex, drug use, and age ($P>0.05$).

Table 2: Demographic information (chi-square tests)

variable	levels	group		Chi-Square	p
		control	Acupuncture		
Gender	Female	26	33	1.855	0.173
	male	35	27		
Medication	Not use	8	4	1.408	0.235
	Use of medicine	53	56		

Table 3- Results of Mann-Whitney U

	Age
Mann-Whitney U	1638.500
Wilcoxon W	3529.500
Z	-.993
Asymp. Sig. (2-tailed)	.321

Mean ± SD of the control and acupuncture groups were 54.98±16.24 and 55.26±16.56, respectively, in the pre-test, 50.78±18.48 and 41.76±41.76, respectively, in the post-test, and 50.40±18.91, 40.55±18.74, respectively, in follow-up. The results are summarized in Table 4.

Table 4: Descriptive statistics

	Group	Mean	Std. Deviation
Pretest	Control	54.9836	16.24858
	Acupuncture	55.2667	16.59269
Posttest	Control	50.7869	18.48613
	Acupuncture	41.7667	17.32185
Follow-up	Control	50.4098	18.91770
	Acupuncture	40.5500	18.74940

To use parametric statistics and the normality of data distribution, the Kolmogorov-Smirnov test was used. Table 5 presents a summary of the results.

Table 5: Kolmogorov-Smirnov

	Group	Kolmogorov-Smirnov		
		Statistic	df	Sig.
Pretest	Control	.049	61	.200
	Acupuncture	.058	60	.200
Posttest	Control	.073	61	.200
	Acupuncture	.070	60	.200

Follow-up	Control	.060	61	.200
	Acupuncture	.052	60	.200

The assumption of homogeneity of the covariance matrix

To examine the assumption of homogeneity of the covariance matrix, Box's M test was used, the results of which are reported in Table 6. As shown in this table, the obtained F is not significant at the $P<0.05$ level. Therefore, the assumption of homogeneity of the covariance matrix has been fulfilled. Thus, Pillai's Trace was used.

Table 6: Box's Test of Equality of Covariance Matrices

Box's M	10.651
F	1.727
df1	6
df2	102522.855
Sig.	.110

The assumption of the equality of error variance

Levene's test was used to examine the assumption of the equality of error variance. The results indicated that the error variance was equal in the research groups since the observed F was not significant at the $P<0.05$ level. Table 7 shows a summary of the results related to the assumption of equality of the error variance.

Table 7: Levene's Test of Equality of Error Variance

		Levene Statistic	df1	df2	Sig.
Pretest	Based on Mean	.011	1	119	.919
Posttest	Based on Mean	.190	1	119	.664
Follow-up	Based on Mean	.015	1	119	.902

The assumption of the equality of covariances

Mauchly's Test of Sphericity was used to examine the assumption of equality of covariances. The results showed that the assumption of equality of covariances has been fulfilled because the obtained F is not significant at the $P<0.05$ level. Therefore, the Sphericity Assumed test was used. Table 8 presents a summary of the results related to this assumption. Based on the results of Tables 6, 7, and 8, all three assumptions of repeated analysis of variance have been fulfilled. The results of Pillai's Trace test (Table 9) indicated that the null hypothesis is rejected and there is a significant difference between the acupuncture and control groups at different times at least in one case ($P<0.05$).

To further examine these results, they were reported in Tables 10 and 12. The results of the Sphericity Assumed test reported in Table 10 showed that the severity of pain at different pre-test, post-test, and follow-up were significantly different ($F=35.57$, $P<0.05$). Based on this table, the interaction effect of group and time is also significant ($F=9.83$, $P<0.05$). Hence, the headache scores of the participants of different groups changed differently in the pre-test, post-test, and follow-up stages. To identify these changes, the post-hoc LSD test was used. Table 11 shows the results of this test. It indicates that there is a significant difference between the headache severity scores of the participants in the pre-test compared to the post-test and follow-up stages ($P<0.05$). However, no significant difference was found between post-test and follow-up scores ($P>0.05$). Additionally, the results of Tests of Between-Subjects Effects, which are reported in Table 12, indicated that the severity of headache is different in the experimental and control groups ($F=4.64$, $P<0.05$). Chart 2 presents a summary of the above results.
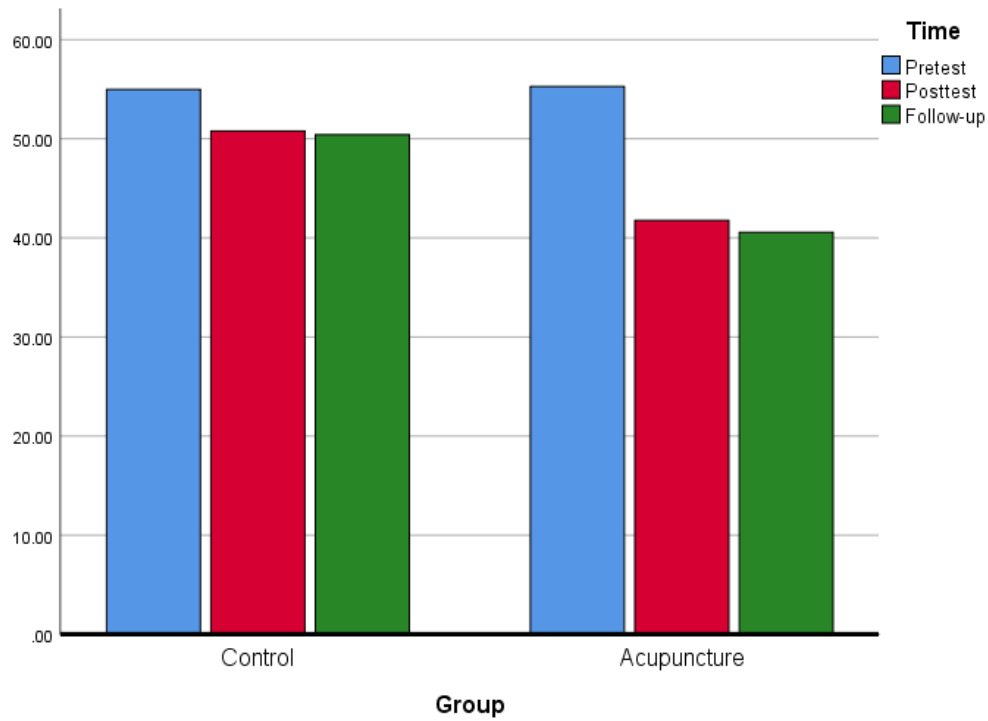
Figure 2: Interaction effect of group and time on headache severity

Table 8: Mauchly's Test of Sphericity

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
Time	.977	2.796	2	.247	.977	1.000	.500

Table 9: Multivariate Tests

Effect	Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
Time	.373	35.128	2.000	118.000	.000	.373
Time * Group	.141	9.710	2.000	118.000	.000	.141

Table 10: Tests of Within-Subjects Effects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Time	6935.194	2	3467.597	35.573	.000	.230
Time * Group	1917.057	2	958.528	9.833	.000	.076
Error(Time)	23200.084	238	97.479			

Table 11: Pairwise Comparisons

(I) Time	(J) Time	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Pretest	Posttest	8.848[*]	1.184	.000	6.504	11.193
	Follow-up	9.645[*]	1.352	.000	6.968	12.323
Posttest	Pretest	-8.848[*]	1.184	.000	-11.193	-6.504
	Follow-up	.797	1.266	.530	-1.711	3.304
Follow-up	Pretest	-9.645[*]	1.352	.000	-12.323	-6.968
	Posttest	-.797	1.266	.530	-3.304	1.711

[*]The mean difference is significant at the .05 level.

Table 12: Tests of Between-Subjects Effects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	870102.877	1	870102.877	1159.420	.000	.907
Group	3487.065	1	3487.065	4.647	.033	.038
Error	89305.200	119	750.464			

Discussion

The results of the present study showed that acupuncture can reduce the severity of migraine headaches of the participants compared to the control group. The results also showed that the severity of migraine headaches decreased significantly in the post-test and follow-up stages compared to the pre-test stages. However, no significant difference was observed between the post-test and the follow-up stages. Urits et al. (2020) indicated acupuncture is a safe, useful, and accessible alternative treatment for some migraine patients (27). The results of a study revealed that manual acupuncture can reduce headache days and migraine attacks compared to sham acupuncture (63). Another study also showed that acupuncture can reduce headache days and can be used as an adjunctive treatment in migraine prevention. Acupuncture also reduced medication use in the short and long term (43).

Another study also revealed that acupuncture was more effective in reducing migraine recurrence in the long term (20 weeks after treatment) compared to sham acupuncture or control (64). However, the results of a study in the first trimester after treatment showed that patients treated with real acupuncture compared to sham acupuncture had fewer migraine days and lower pain severity. The patient's pain threshold also increased. However, after one year of follow-up, these effects were lost (65). Supasiri et al. (2022) showed that groups with 5-session and 10-session treatment did not differ from each other in migraine prevention, headache severity, and improvement of quality of life (53). The results of other human studies also support the effectiveness of acupuncture (49, 51, 52, 66, and 67). A number of systematic reviews and meta-analyses also support this result (27, 46-48). The results of a meta-analysis in 2023 indicated that the right thalamus, the right insula, the left anterior cingulate, the right superior frontal gyrus, the right middle frontal gyrus, and the postcentral gyrus regions are involved in brain responses to acupuncture (45). A systematic review conducted on rats suffering from migraine also showed that acupuncture can reduce migraine in rats by inhibiting the dilation of meningeal vessels and reducing neuro-inflammation (42).

Despite much evidence about the effectiveness of acupuncture in reducing the severity of migraine, studies did not show the effectiveness of acupuncture compared to control groups. Linde et al. (2005) showed that real and fake acupuncture was more effective than the waiting group in reducing migraine headaches, which is in line with the present study. However, there was no statistically significant difference between real and fake acupuncture (54). Since the control group of the present study was on the waiting list and sham acupuncture was not used, we could compare the results in this field. However, as noted, sham acupuncture has physiological effects on patients and can have greater effects than untreated control groups (60, 62).

The study by Farahmand et al. (56) can also be explained by the same mechanism. Lavies et al. (1998) investigated 12 patients with chronic migraine and showed that laser acupuncture compared to placebo (dummy laser acupuncture) does not significantly affect the patients' migraine (55). This inconsistency of results can be attributed to the different treatment methods used in these two studies. The present study suffered some limitations. The use of a convenience sampling method and access to only one Clinic (Masih Clinic) in Tehran can affect the generalizability of the data. Also, since the study with a one-year follow-up showed that the effects of real acupuncture compared to sham acupuncture were lost in the one-year follow-up (65), it is recommended to use long follow-ups in future studies for other control groups such as the waiting list.

Conclusion

The results of this study revealed that acupuncture can significantly reduce migraine headaches compared to the control group, so the scores of the patients decreased significantly in the post-test and follow-up stages compared to the pre-test stage. However, no significant was found between the post-test and the follow-up stages.

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