Journal of Scientific and Technology Research (TUBITTUM)
Volume 4 Issue 2, 2025, pp: 44-64 www. Tubittumjournal.com ISSN: 2822-5295

Effects of Progressive Muscle Relaxation (PMR) on Reducing Migraine Headaches; A Randomized Clinical Trial

***Samaneh Mollaei* [*1], *Abolfazl Moradi*[2], *Mojtaba Valizadegan Arjomand*[3] *Faezeh Dorisefat,*[4]**

[1*] *Doctorate in Naturopathic Medicine, Technofest Institute of Technology University (TITU), Erquelinnes, Belgium*
[2] *Assistant Professor, Department of Naturopathic Medicine, Technofest Institute of Technology, Erquolinnes, Belgium*
[3] *Doctorate in Naturopathic Medicine, Technofest Institute of Technology University (TITU), Erquelinnes, Belgium. Orcid number: 0009-0002-6559-1107*
[4] *Doctorate in Naturopathic Medicine, Technofest Institute of Technology University (TITU), Erquelinnes, Belgium*

Received 08/05/2025 **Accepted** 09/06/2025

Abstract

Introduction: The present study aimed to investigate the effects of relaxation on mitigating the severity of headaches in migraine patients.

Method: The number of 126 people were selected through convenience sampling and randomly assigned to two experimental and control groups. Visual Analogue Scale (VAS) was used to measure the severity of headaches in pre-test, post-test and follow-up stages. Data were analyzed by SPSS-26 software.

Results: Data analysis indicated that age, gender and taking pills in the pretest did not show a significant difference in the two groups ($P>0.05$). However, PMR significantly reduced severe headache scores in the experimental group in post-test and follow-up stages compared to the control group ($P<0.05$).

Conclusion: Findings indicated that PMR is an effective treatment to relieve the severity of migraine in sufferers; however, it is required to perform more clinical trials in this connection.

Keywords: migraine, headaches, progressive muscle relaxation (PMR)

Journal of Scientific and Technology Research (TUBITTUM)
Volume 4 Issue 2, 2025, pp: 44-64 www. Tubittumjournal.com ISSN: 2822-5295

Introduction

Migraine is a frequently recurring chronic disturbance with mild to severe headaches, which is sometimes associated with aura signs, sensitivity to auditory and olfactory stimuli, nausea and vomiting [1-6]. Migraine is one of the leading causes of inability in females, which can negatively affect economic conditions [7]. This disease also puts much medical costs on people and society [8]. A study has shown that the prevalence of migraine with and without aura was close to 7 and 2%, respectively. In the meantime, 67% of people have experienced headaches at least once during their lives [9]. A review of 19 studies reported the prevalence of definite and possible migraines to be 11.5 and 7%, respectively [10]. The prevalence of migraine in women and people with low social-economic situation was also reported to be higher [11]. Findings of a study suggested that neurologists report migraine headaches to be 2-3 times more than other headaches, which indicates peoples' unawareness of this disease [12]. Migraines are associated with unhealthy lifestyles such smoking [13], medical and psychiatric diseases such as thyroid [14,15] and depression [16] and pain-related diseases such as fibromyalgia [17] [18]. Other factors such as ineffective and unreliable acute migraine treatments, obesity, depression and stressful events can turn acute migraines into chronic ones [3]. Findings of a 2016 study that examined genes identified from prior study indicated that none of the 27 candidate genes were statistically significant [3]. A review of FMRI studies on migraines demonstrated that the brain's unusual activation in response to unusual painful, olfactory, visual and functional connectivity stimuli occur in people with migraines. Evidence suggests that people with prolonged history of migraine have their brain functioning subjected to cumulative migraine effects, as underlying abnormalities may also relate to severe migraine risks [20]. A review study in 2022 used FMRI to demonstrate that migraines strike by stimulating the hypothalamus and reorganizing ascending pain and trigeminovascular pathways. However, in the headache phase, hypothalamic connectivity is normalized but pontine and thalamic, sensory-motor as well as visual networks are disrupted. In the postdromal phase, the activity of the visual cortex remains hyperexcitable [21]. In another systematic review of 2022, structures such as insula, brainstem, limbic system, hypothalamus, thalamus and functional networks are involved in migraines [22]. The differences in the findings suggests that we have not yet understood the etiology of migraines and more studies in this connection are warranted.

Migraine treatments vary in different people, with 49%, 23% and 23% of sufferers using over-the-counter medications, prescribed medications, and prescribed and non-prescribed medications, respectively, while 5% do not receive any medications [23]. Common medications for migraines consist in: NSAID, Triptans, Gepants and Iasmiditan for acute migraines and onabotulinumtoxinA medications for chronic migraines [1,24-29]. Despite their desirable effects on migraines, these medications produce some mild-to-severe complications, prompting sufferers to replace them with therapeutic alternatives such as relaxation [30, 31], sports exercises [32,33), psychological treatments [34,35], non-invasive neuromodulation therapies [36,37] and acupuncture [38,40].

Relaxation refers to a non-pharmacological intervention to treat stress caused by chronic diseases or diseases with side effects; these exercises are also used to mitigate pains, anxiety and depression [41-43]. Relaxation treatments involve different types, including PMR [44], deep breathing exercise [45], and guided imagery [46]. PMR, first developed by Edmund Jacobson in the 1920s [47] and used to treat migraine in the 1970s [48], is a technique by which the individual acquires a sense of relief and comfort by way of active contraction and then relaxing specific muscular groups in a progressive state [49]. Theoretically, PMR follows the bottom-up and top-down neural processing principles [50,51], as pain and anxiety are associated with the increased activation of the autonomic system, thus facilitating and deteriorating arousal, emotional stress and physical signs [52]. In the top-down processing, PMR activates cortical regions for muscle contraction, while in the bottom-up processing, it stimulates the proprioception of peripheral muscles by tightening and relaxing the tension, thus ascending from the spinal cord to the brainstem and then to the brain; when both pathways are activated by PMR, pain is immediately mitigated [50]. In general, PMR appears to mitigate pain and anxiety in people by inhibiting the sympathetic system and activating the parasympathetic system, especially through the vagus nerve [52]. Anxiety is related to migraines and PMR can reduce migraine-caused headaches by reducing anxiety, especially the physical signs of anxiety [53]. This therapeutic method affects the body physiology by reducing glucose [54,55], reducing heart rates [56,57], changing brain waves [58,59], and blood pressure [60,61]. An FMRI study also investigated PMR effects, finding that the technique could potentially reduce brain activities, especially in superior frontal gyrus (SFG), inferior frontal gyrus (IFG), and posterior cingulate cortex (PCC) regions [62].

Studies that have investigated the effects of relaxation on migraines have generally confirmed the efficacy of this technique [44,49, 63-66]. However, most studies in this

connection date back to the 1990s [67-69], while after a period of hiatus in research on migraines and PMR, the years 2000 to 2020 saw a renewed interest in this area [30, 63, 70-72]. On the one hand, the rising interest pertained to the combination of PMR with other treatments and the comparison of them with control groups, as PMR was less focused on [71, 72]. Despite the desirable effects of PMR on mitigating migraine headaches, some studies have reported different results. Klan et al. demonstrated that migraine patients with inability or low anxiety can use PMR if there are no comorbid signs [70]. In another study, smartphone-related PMR was shown to reduce migraine-induced inability, though this reduction was not significant [30]. Fewer English systematic reviews and metanalyses in recent years indicate the lack of high-quality clinical trials in this regard. Thus, the goal of the present study was to investigate the effects of PMR on reliving migraine headaches between experimental and control groups.

Method

Study Method

This study was a randomized clinical trial study with an experimental and a control group at three pretest, posttest and follow-up stages.

Statistical Population

The statistical population of this study consisted of all migraine patients presenting to the Masiha Clinic in Tehran in 2023.

Samples and Sampling Procedure

The present study consisted of 126 subjects, who were elected using convenience sampling and randomly assigned to two PMR (n=65) and control (n=61) groups. Inclusion criteria were: having the literacy of reading and writing, a history of episodic or chronic migraine as diagnosed by a neurologist, a report of migraine for at least three times a month, aged between 20-50 years, no history of chronic psychological disorders such as anxiety and depression and no acute and chronic physical diseases, treatment with PMR, no use of antipsychotic drugs, no participation in another clinical trial in the past six months and informed consent to attend the study; meanwhile, exclusion criteria were failure to cooperate, unwillingness to continue the study and pregnancy during the study. Also, no other drugs except for mitigating medications were allowed in the course of study.

Journal of Scientific and Technology Research (TUBITTUM)
Volume 4 Issue 2, 2025, pp: 44-64 www. Tubittumjournal.com ISSN: 2822-5295

Tools

Visual Analogue Scale (VAS)

To examine pain, the Visual Analogue Scale (VAS) tool was used, which is a straight horizontal line of 100 mm. The individual marks the amount of pain he feels most of the time on this line, with scores 0-10 mm indicating no pain, 10-20 mm low pain, 20-50 medium pain, 50-80 severe pain and 80-100 very severe [73].

The summary Intraclass correlation coefficients (ICC) for all paired VAS scores was 0.97 (74).

Interventions

Progressive Muscle Relaxation Group

The PMR therapy was carried out for three times of a week of 15 minutes each for four weeks. To exercise the PMR, the muscles of hands, arms, the head and facial parts, the neck, shoulders, the spinal cord, the chest, the abdomen and leg parts were respectively contracted for nearly 5 seconds and then relaxed for 15 to 30 seconds. Also, a video clip, downloaded from the Greenolive.ir channel of the Aparat Site, was provided to participants to exercise at home. The following tips were explained to the subjects to properly exercise PMR:

1. Breath when contracting and relaxing muscles normally, and hold no breath.
2. When you contract and relax the muscles, you feel the difference between these two practices. If you feel nothing initially, then you will feel this difference after a while.
3. When you tense the muscles, focus on them, which affects the body and gradually relaxes the muscles.
4. Repeat the exercise for each muscular group twice.

Control Group

Placing people in no-treatment groups could cause nocebo effects in which the control group has a worsening feeling due to the lack of drugs or treatments they tend to receive [75]. For this, the control group of the present study included the people on the waiting list, who after the end of the study managed to receive their favorable drugs.

Journal of Scientific and Technology Research (TUBITTUM)
Volume 4 Issue 2, 2025, pp: 44-64 www. Tubittumjournal.com ISSN: 2822-5295

Administration Procedure

As many as 149 people at a Tehran's Clinic were selected via convenience sampling and were randomly assigned to two PMR and control groups after meeting inclusion and exclusion criteria. After some of the subjects withdrew in the posttest and follow-up stages, the number of 126 people were analyzed. A summary of participant assignment from the beginning of the study to the follow-up stages is illustrated in Diagram 2.1. Prior to the pre-stage, the subjects filled in the informed consent form, while completing the VAS tool in the post-stage. The PMR therapy was administered for three times of a week of 15 minutes each for four weeks. The control group, which included the people on the waiting list, could receive their desired drugs after the study ended. VAS in the post-test and follow-up stages (four months after the post-stage) was repeated, and data were statistically analyzed by SPPS-26.

Data Analysis

This study used descriptive statistics such as mean and standard deviation. Also, Kolmogorov-Smirnov test was used to determine the normality of data distribution. After examining the normality of data, the repeated measures ANOVA was used for data analysis. The significance level was considered to be $P<0.05$, and this statistical method was performed by the SPPS-26 software.

Results

The chi-square result from comparing frequencies in the two control and PMR groups in two men and women classes was 1.59, which was not statistically significant ($P =0.69$). Therefore, the two groups under study did not have a significant difference based on gender. Also, chi-square from comparing the frequencies of the two control and PMR groups in the two no drug use and drug use classes was 1.77, which was not statistically significant ($P =0.183$). Thus, the two groups under study were not significantly different in terms of drug use for relieving headache severity. A summary of the results is given in Table 1. Also, the Mann-Whitney U test findings, as given in Table 2, suggest that there is no significant difference of age between the studied groups. The mean and standard deviation of the subjects' age were 33.627±8.53. Meanwhile, the mean ± SD of control and PMR groups in the pretest were 54.98±16.24 and 56.53±16.95, in the post stage

Journal of Scientific and Technology Research (TUBITTUM)
Volume 4 Issue 2, 2025, pp: 44-64 www. Tubittumjournal.com ISSN: 2822-5295

50.78±18.48 and 40.10±18.24 and in the follow-up stage 50.40±18.91 and 39.38±18.20, respectively. Table 3 gives the results.

Table 1: Demographic data (Chi-square tests)

Variable	levels	Group		Chi-Square	P
		Control	PMR		
Gender	Female	26	30	1.59	0.690
	male	35	35		
Medication	No use	8	4	1.77	0.183
	Use of medication	53	61		

Table 2: Mann-Whitney U test results

	Age
Mann-Whitney U	1785.000
Wilcoxon W	3930.000
Z	-.965
Asymp. Sig. (2-tailed)	.335

Table 3: Descriptive statistics

	Group	Mean	Std. Deviation
Pretest	Control	54.9836	16.24858
	PMR	56.5385	16.95497
Posttest	Control	50.7869	18.48613
	PMR	40.1077	18.24154
Follow-up	Control	50.4098	18.91770
	PMR	39.3846	18.20945

Journal of Scientific and Technology Research (TUBITTUM)
Volume 4 Issue 2, 2025, pp: 44-64 www. Tubittumjournal.com ISSN: 2822-5295

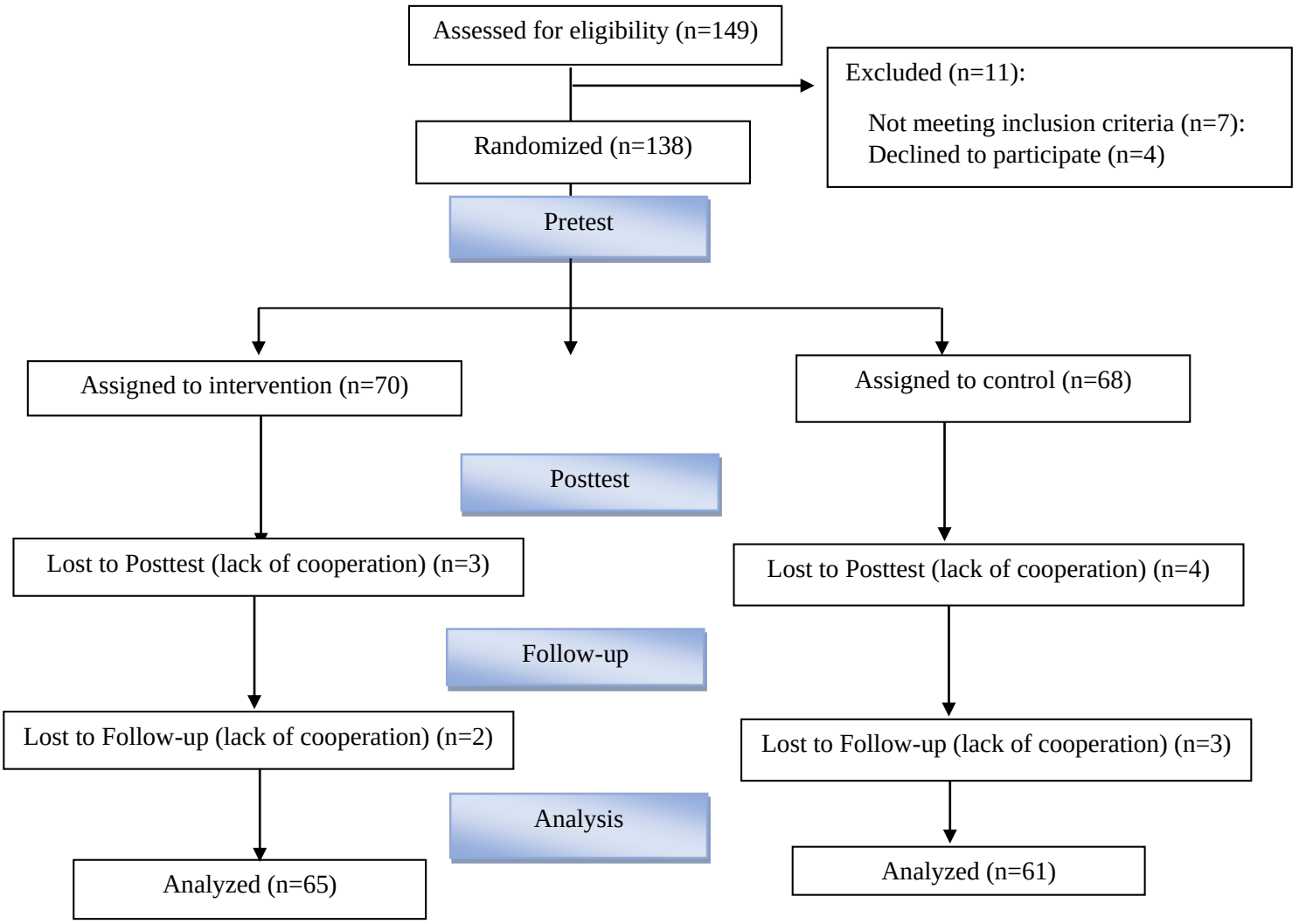


Diagram 1: Random assignment of the samples in experimental and control groups

The Assumption of Homogeneity of Covariance Matrix

To examine the assumption of the homogeneity of covariance matrix, the Box's M Test was used, as seen in Table 4. F in this table is not significant at $P < 0.05$; thus, the assumption is satisfied. For this the Pillai's trace is used.

Journal of Scientific and Technology Research (TUBITTUM)
Volume 4 Issue 2, 2025, pp: 44-64 www. Tubittumjournal.com ISSN: 2822-5295

Table 4: Box's Test of Equality of Covariance Matrices

Box's M	6.366
F	1.033
df1	6
df2	110172.702
Sig.	.401

Assumption of Homogeneity of Error Variance

Levene's test was used to examine the homogeneity of error variance assumption. Results indicated that error variance in the studied groups was homogenous, because the observed F was not significant at P <0.05. A summary of results of the homogeneity of error variance assumption is given in Table 5.

Table 5: Levene's Test of Equality of Error Variances

		Levene's Statistic	**df1**	**df2**	**Sig.**
Pretest	**Based on Mean**	.120	1	124	.729
Posttest	**Based on Mean**	.007	1	124	.933
Follow-up	**Based on Mean**	.001	1	124	.969

Equality of Covariances Assumption

Mauchly's Test of Sphericity was used to examine the assumption of the equality of covariances. Results indicated that the assumption of the equality of covariances had been satisfied because the F obtained at P<0.05 was not significant. Thus, the Sphericity Assumed Test was used. A summary of the assumption results is given Table 6. According to Tables 4, 5 and 6, all three assumptions of repeated measures ANOVA had been satisfied. Table 7 gives Pillai's Traces and shows that the assumption is rejected and there is at least a significant difference between different groups at different times (P <0.05). Tables 8 and 10 are also provided to better examine the results. Results from the Sphericity Assumed Test, given in Table 8, suggested that pain severity at different times of the

Journal of Scientific and Technology Research (TUBITTUM)
Volume 4 Issue 2, 2025, pp: 44-64 www. Tubittumjournal.com ISSN: 2822-5295

pretest, posttest and follow-up stages was not significantly different (F=50.80, P <0.05). This table also shows that the interactive effect of the group and time is significant (F=17.41, P <0.05), as subjects' migraine pain severity scores in various groups have significantly changed at pre-test, post-test and follow-up stages. An LSD post Hoc Test was used to determine these changes, as given in Table 9. Accordingly, there is a significant difference between subjects' migraine pain severity scores in the pretest compared to the posttest and follow-up stages (P <0.05). However, there is no significant difference between posttests and follow-up scores (P >0.05). Also, the results of the Between-Subjects Effects Test, given in Table 10, indicates that the severity of pain was significantly different in various experimental and control groups (F=5.51, P<0.05). A summary of above results is given in Tables 2,3 and 4.

Table 6: Mauchly's Test of Sphericity

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	Df	Sig.	Epsilon		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
Time	.954	5.739	2	.057	.956	.979	.500

Table 7: Multivariate Tests

Effect	Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
Time	.460	52.313	2.000	123.000	.000	.460
Time * Group	.227	18.090	2.000	123.000	.000	.227

Table 8: Tests of Within-Subjects Effects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Time	9427.815	2	4713.908	50.809	.000	.291
Time * Group	3231.265	2	1615.632	17.414	.000	.123
Error (Time)	23008.768	248	92.777			

Journal of Scientific and Technology Research (TUBITTUM)
Volume 4 Issue 2, 2025, pp: 44-64 www. Tubittumjournal.com ISSN: 2822-5295

Table 9: Pairwise Comparisons

(I) Time	(J) Time	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Pretest	Posttest	10.314*	1.093	.000	8.150	12.477
	Follow-up	10.864*	1.319	.000	8.254	13.474
Posttest	Pretest	-10.314*	1.093	.000	-12.477	-8.150
	Follow-up	.550	1.220	.653	-1.865	2.965
Follow-up	Pretest	-10.864*	1.319	.000	-13.474	-8.254
	Posttest	-.550	1.220	.653	-2.965	1.865

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

Table 10: Tests of Between-Subjects Effects

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	895663.346	1	895663.346	1160.222	.000	.903
Group	4258.753	1	4258.753	5.517	.020	.043
Error	95724.985	124	771.976			

Journal of Scientific and Technology Research (TUBITTUM)
Volume 4 Issue 2, 2025, pp: 44-64 www. Tubittumjournal.com ISSN: 2822-5295

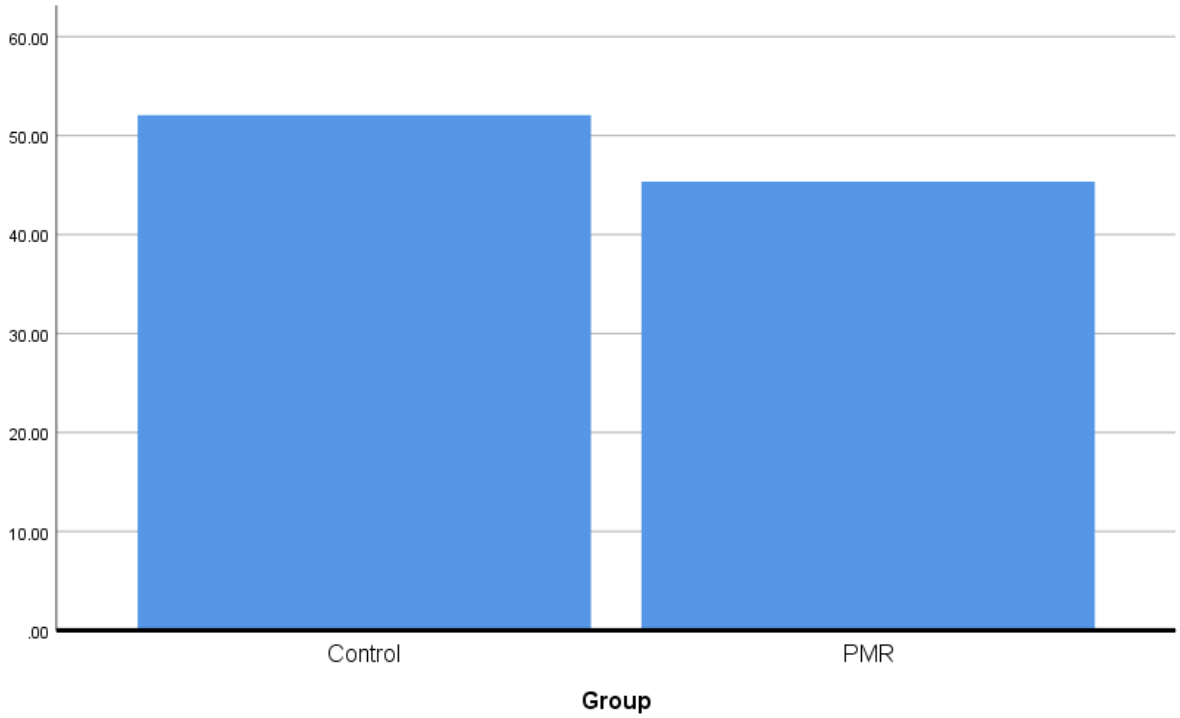
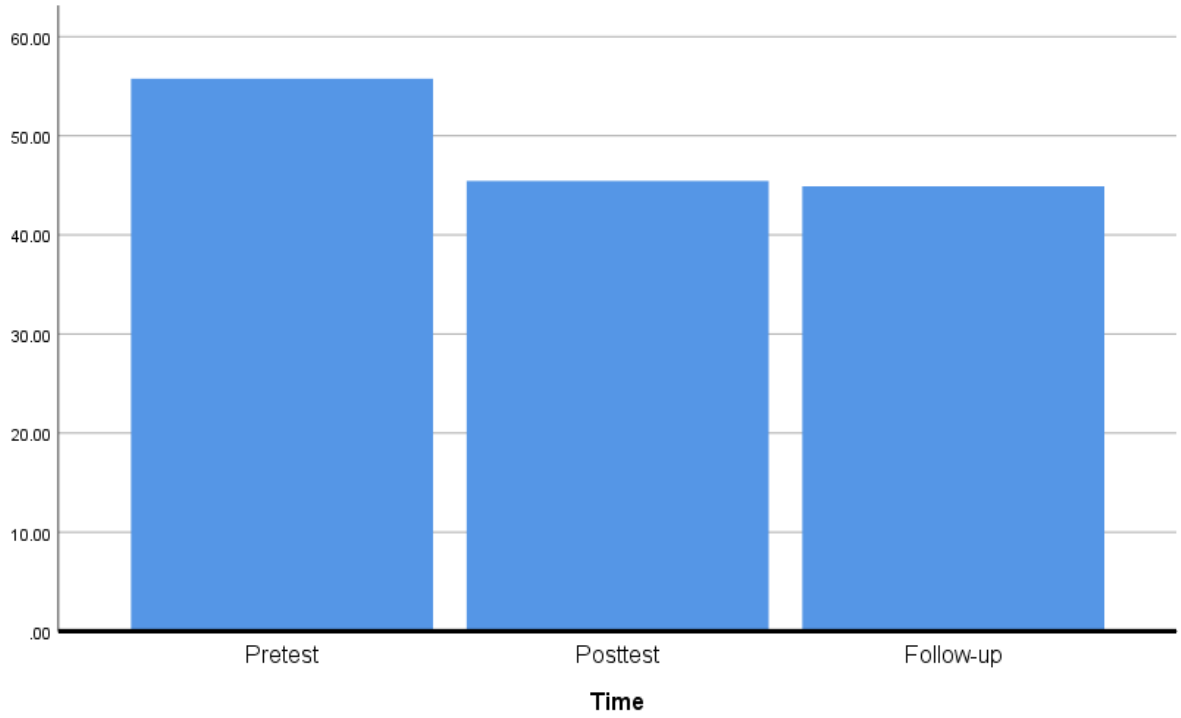


Diagram 2: Differences in headache severity changes in the experimental and control groups



Journal of Scientific and Technology Research (TUBITTUM)
Volume 4 Issue 2, 2025, pp: 44-64 www. Tubittumjournal.com ISSN: 2822-5295

Diagram 3: Headache severity changes in the pretest, posttest and follow-up

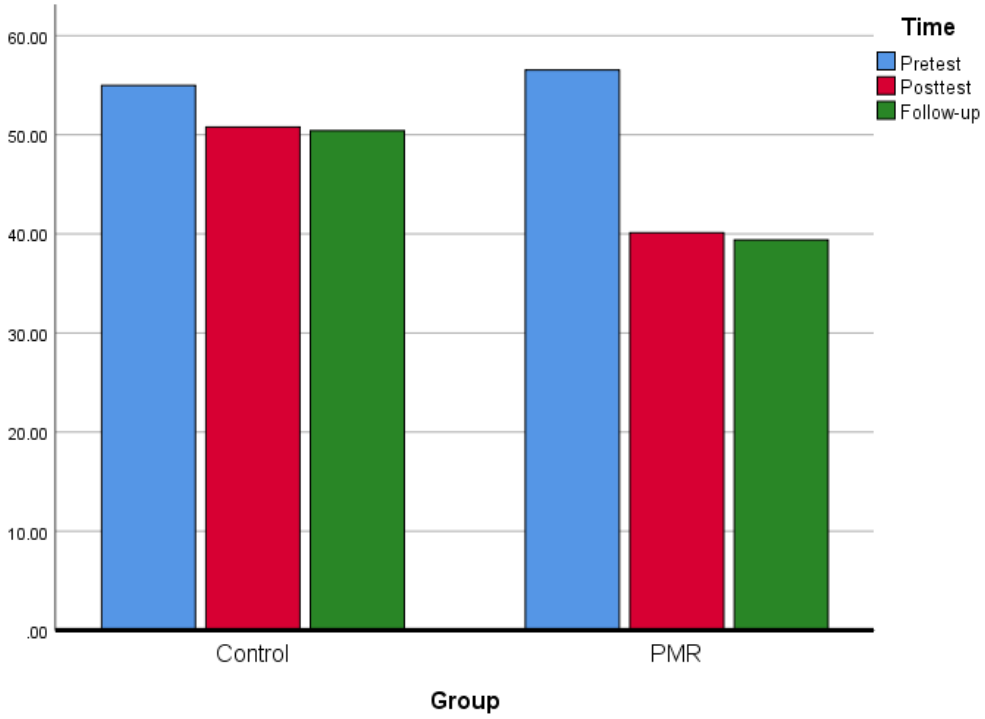


Diagram 4: Interactive Effects of group and time in headache severity

Discussion

The findings of the first hypothesis indicated that PMR could relieve the migraine headaches of the subjects compared to the control group. It was also found that the severity of migraine headaches in posttest and follow-up stages saw a significant relief compared to the pretest. However, there was no significant difference between posttest and follow-up stages.

The findings of the presents study were consistent with those of Khah et al. (2020), who demonstrated that relaxation therapy could relive headaches in migraine patients [49]. In another study, PMR was found to create lower migraine frequencies in patients, suggesting that the PMR neural mechanism could be possibly carried out through serotonin metabolism [44]. Varkey et al. (2011) also argued that PMR was as effective as sports exercises and topiramate in migraine prevention [64]. Another study that compared relaxation exercises with Written Emotional Disclosure (WED) and a control group indicated that relaxation exercises resulted in greater recovery both in terms of headaches

attacks and inability compared to the control group [65]. Another study showed that relaxation exercises could reduce long-term migraine headaches and helped take fewer medications, thus reducing secondary effects such as depression and external stress [69]. It was also demonstrated in another study that compared to biofeedback, relaxation could reduce headaches in migraine sufferers [67]. The results of a review study indicated that relaxation, together with pharmacological treatments, could help sufferers recover from the disease [63]. Today, interest in combining relaxation and other treatments is on the rise. Another study also examined the effects of combining the intervention of education and relaxation (GIER) with remote electrical neuromodulation (REN) to show that the combination of these two therapies could reduce headaches and help return to the normal functioning [72]. In another study, it was found that the combination of aerobic sports, migraine-prevention drugs and relaxation were found to be more effective in treating migraine than migraine-prevention drugs alone [71]. Dittrich et al. (2008) demonstrated that combining aerobic exercises, music and PMR could relieve migraine headaches and depression signs compared to the depression group [66]. Although the findings of the cited research have been consistent with those of the presents study, there are also some studies that are inconsistent with the preset study [30, 70]. Klan et al. (2003) investigated cognitive-behavioral therapies and relaxation treatments, arguing that cognitive behavioral treatments were more effective for migraine sufferers who had higher levels of anxiety and inability and another mental disorder; while relaxation worked more effectively for migraine people who had low levels of inability and anxiety and no other mental disorder work [70]. This finding is partly inconsistent with those of the present study, because the present study demonstrated that PMR could significantly reduce pain severity at different time intervals. Thus, interventional and research methods are said to justify these differences. The present study investigated the severity of migraine headaches; however, in Klan's study, inability, anxiety, headache days and mental disorders were investigated. Minen et al. (2020) showed that smartphone-delivered PMR could insignificantly reduce Migraine Disability Assessment Scale (MIDAS) scores [30]. This justifies the use of various interventions and various measuring scales, which make it difficult to compare these studies.

Limitations

The main limitation of the study was the use of convenience sampling that can affect the generalization of the findings. Future research is proposed to use random sampling methods. Other limitations included the use of a measurement scale to measure headache severity, and for this, future studies are suggested to not only use VAS but also to use other tools such as headache days and Life Quality Questionnaires to check for the secondary outcomes of migraine headaches.

Conclusion

Findings revealed that PMR reduced the severity of migraine headaches as compared to the control group; meanwhile, subjects' scores had significantly decreased in and posttest and follow-up stages compared to the pretest and no significant difference was noted between posttest and follow-up stages.

References

1. Ferrari MD, Goadsby PJ, Burstein R, Kurth T, Ayata C, Charles A, et al. Migraine. Nature reviews Disease primers. 2022;8(1).
2. Hansen JM, Charles A. Differences in treatment response between migraine with aura and migraine without aura: lessons from clinical practice and RCTs. The journal of headache and pain. 2019;20(1):1-10.
3. May A, Schulte LH. Chronic migraine: risk factors, mechanisms and treatment. Nature Reviews Neurology. 2016;12(8):455-64.
4. Sjöstrand C, Savic I, Laudon-Meyer E, Hillert L, Lodin K, Waldenlind E. Migraine and olfactory stimuli. Current pain and headache reports. 2010;14:244-51.
5. Demarquay G, Caclin A, Brudon F, Fischer C, Morlet D. Exacerbated attention orienting to auditory stimulation in migraine patients. Clinical neurophysiology. 2011;122(9):1755-63.
6. Chan TLH, Cowan RP, Woldeamanuel YW. Calcitonin Gene-Related Peptide Receptor Antagonists (Gepants) for the Acute Treatment of Nausea in Episodic Migraine: A Systematic Review and Meta-Analysis. Headache: The Journal of Head and Face Pain. 2020;60(7):1489-99.
7. Ashina M, Katsarava Z, Do TP, Buse DC, Pozo-Rosich P, Özge A, et al. Migraine: epidemiology and systems of care. The Lancet. 2021;397(10283):1485-95.
8. Schwedt TJ. Chronic migraine. Bmj. 2014;348.

9. Bank J, Marton S. Hungarian migraine epidemiology. Headache: The Journal of Head and Face Pain. 2000;40(2):164-9.
10. Merikangas KR. Contributions of epidemiology to our understanding of migraine. Headache: The Journal of Head and Face Pain. 2013;53(2):230-46.
11. Lipton RB, Bigal ME. Migraine: epidemiology, impact, and risk factors for progression. Headache: The Journal of Head and Face Pain. 2005;45:S3-S13.
12. Yeh WZ, Blizzard L, Taylor BV. What is the actual prevalence of migraine? Brain and behavior. 2018;8(6):e00950.
13. López-Mesonero L, Márquez S, Parra P, Gámez-Leyva G, Munoz P, Pascual J. Smoking as a precipitating factor for migraine: a survey in medical students. The journal of headache and pain. 2009;10(2):101-3.
14. Spanou I, Bougea A, Liakakis G, Rizonaki K, Anagnostou E, Duntas L, et al. Relationship of migraine and tension-type headache with hypothyroidism: a literature review. Headache: The Journal of Head and Face Pain. 2019;59(8):1174-86.
15. Tasnim S, Wilson SG, Walsh JP, Nyholt DR, Consortium IHG. Shared genetics and causal relationships between migraine and thyroid function traits. Cephalalgia. 2023;43(2):03331024221139253.
16. Zhang Q, Shao A, Jiang Z, Tsai H, Liu W. The exploration of mechanisms of comorbidity between migraine and depression. Journal of cellular and molecular medicine. 2019;23(7):4505-13.
17. Giamberardino MA, Affaitati G, Martelletti P, Tana C, Negro A, Lapenna D, et al. Impact of migraine on fibromyalgia symptoms. The journal of headache and pain. 2016;17:1-9.
18. Yin JH, Lin YK, Yang CP, Liang CS, Lee JT, Lee MS, et al. Prevalence and association of lifestyle and medical-, psychiatric-, and pain-related comorbidities in patients with migraine: A cross-sectional study. Headache: The Journal of Head and Face Pain. 2021;61(5):715-26.
19. de Vries B, Anttila V, Freilinger T, Wessman M, Kaunisto MA, Kallela M, et al. Systematic re-evaluation of genes from candidate gene association studies in migraine using a large genome-wide association data set. Cephalalgia. 2016;36(7):604-14.
20. Schwedt TJ, Chiang C-C, Chong CD, Dodick DW. Functional MRI of migraine. The Lancet Neurology. 2015;14(1):81-91.
21. Messina R, Gollion C, Christensen RH, Amin FM. Functional MRI in migraine. Current Opinion in Neurology. 2022;35(3):328-35.

22. Schramm S, Börner C, Reichert M, Baum T, Zimmer C, Heinen F, et al. Functional magnetic resonance imaging in migraine: A systematic review. Cephalalgia. 2023;43(2):03331024221128278.
23. Lipton RB, Scher A, Kolodner K, Liberman J, Steiner T, Stewart W. Migraine in the United States: epidemiology and patterns of health care use. Neurology. 2002;58(6):885-94.
24. Becker WJ. Acute migraine treatment. Continuum: Lifelong Learning in Neurology. 2015;21(4):953-72.
25. Pardutz A, Schoenen J. NSAIDs in the acute treatment of migraine: a review of clinical and experimental data. Pharmaceuticals. 2010;3(6):1966-87.
26. Johnston MM, Rapoport AM. Triptans for the management of migraine. Drugs. 2010;70:1505-18.
27. Negro A, Martelletti P. Gepants for the treatment of migraine. Expert opinion on investigational drugs. 2019;28(6):555-67.
28. Capi M, de Andrés F, Lionetto L, Gentile G, Cipolla F, Negro A, et al. Lasmiditan for the treatment of migraine. Expert opinion on investigational drugs. 2017;26(2):227-34.
29. Burstein R, Blumenfeld AM, Silberstein SD, Manack Adams A, Brin MF. Mechanism of action of onabotulinumtoxinA in chronic migraine: a narrative review. Headache: The Journal of Head and Face Pain. 2020;60(7):1259-72.
30. Minen MT, Adhikari S, Padikkala J, Tasneem S, Bagheri A, Goldberg E, et al. Smartphone-delivered progressive muscle relaxation for the treatment of migraine in primary care: a randomized controlled trial. Headache: The Journal of Head and Face Pain. 2020;60(10):2232-46.
31. Meyer B, Keller A, Müller B, Wöhlbier H-G, Kropp P. Progressive muscle relaxation according to Jacobson for migraine prophylaxis: Clinical effectiveness and mode of action. Manuelle Medizin. 2019;57:91-9.
32. La Touche R, Fernandez Perez JJ, Proy Acosta A, Gonzalez Campodonico L, Martinez Garcia S, Adraos Juarez D, et al. Is aerobic exercise helpful in patients with migraine? A systematic review and meta-analysis. Scandinavian journal of medicine & science in sports. 2020;30(6):965-82.
33. Song T-J, Chu MK. Exercise in treatment of migraine including chronic migraine. Current Pain and Headache Reports. 2021;25:1-11.
34. Bae J-y, Sung H-K, Kwon N-Y, Go H-Y, Kim T-j, Shin S-M, et al. Cognitive behavioral therapy for migraine headache: a systematic review and meta-analysis. Medicina. 2022;58(1):44.

35. Dudeney J, Sharpe L, McDonald S, Menzies RE, McGuire B. Are psychological interventions efficacious for adults with migraine? A systematic review and meta-analysis. Headache: The Journal of Head and Face Pain. 2022;62(4):405-19.
36. Lloyd J, Biloshytska M, Andreou AP, Lambru G. Noninvasive neuromodulation in headache: an update. Neurology India. 2021;69(7):183.
37. Reuter U, McClure C, Liebler E, Pozo-Rosich P. Non-invasive neuromodulation for migraine and cluster headache: a systematic review of clinical trials. Journal of Neurology, Neurosurgery & Psychiatry. 2019;90(7):796-804.
38. Li Y-X, Xiao X-l, Zhong D-L, Luo L-J, Yang H, Zhou J, et al. Effectiveness and safety of acupuncture for migraine: an overview of systematic reviews. Pain Research and Management. 2020;2020.
39. Zhang N, Houle T, Hindiyeh N, Aurora SK. Systematic review: acupuncture vs standard pharmacological therapy for migraine prevention. Headache: The Journal of Head and Face Pain. 2020;60(2):309-17.
40. Mollaei S, Jaybashi B, Hemmatpour R, Fojlaley M, Lopes FM. The Effect of Acupuncture in Reducing the Severity of Migraine Headaches: A Randomized Controlled Clinical Trial. Telematique. 2023 Aug 23;22(01):2280-93.
41. De Paolis G, Naccarato A, Cibelli F, D'Alete A, Mastroianni C, Surdo L, et al. The effectiveness of progressive muscle relaxation and interactive guided imagery as a pain-reducing intervention in advanced cancer patients: A multicentre randomised controlled non-pharmacological trial. Complementary therapies in clinical practice. 2019;34:280-7.
42. Harorani M, Davodabady F, Masmouei B, Barati N. The effect of progressive muscle relaxation on anxiety and sleep quality in burn patients: A randomized clinical trial. Burns. 2020;46(5):1107-13.
43. Merakou K, Tsoukas K, Stavrinos G, Amanaki E, Daleziou A, Kourmousi N, et al. The effect of progressive muscle relaxation on emotional competence: Depression–anxiety–stress, sense of coherence, health-related quality of life, and well-being of unemployed people in Greece: An intervention study. Explore. 2019;15(1):38-46.
44. Meyer B, Keller A, Wöhlbier H-G, Overath CH, Müller B, Kropp P. Progressive muscle relaxation reduces migraine frequency and normalizes amplitudes of contingent negative variation (CNV). The Journal of Headache and Pain. 2016;17:1-9.
45. Ariga RA. Decrease anxiety among students who will do the objective structured clinical examination with deep breathing relaxation technique. Open access Macedonian journal of medical sciences. 2019;7(16):2619.

46. dos Santos Felix MM, Ferreira MBG, da Cruz LF, Barbosa MH. Relaxation therapy with guided imagery for postoperative pain management: an integrative review. Pain Management Nursing. 2019;20(1):3-9.
47. Mackereth PA, Tomlinson L. 6 Progressive muscle relaxation: therapists and patients. Integrative hypnotherapy: Complementary approaches in clinical care. 2010:82.
48. Meyer B, Keller A, Müller B, Wöhlbier H-G, Kropp P. Progressive muscle relaxation according to Jacobson for migraine prophylaxis: Clinical effectiveness and mode of action. Der Schmerz. 2018;32:250-8.
49. Izadi Khah A, Ansari Shahidi M, Rezaei Jamaloei H, Haghayegh A. Comparing the Effectiveness of Mindfulness Therapy and Relaxation on Painin Patients with Migraine. Anesthesiology and Pain. 2020;11(3):28-42.
50. Toussaint L, Nguyen QA, Roettger C, Dixon K, Offenbächer M, Kohls N, et al. Effectiveness of progressive muscle relaxation, deep breathing, and guided imagery in promoting psychological and physiological states of relaxation. Evidence-Based Complementary and Alternative Medicine. 2021;2021.
51. Keptner KM, Fitzgibbon C, O'Sullivan J. Effectiveness of anxiety reduction interventions on test anxiety: a comparison of four techniques incorporating sensory modulation. British Journal of Occupational Therapy. 2021;84(5):289-97.
52. Taylor AG, Goehler LE, Galper DI, Innes KE, Bourguignon C. Top-down and bottom-up mechanisms in mind-body medicine: development of an integrative framework for psychophysiological research. Explore. 2010;6(1):29-41.
53. Peres MFP, Mercante JP, Tobo PR, Kamei H, Bigal ME. Anxiety and depression symptoms and migraine: a symptom-based approach research. The journal of headache and pain. 2017;18(1):1-8.
54. Antoni A. The effect of progressive muscle relaxation on blood glucose levels and fatiguesymptom of people with type 2 diabetes mellitus. Jurnal Kesehatan Ilmiah Indonesia/Indonesian Health Scientific Journal. 2017;2(3):21-6.
55. Akbar MA, Malini H, Afriyanti E. Progressive muscle relaxation in reducing blood glucose level among patients with type 2 diabetes. Jurnal Keperawatan Soedirman. 2018;13(2):77-83.
56. Wilk C, Turkoski B. Progressive muscle relaxation in cardiac rehabilitation: a pilot study. Rehabilitation Nursing. 2001;26(6):238-42.
57. Khanna A, Paul M, Sandhu JS. Efficacy of two relaxation techniques in reducing pulse rate among highly stressed females. Calicut Medical Journal. 2007;5(2):23-5.

58. Simon KC, McDevitt EA, Ragano R, Mednick SC. Progressive muscle relaxation increases slow-wave sleep during a daytime nap. Journal of Sleep Research. 2022;31(5):e13574.
59. Lee E-J, Bhattacharya J, Sohn C, Verres R. Monochord sounds and progressive muscle relaxation reduce anxiety and improve relaxation during chemotherapy: a pilot EEG study. Complementary therapies in medicine. 2012;20(6):409-16.
60. Sheu S, Irvin BL, Lin H-S, Mar C-L. Effects of progressive muscle relaxation on blood pressure and psychosocial status for clients with essential hypertension in Taiwan. Holistic nursing practice. 2003;17(1):41-7.
61. Ermayani M, Prabawati D, Susilo WH. The effect of progressive muscle relaxation on anxiety and blood pressure among hypertension patients in east Kalimantan, Indonesia. Enfermería Clínica. 2020;30:121-5.
62. Kobayashi S, Koitabashi K. Effects of progressive muscle relaxation on cerebral activity: An fMRI investigation. Complementary therapies in medicine. 2016;26:33-9.
63. Müller B, Dresler T, Rimmele F, Jürgens T, Niederberger U, Schwarz C, et al. Interdisciplinary multimodal pain therapy in headache disorders. Schmerz (Berlin, Germany). 2023.
64. Varkey E, Cider Å, Carlsson J, Linde M. Exercise as migraine prophylaxis: a randomized study using relaxation and topiramate as controls. Cephalalgia. 2011;31(14):1428-38.
65. D'Souza PJ, Lumley MA, Kraft CA, Dooley JA. Relaxation training and written emotional disclosure for tension or migraine headaches: a randomized, controlled trial. Annals of Behavioral Medicine. 2008;36(1):21-32.
66. Dittrich SM, Günther V, Franz G, Burtscher M, Holzner B, Kopp M. Aerobic exercise with relaxation: influence on pain and psychological well-being in female migraine patients. Clinical Journal of Sport Medicine. 2008;18(4):363-5.
67. Attfield M, Peck D. Temperature self-regulation and relaxation with migraine patients and normals. Behaviour Research and Therapy. 1979;17(6):591-5.
68. Richter IL, McGrath PJ, Humphreys PJ, Goodman JT, Firestone P, Keene D. Cognitive and relaxation treatment of paediatric migraine. Pain. 1986;25(2):195-203.
69. Sorbi M, Tellegen B, Long AD. Long-term effects of training in relaxation and stress-coping in patients with migraine: A 3-year follow-up. Headache: The Journal of Head and Face Pain. 1989;29(2):111-21.

70. Klan T, Gaul C, Liesering-Latta E, Witthöft M, Hennemann S. Behavioral treatment for migraine prophylaxis in adults: Moderator analysis of a randomized controlled trial. Cephalalgia. 2023;43(6):03331024231178237.
71. Butt MN, Maryum M, Amjad I, Khan OJ, Awan L. Effects of aerobic exercise and progressive muscle relaxation on migraine. JPMA The Journal of the Pakistan Medical Association. 2022;72(6):1153-7.
72. Buse DC, Rabany L, Lin T, Ironi A, Connelly MA, Bickel JL. Combining guided intervention of education and relaxation (GIER) with remote electrical neuromodulation (REN) in the acute treatment of migraine. Pain Medicine. 2022;23(9):1544-9.
73. Seydi P, Bagheri-Nesami M, Mohammadpour-Tahamtan RA, Cheraghmakani H, Madani Z. Efficacy of Acupressure on Intensity of Acute Migraine in Patients Attending an Emergency Department: A Randomized Clinical Trial. Journal of Mazandaran University of Medical Sciences. 2021;31(203):83-94.
74. Bijur PE, Silver W, Gallagher EJ. Reliability of the visual analog scale for measurement of acute pain. Academic emergency medicine. 2001;8(12):1153-7.
75. Enck P, Benedetti F, Schedlowski M. New insights into the placebo and nocebo responses. Neuron. 2008;59(2):195-206.