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Does Acupuncture Help Reduce Headache Intensity in Patients Who Have Migraine Without Aura?

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ABSTRACT

Objective: The objective of this selective EBM review is to determine whether or not “Does acupuncture help reduce headache intensity in patients who have migraine without aura?”

Study Design: A systematic review of three randomized controlled trials (RCTs) all published between 6/29/2016 and 2022.

Data Sources: All three RCTs were peer-reviewed articles published in English on PubMed. Each article was relevant to the clinical question and had patient-oriented outcomes that included headache intensity.

Outcome Measured: Headache intensity was measured using the visual analogue scale (VAS) in all three RCTs. The VAS is a scale from 0-10 with correlating cartoon faces showing visuals of no pain to worst pain. Each article reported mean changes from baseline and p-values.

Results: In the RCT by Zhao et al., true acupuncture led to a reduction in headache intensity by -2.5 points on the VAS, and the difference between the mean change from baseline was statistically significant with a P value of <0.001 in each group and the difference between the true and sham acupuncture group was 1.1 points. In the RCT by Li et al., true acupuncture led to a reduction in headache intensity by -2.16 points on the VAS, and the difference between the mean change from baseline between the true and sham acupuncture group was 1.02 with a treatment group P value of 0.000 and sham acupuncture group P value of 0.158. In the RCT by Xu et al., true acupuncture led to a reduction in headache intensity by -2.2 points on the VAS, and the difference between the mean change from baseline was statistically significant with a P value of <0.001 in each group and the difference between the true and sham acupuncture group was 1.3 points.

Conclusions: All three RCTs showed that migraine patients without aura in true acupuncture treatment groups experienced a statistically significant reduction in headache intensity as measured by the VAS. However, the change between true and sham acupuncture was minimal at no more than 1.3 points on the VAS. Further studies should be completed in other locations to allow for more generalizability and should study how effective acupuncture and migraine medication are together in reducing headache intensity and compare its effectiveness to acupuncture or medication alone.

Key Words: Migraine, Acupuncture

INTRODUCTION

Migraines are a recurrent and often disabling disease that can have sensory disturbances called an aura, and migraine without aura is the most common type. A migraine diagnosis includes repeated attacks of headaches lasting 4-72 hours with at least two pain characteristics (unilateral pain, throbbing pain, aggravation by movement, moderate or severe intensity) and at least one accompanying feature of nausea/vomiting or photophobia and phonophobia.[1] This topic is relevant to patients and the PA profession as about 12% of the US population is affected by migraines each year.[2] In a 2016 Global Burden of Disease Study 1.04 billion people were estimated to have migraines worldwide.[2] This common and potentially disabling condition disproportionately affects women three times more than their male counterparts.[2] Ultimately, treating migraines is important as a vast amount of the population is affected.

Not only is this disease common, but it's also costly. Those with migraine can have direct costs such as healthcare visits and indirect costs like less ability to focus or absenteeism from migraine attacks. In a study that collected data from 2008-2013, researchers found the cost to the individual is about $9,000 more per year as compared to individuals without migraine.[2] This is financially detrimental to the patient, but also to companies as it costs them about $2,600 more annually to have an employee with migraines compared to an employee without migraines.[2] Additionally, healthcare providers feel the impact of this common disease, as chronic migraine patients have double the number of primary care visits and triple the number of neurology visits as compared to patients with episodic migraine.[2] In total, the effects of migraines are not limited to a physically intense headache but are far-reaching. Migraines are common amongst the population, affect the financial well-being of the companies, and significantly utilize healthcare system resources.

Despite migraines being as common as they are, there are still areas of pathophysiology that need further study. The phases of migraine are known and are divided into prodromal, aura (not all patients have this), headache, and postdrome. [4] In patients with migraines the brain is in a constant state of neuronal vulnerability, likely due to a dysfunction in the trigeminal system. There is thought that the hypothalamus activates nociceptive and trigeminal pathways with increased parasympathetic tones.[4] Ultimately, there is a release of vasoactive neuropeptides causing vasodilation resulting in pain that is usually throbbing and unilateral.[4] Although migraine pathophysiology is not fully understood, there are plenty of treatment options available today. Non-pharmacologic treatment involves avoiding known triggers, regulating sleep, and stress relief. For an acute attack resting in a quiet dark room is recommended. For mild to moderate pharmacologic treatment, NSAIDs and acetaminophen are first line. Excedrin Migraine is also an option. For prophylactic and abortive treatment triptans are first line and taken at the sign of an impending migraine or during an attack. Options for preventative treatment include beta-blockers, antiepileptics like topiramate, and antidepressants like amitriptyline, or Botox. There is a wide array of pharmacological options that have appealed to western society, yet not all patients are interested in these kinds of interventions.

Acupuncture has been used in China as a preventative treatment and is currently being studied for its potential efficacy in reducing headache intensity.[5,6,7] This is an important field of research as only 13% of patients with migraine who are prescribed prophylactic drugs report current use of these drugs.[5] Additionally, not all the prophylactic medications work well for every patient as there are some contraindications.[5] So there is a need for non-pharmacologic preventative treatment of migraines such as acupuncture. Some scientists theorize acupuncture stimulates the brain to release certain hormones that promote healing; however, the

pathophysiology of how acupuncture works is still unclear. [5] This paper evaluates three randomized controlled trials (RCTs) that research the efficacy of acupuncture in reducing headache intensity in patients who have migraine without aura.

OBJECTIVE

The objective of this selective EBM review is to determine "Does acupuncture help reduce headache intensity in patients who have migraine without aura?"

METHODS

All three studies in this selective review were chosen as they were credible and relevant to the objective question. It was required that each of these studies met criteria including population, intervention, comparison, and outcome measure. To find these articles, I used the keywords "migraine" and "acupuncture" in the PubMed search engine and looked for articles that had the patient-oriented outcome of headache intensity. The population of interest for the studies in this review was migraine patients without aura and the intervention was acupuncture. The comparison group was sham acupuncture and the outcome measured was headache intensity measured via the patients rating their own visual analog scale (VAS). All three studies were RCTs that were peer-reviewed and published in English on Pub Med. Studies had to meet the inclusion criteria of being a clinical trial published after 6/28/2016 and were excluded if they were published prior to 6/29/2016 and/or did not use a VAS. Studies were excluded based on that date as the last Cochrane Review regarding the topic of migraines and acupuncture was published in June 2016. Lastly, to report statistics of their collected VAS data, all of the studies used mean changes from baseline and p-values.

OUTCOMES MEASURED

In all three studies, the outcome measured was headache intensity and it was measured by using a common scale in research, the VAS. Headache intensity is patient-oriented evidence that

Table 1. Demographics & Characteristics of Included Studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W /D	Interventions
Zhao 2017 (1)	RCT	249	18-65	18-65 yrs old with initial onset of migraines prior to 50 yrs old; a frequency of acute migraine attacks 2-8 times per months 3 months before inclusion; experience of migraine attacks for at least 1 year; completion of a baseline HA diary; and provision of written, informed consent by the patients.	HA d/t organic disorders (eg, SAH, cerebral hemorrhage or embolism, cerebral thrombosis, vascular malformation, arteritis, HTN, or arteriosclerosis); the presence of neurological diseases, immunodeficiency, bleeding disorders, or allergies; prophylactic HA tx with drugs during the previous 3 months; pregnancy, lactation, or plans to become pregnant within 6 months; or involvement in other clinical trials.	10	Participants in the true acupuncture and sham acupuncture groups received treatment 5 days per week for 4 weeks for a total of 20 sessions.
Li 2017 (2)	RCT	100	17-45	All patients (1) were 17-45 yrs old and were righthanded, (2) had not taken any prophylactic HA medicine nor had acupuncture tx during the last three months, (3) had at least six months migraine duration, and (4) had at least one HA attack per month during the last three months.	Patients were excluded if they (1) were alcohol or drug abusers, (2) were pregnant or lactating, (3) suffered from psychiatric, neurological, cardiovascular, respiratory, or renal illnesses, (4) suffered from any other chronic pain conditions or had a history of head trauma with loss of consciousness, (5) had MRI contraindications, such as claustrophobia, and (6) had acupuncture contraindications, such as a bleeding tendency.	38	The tx for the acupuncture groups consisted of 20 sessions of acupuncture tx with a duration of 30 min per session, each administered over a period of 4 weeks (5 sessions per week). No verum acupuncture.
Xu 2020 (3)	RCT	150	15-65	A neurologist made the Dx of episodic migraine w/o aura according to International Classification of HA Disorders, 3rd edition β version; 15-65 yrs of age, hx of migraine w/o aura for more than 12 months, initial onset of migraine before 50 y/o, between 2-8 migraine attacks during the baseline phase, naivety to acupuncture, and ability to give informed consent.	Exclusion criteria included all other types of primary and secondary headaches, history of a clinically significant disorder (for example, severe mental illness), pregnancy or breast feeding, and non-adherence to the baseline diary. In addition, all patients were instructed not to take any other analgesics and to avoid starting other interventions.	6	20 sessions of manual acupuncture at true acupuncture points plus usual care, 20 sessions of non-penetrating sham acupuncture at heterosegmental non-acupuncture points plus usual care, or usual care alone over 8 weeks.

matters (POEM) as reducing pain from migraines is important to patients since their pain can be debilitating and make it difficult to focus on the task at hand. The VAS is a scale from 0-10 with correlating cartoon faces that allow the patient to subjectively rate their pain.[5,6,7] A zero on the scale has a correlating smiling face and a ten on the scale has a frowning face with streaming tears. So, the VAS scale was used in these studies to see if a patient's headache intensity is improving, worsening, or staying the same with acupuncture.

RESULTS

The three RCTs in this study looked at acupuncture as an intervention for migraine patients without aura. Zhao et al. led an RCT study with 249 enrolled participants 18-65 years old who had migraine without aura.[6] The participants were randomized into true acupuncture (83 participants), sham acupuncture (80 participants), and waitlist groups (82 participants).[6] The study involved one month of treatment and then twenty weeks of follow-up during 2012-2014 in three different locations in China.[6] During the month of treatment, the true acupuncture and sham acupuncture group participants had five treatment days a week totaling twenty sessions.[6] Change in migraine frequency was the primary outcome of this study, and headache severity was a secondary outcome measure. The patients in the treatment group, sham acupuncture group, outcome assessors, and statisticians were able to be kept blind during this study; however, the acupuncturists could not be blinded as they needed to know who was receiving what treatment in order to perform acupuncture.[6] Four patients from the 249 that were randomized were excluded due to misdiagnosis or missing primary outcomes.[6] In total the study had a low loss to follow-up percentage at <20%, two dropped in the true acupuncture group, three dropped in the sham acupuncture group, and one dropped in the waitlist group and all the dropouts were analyzed with intention to treat analysis and a worst-case analysis was done.[6]

For this review, the mean VAS score of each group was reported as well as the standard deviation (SD). The treatment group baseline was a VAS score of 5.7 (SD 1.9), and 21-24 weeks after treatment the VAS score was lower at 3.2 (SD 2.0), so the mean change from baseline was -2.5 points.[6] The sham acupuncture group baseline was a VAS score of 5.6 (SD 1.6), and 21-24 weeks after treatment the VAS score was lower at 4.2 (SD 1.7), so the mean change from baseline was -1.4.[6] The p-value for both groups was <0.001 so the findings were statistically significant.[6] True acupuncture led to a reduction in headache intensity; however, no P-value was listed for the difference between the mean change from baseline between the true and sham acupuncture groups. Therefore, it cannot be stated the difference of 1.1 points on the VAS between these groups is statistically significant.[6]

Table 2. Zhao et al. Change in Headache Intensity

Group	Baseline mean VAS score	21-24 weeks after treatment mean VAS score	VAS Mean Change from Baseline	P-value
acupuncture	5.7 (SD 1.9)	3.2 (SD 2.0)	-2.5	<0.001
Sham acupuncture	5.6 (SD 1.6)	4.2 (SD 1.7)	-1.4	<0.001

In the RCT by Li et al., the study had the same groups with a true acupuncture group, sham acupuncture group, and a waitlist group. There were 100 patients with migraine without aura and 46 healthy controls who were 17-45 years old and recruited from the outpatient department at Chengdu University of Traditional Chinese Medicine in China.[7] Participants were blinded and randomly assigned to these groups and received four weeks of the assigned treatment and 20 sessions in total.[7] Patients were responsible for reporting their pain on the VAS. The true acupuncture group had 35 patients, the sham acupuncture group had 11 patients, and the wait list group had 16 patients.[7] The total number of withdrawals from the 100 patients originally

enrolled was 38, so the study had a >20% loss of follow-up for the study. [7] The patients that were excluded due to excessive head movements or incomplete fMRI scans were not included in the data analysis.[7] The primary outcome of this study was spontaneous brain activity using BOLD-fMRI, however, headache intensity was a secondary outcome measure self-rated using a VAS.[7]

The results section for this review used mean VAS score at baseline and end of treatment to show the change in headache intensity in each group and had a 95% confidence interval. For the treatment group, the mean VAS score at baseline was 5.50 with a CI of (5.13; 5.87) and the end-of-treatment mean VAS score was lower at 3.34 with a CI of (2.87; 3.81).[7] So the change from baseline in the treatment group was -2.16 and since the group's p-value was 0.000, it was a statistically significant change.[7] For the sham acupuncture group, the mean VAS score at baseline was 5.18 with a CI of (4.19; 6.17) and the end-of-treatment mean VAS score was lower at 4.04 with a CI of (3.09; 5.00).[7] However, headache intensity in the sham acupuncture group had a p-value of > 0.05 at 0.158 so the reduction in the VAS scale was not statistically significant.[7] So, true acupuncture led to a statistically significant reduction in headache intensity; however, the confidence intervals overlap between the groups both before and after treatment. Therefore, it cannot be stated the groups had different outcomes despite the difference of 1.02 points on the VAS between the mean change from baseline between the true and sham acupuncture groups.[7]

Table 3. Li et al. Change in Headache Intensity

Group	Before Tx mean VAS score and CI	After Tx mean VAS score and CI	VAS score Mean Change from Baseline	P-value
Treatment Group	5.50 with a CI of (5.13; 5.87)	3.34 with a CI of (2.87; 3.81)	-2.16	0.000
Sham acupuncture	5.18 with a CI of (4.19; 6.17)	4.04 with a CI of (3.09; 5.00)	-1.14	0.158

In the RCT by Xu et al., there were 150 patients between 15-65 years old enrolled in the study across seven hospitals in China.[5] The study lasted 6 months with a month of collecting baseline data, 2 months of the intervention, and 3 months of follow-up.[5] Patients were randomized into three groups in a 2:2:1 ratio. So there were 60 patients in the manual acupuncture group, 60 patients in the sham acupuncture group, and 30 patients in the usual care group.[5] Two patients were excluded after randomization before the intervention because of loss to contact and only four patients stopped after the intervention started, so the losses to follow-up ratio was <20%.[5] Intention to treat analysis was used and the last observation carried forward method for any missing data. The three groups were 20 sessions of true acupuncture plus usual care, 20 sessions of sham acupuncture plus usual care, or just usual care.[5] Participants, outcome assessors, and statisticians were all blinded, however, the acupuncturists needed to know what participants were receiving true acupuncture.[5] Primary outcomes were a change in the frequency of migraine attacks and headache intensity was listed as a secondary outcome.

For this study, the manual acupuncture group and sham acupuncture group had VAS mean change from baseline reported and the corresponding SD for each group. The mean change from baseline for the true acupuncture group was -2.2 on the VAS with a SD of 2.5 and the sham acupuncture group had a smaller difference with a mean change from baseline of -0.9 on the VAS and SD of 1.9.[5] True acupuncture led to a reduction in headache intensity; however, no P-value was listed for the difference between the mean change from baseline between the true and sham acupuncture groups. Therefore, it cannot be stated the difference of 1.3 points on the VAS between these groups is statistically significant.

Table 4. Xu et al. Change in Headache Intensity

	VAS Mean Change from Baseline and SD	P-value

True acupuncture	-2.2, SD 2.5	<0.001
Sham acupuncture	-0.9, SD 1.9	<0.001

DISCUSSION

In this systematic review the efficacy of acupuncture as an intervention for headache intensity in migraine patients without aura was evaluated. All three RCTs had statistically significant reductions in headache intensity as reported by patients with the VAS after twenty sessions of true acupuncture.[5,6,7] Each study reported a mean change from baseline for the true acupuncture group, and all of them found point reductions in the VAS for headache intensity. However, as there was no statistical measure given for the differences between the true acupuncture and sham acupuncture groups, the reduction in headache intensity between these groups were no different. Still some patients may choose to add acupuncture into their lives to reduce headache intensity. However, barriers to acupuncture still exist, as not all patients' insurance will cover acupuncture even with a referral. Additionally, patients must be able to take the time and transportation necessary to benefit from regular in person appointments, and this may be difficult for low-income patients. Ultimately, providers writing referrals for acupuncture is not new, as acupuncture is a treatment option for painful conditions like osteoarthritis.[8] There are no absolute contraindications to acupuncture, however, relative contraindications include fever and areas of infected skin as a possible adverse effect of acupuncture includes infection.[8]

The studies also had their limitations, for example, all three were not able to blind the acupuncturists in the study. In each study, the acupuncturists had to know if they were to perform true acupuncture or in the sham acupuncture groups use non-acupressure points or retracting needles which introduce performance bias into the studies.[5] Additionally, since all three studies

were performed in China this limits the generalizability, and the study findings for this population are less likely to apply to patients outside of China. In Zhao et al., the authors mentioned in their limitations section that the full benefit of acupuncture could not be realized as the acupuncturists had to subscribe to the studies outlined acupressure points and could not personalize the session based on the patient's symptoms.[6] Li et al. had a high loss to follow-up percentage at greater than 20% with an already small study, and the researchers decided to exclude the participants that were lost to follow up from the data analysis instead of performing worst-case analysis.[7] This is problematic as excluding them from the data analysis can skew the results of the study, usually towards a larger treatment benefit than actually experienced. Lastly, in Xu S et al. the researchers allowed participants to take diclofenac sodium enteric-coated tablets as a "rescue medication" if they had pain worse than 8 on the VAS.[5] Therefore, the use of the rescue medication could have an impact on how the participants rated their pain on the VAS and affect the validity of the study.

CONCLUSION

This selective review of three RCTs ultimately shows acupuncture does reduce headache intensity in patients who have migraine without aura; although, without a precision measure it cannot be stated this reduction is any different from sham acupuncture. Each article found that 20 sessions of acupuncture reduced the headache intensity as reported by patients on a VAS.[5,6,7] Looking at all three RCTs, the mean change from baseline is at least a 2.16-point reduction on the VAS, and this is statistically significant as every study had p-values of <0.05 in the treatment group. However, the change between true and sham acupuncture was minimal at no more than 1.3 points on the VAS. So, the answer to the objective question is yes, as acupuncture does reduce headache intensity. When offering acupuncture as a treatment option, migraine patients

without aura should know the intervention may moderately reduce their headache intensity by 2.16 on the VAS. As always, it is up to the patient to decide if an intervention is worth their time and money.

There are ways in which the methods section of this selective review and the studies within it could be improved. Since the studies in this review were all done in China, including studies done in other countries would allow for larger generalizability of a systematic review's results in the future. There is currently a clinical trial of acupuncture in migraine treatment with an expected study completion date of February 28th, 2023.[9] This ongoing study is comparing headache intensity in two groups: acupuncture with a placebo medication vs. acupuncture and flunarizine hydrochloride which is a preventative medication for migraines.[9] However, this study is being completed at the Zhejiang Medical University in China.[9] So, the ongoing study's results will also lack generalizability to other countries.

Additionally, in Xu et al. the authors wrote that often other studies have patients take prophylactic medication before the intervention; however, their study chose not to.[5] The authors in Xu et al. defended this choice as they wanted to respect the participants' decision on whether or not to take medication, but allowed participants to take a rescue medication if needed.[5] So, to research acupuncture's full treatment potential while still respecting the patient's decision to take medication, future studies should consider using a comparison group with patients who already use acupuncture alongside migraine medication. With this, future studies could look at how effective acupuncture and migraine medication are together in reducing headache intensity and compare its effectiveness to acupuncture or medication alone. Overall, to help migraine patients without aura improve their quality of life it's important that clinical research trials continue to study what treatments help to reduce headache intensity, a patient-oriented outcome that matters.

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