The Long-term Effect of Acupuncture for Migraine Prophylaxis: A Randomized Clinical Trial

Mitchell Goodwin, PharmD Candidate

BACKGROUND:

- Migraines are a common neurologic disorder that often requires preventative therapy. Excessive use of analgesics for relief can cause headaches and increase the frequency of headaches
- Acupuncture is often used in China for medication-refractory migraines, thought to achieve both acute relief and prevention of further migraines

OBJECTIVE

- This study aims to test the long-term benefit of acupuncture for the prevention of migraines without aura

METHODS

- **Design:** 24-week, multicenter, 3-arm, parallel randomized clinical trial
- **Inclusion Criteria:** 18-65 years old with migraines without aura that started before age 50, 2-8 migraines per month for 3 months before the study, suffered acute migraine attacks for at least one year, completion of a baseline headache diary, and written informed consent
- **Exclusion Criteria:** Headache from an organic disorder, neurological diseases, immunodeficiency, bleeding disorders, allergies, pharmacologic prophylactic headache treatment in the past 3 months, patients who were pregnant or planning to become pregnant within 6 months, patients enrolled in another clinical trial
- Outcomes were reported by patients in a migraine diary that was collected every 4 weeks via email or outpatient visit. Patients were reminded every 4 weeks via phone call or text message
- **Primary Outcome Measure:** Decrease in frequency of migraine attacks at 16 weeks
- **Secondary Outcome Measures:** Duration of migraine attacks, change in VAS scores, medication intake every 4 weeks within 24 weeks.
- This study utilized intention-to-treat as long as patients had at least 1 treatment and 1 primary outcome measure
- The primary outcome measure was analyzed using the Kruskal-Wallis test
- Secondary outcome measures were analyzed with the Chi-square test for categorical data and Kruskal-Wallis tests for quantitative variables
- Pairwise comparisons were made using the Fisher's Least Significant Difference test

RESULTS

- 249 patients were randomized. 4 were excluded (1 was misdiagnosed and 3 did not experience primary outcome).
- 245 patients were included in the study
    - 83 in the acupuncture group (1 changed their phone number and 1 dropped out due to intercurrent illness)
    - 80 in the sham acupuncture group (2 were unsatisfied with treatment outcome and 1 had a time restriction)

    - 82 in the waiting list group (1 was unwilling to follow-up)
- Primary Outcome:
    - **Acupuncture group:** 3.2 fewer attacks, SD 2.1; **sham acupuncture group:** 2.1 fewer attacks, SD 2.5; **waiting list group:** 1.4 fewer attacks, SD 2.5 (P <0.001)
    - **Acupuncture vs sham acupuncture:** effect size 0.5 (95% CI: 0.2-0.8, P=0.002)
    - **Acupuncture vs waiting list:** effect size 0.8 (95% CI 0.5-1.1, P<0.001)
    - **Sham acupuncture vs waiting list:** effect size 0.3 (95% CI 0.0-0.6, P=0.07)
- Secondary Outcomes:

Outcome Measure	TA (n = 83)	SA (n = 80)	WL (n = 82)	*P* Value
Days With Migraine per 4 Weeks, Mean (SD), No.[b,d]				
Baseline	5.9 (3.9)	6.2 (4.4)	6.0 (4.6)	.80
Treatment, 1-4 wk	2.4 (1.7)	4.0 (2.9)	4.5 (2.4)	<.001
After treatment, wk				
5-8	1.8 (1.9)	3.3 (2.3)	4.4 (2.3)	<.001
9-12	2.1 (3.2)	3.2 (2.3)	4.2 (2.2)	<.001
13-16	2.0 (3.2)	3.1 (2.1)	3.8 (2.1)	<.001
17-20	2.0 (3.2)	3.0 (2.3)	3.9 (2.2)	<.001
21-24	2.1 (3.3)	3.1 (2.2)	3.8 (1.8)	<.001
VAS Score, Mean (SD)[b]				
Baseline	5.7 (1.9)	5.6 (1.6)	5.1 (1.5)	.10
Treatment, 1-4 wk	3.6 (1.9)	4.2 (1.7)	4.9 (1.6)	.001
After treatment, wk				
5-8	3.7 (2.3)	4.3 (1.9)	5.0 (1.8)	.002
9-12	3.4 (2.1)	4.1 (1.9)	5.1 (1.5)	<.001
13-16	3.4 (2.3)	4.2 (1.9)	4.9 (1.4)	<.001
17-20	3.4 (2.0)	4.3 (1.8)	4.9 (1.4)	<.001
21-24	3.2 (2.0)	4.2 (1.7)	4.9 (1.3)	<.001
Use of Acute Pain Medication, No. (%)[e]				
Baseline	36 (43.4)	24 (28.9)	29 (34.9)	.15
Treatment, 1-4 wk	5 (6.0)	4 (4.8)	13 (8.8)	.03
After treatment, wk				
5-8	3 (3.6)	3 (3.6)	15 (18.1)	.001
9-12	5 (6.0)	4 (4.8)	13 (8.8)	.03
13-16	5 (6.0)	5 (6.0)	16 (19.3)	.006
17-20	5 (6.0)	7 (8.4)	18 (21.7)	.004
21-24	5 (6.0)	7 (8.4)	19 (22.9)	.002

Pairwise Comparison					
TA vs SA		TA vs WL		SA vs WL	
Effect Size (95% CI)	*P* Value[a]	Effect Size (95% CI)	*P* Value[a]	Effect Size (95% CI)	*P* Value[a]
Days with Migraine per 4 weeks, Mean (SD), No.					
NA		NA		NA	
−0.7 (−1.0 to −0.4)	<.001	−1.0 (−1.3 to −0.7)	<.001	−0.2 (−0.5 to 0.1)	.18
−0.7 (−1.0 to −0.4)	<.001	−1.2 (−1.6 to −0.9)	<.001	−0.5 (−0.8 to −0.2)	.001
−0.4 (−0.7 to −0.1)	.008	−0.8 (−1.1 to −0.4)	<.001	−0.4 (−0.8 to −0.1)	.01
−0.4 (−0.7 to −0.1)	.005	−0.7 (−1.0 to −0.4)	<.001	−0.3 (−0.6 to 0.0)	.06
−0.4 (−0.7 to −0.1)	.01	−0.7 (−1.0 to −0.4)	<.001	−0.4 (−0.7 to −0.1)	.03
−0.4 (−0.7 to −0.1)	.01	−0.6 (−0.9 to −0.3)	<.001	−0.3 (−0.7 to 0.0)	.07
VAS Score, Mean (SD)					
NA		NA		NA	
−0.3 (−0.6 to 0.0)	.04	−0.7 (−1.1 to −0.4)	<.001	−0.4 (−0.7 to −0.1)	.02
−0.3 (−0.6 to 0.0)	.04	−0.6 (−0.9 to −0.3)	<.001	−0.4 (−0.7 to −0.1)	.04
−0.3 (−0.7 to −0.0)	.01	−0.9 (−1.2 to −0.6)	<.001	−0.6 (−0.9 to −0.3)	.001
−0.4 (−0.7 to −0.1)	.01	−0.8 (−1.1 to −0.5)	<.001	−0.4 (−0.7 to −0.1)	.01
−0.5 (−0.8 to −0.2)	<.001	−0.9 (−1.2 to −0.5)	<.001	−0.4 (−0.7 to −0.1)	.03
−0.5 (−0.8 to −0.2)	<.001	−1.0 (−1.3 to −0.7)	<.001	−0.5 (−0.8 to −0.1)	.01

- **Authors' Conclusion:** Acupuncture shows statistical and clinical significance compared to sham acupuncture and patients on a waiting list for the prevention of migraine headaches as well as reducing migraine intensity.

STRENGTHS

- Patients came from multiple centers
- Appropriate power
- Study showed acupuncture to be more efficacious than sham acupuncture and no treatment
- Inclusion of a waiting list group allowed for measurement of potential placebo effect

LIMITATIONS

- Authors have affiliations with schools of acupuncture, and this potential bias may have had an effect on the study
- Inclusion criteria included a large range of migraine severity
- Non-normally distributed data was represented by mean and standard deviation
- Unblinding likely due to nature of sham acupuncture and patient familiarity with acupuncture
- Patients had high expectations for acupuncture to be effective and sham acupuncture performed well, showing likely placebo effect
- Patient sample was not diverse (all three centers used for this trial are in China)

CONCLUSION: Due to the likely influence of the placebo effect, poor inclusion criteria, misrepresentation of central tendency and variability of results, and strong potential for unblinding, this study is inconclusive as to the effectiveness of acupuncture in migraine prophylaxis

Citation: Zhao L, Chen J, Li Y, Sun X, Chang X, et al. The Long-term Effect of Acupuncture for Migraine Prophylaxis: A Randomized Clinical Trial. *JAMA Intern Med*. 2017; 177 (4): 508-515.