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Acupuncture for Patients With Chronic Tension-Type Headache: A Randomized Controlled Trial

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ABSTRACT

Background and Objectives: Whether acupuncture is effective for chronic tension-type headache (CTTH) is inconclusive. We aimed to examine the effectiveness of acupuncture with a follow-up period of 32 weeks.

Methods: We conducted a randomized controlled trial, and 218 participants who were diagnosed with CTTH were recruited from June 2017 to September 2020. The participants in the intervention group received 20 sessions of true acupuncture (TA group) over 8 weeks. The acupuncture treatments were standardized across participants, and each acupuncture site was needled to achieve *deqi* sensation. Each treatment session lasted 30 minutes. The participants in the control group received

the same sessions and treatment frequency of superficial acupuncture (SA group)—defined as a type of sham control by avoiding *deqi* sensation at each acupuncture site. The main outcome was the responder rate at 16 weeks after randomization (week 16) and was followed up at week 32. A responder was defined as a participant who reported at least a 50% reduction in the monthly number of headache days (MHDs).

Results: Our study included 218 participants (mean age: 43.1 years, mean disease duration: 130 months, MHDs: 21.5 days). The responder rate was 68.2% in the TA group (n=110) versus 48.1% in the SA group (n=108) at week 16 (odds ratio, 2.65; 95%CI, 1.5 to 4.77; p<0.001); and it was 68.2% in the TA group versus 50% in the SA group at week 32 (odds ratio, 2.4; 95%CI, 1.36 to 4.3; p<0.001). The reduction in MHDs was 13.1±9.8 days in the TA group versus 8.8±9.6 days in the SA group at week 16 (mean difference, 4.3 days; 95%CI, 2.0 to 6.5; p<0.001), and the reduction was 14±10.5 days in the TA group versus 9.5±9.3 days in the SA group at week 32 (mean difference, 4.5 days; 95%CI, 2.1 to 6.8; p<0.001). Four mild adverse events were reported; three in the TA group versus one in the SA group.

Conclusion: The 8-week TA treatment was effective for the prophylaxis of CTTH. Further studies might focus on the cost-effectiveness of the treatment.

Trial Registration Information: ClinicalTrials.gov: NCT03133884 (https://clinicaltrials.gov/ct2/show/NCT03133884)

Classification of Evidence: This study provides Class I evidence that acupuncture (achieving deqi sensation) reduces mean headache days (per month) in patients with chronic tension-type headache.

INTRODUCTION

Tension-type headache (TTH) is one of the most prevalent primary headaches, characterized as dull, bilateral, mild-to-moderate pain.[1,2] It is estimated that the lifetime prevalence of TTH could be 80% in the general population, and the high prevalence of TTH caused a significant socioeconomic impact. Chronic tension-type headache (CTTH) is defined as the TTH that has a higher frequency of headache attacks for at least 15 days per month. Owing to the higher headache frequency, CTTH caused a lower quality of life and higher health expenditure.[2,3]

Acupuncture, having been practiced routinely for primary headaches in China, was reported effective in previous RCTs and a subsequent Cochrane systematic review.[4–6] Acupuncture decreased the number of headache days in patients with TTH without causing any serious adverse events, which therefore has high clinical compliance and attracts patients with TTH. However, several clinical questions remain unanswered in previous studies. First, conflict results were found in previous RCTs. Three RCTs found no efficacy of acupuncture when compared with sham acupuncture, but one RCT with a larger sample size had contradictory findings. The efficacy of acupuncture is therefore still questioned, although it showed a promising effect in reducing headache days in comparison to no acupuncture. Second, none of

the previous RCTs assessed the effect of acupuncture in a period over 6 months. Whether the acupuncture effect persists over 6 months is unknown, as concluded in the Cochrane review.[6] Third, all RCTs recruited both episodic TTH and CTTH patients in a trial, except two small-size RCTs recruited them separately (one recruited patients with episodic TTH only,[7] and the other recruited CTTH only[8]). Whether acupuncture provides benefits for patients with CTTH—a condition with a more significant impact on health—is unknown.

Deqi sensation, defined as a sensation of numbness, soreness, heaviness, or irritating pain in the needling site, is recognized as the key to successful acupuncture treatment in traditional Chinese acupuncture theory; and this assertion is supported by fMRI studies and clinical studies—showing that the effect and working mechanism of acupuncture is different between achieving and avoiding *deqi* sensation. Endres and colleagues—conducted the largest-scale RCT on acupuncture for TTH—hypothesized that *deqi* sensation may play an essential part in the difference between acupuncture and sham acupuncture,[5] since sham acupuncture in their trial was performed without *deqi*. However, since their trial used the design of sham points and avoiding-deqi-sensation in the sham acupuncture group, it is impossible to confirm the hypothesis. Based on these grounds, several questions are raised: (1) Is TA efficacious for CTTH? (2) Does the effect persist over 6 months after initiation of acupuncture? (3) Is *deqi* sensation the key to the specific effect of acupuncture?

We therefore performed an RCT primarily aiming to clarified whether acupuncture achieving deqi sensation reduces mean headache days (per month) in patients with chronic tension-type headache.

METHODS

Study overview

A parallel-design, patient-and-assessor blinded RCT was performed in the Teaching Hospital of Chengdu University of Traditional Chinese Medicine from June 1, 2017, to September 10, 2020. Eligible participants with CTTHs were randomly assigned to receive true acupuncture (TA) or superficial acupuncture (SA) in a 1:1 ratio. The study included a 4-week baseline evaluation (before randomization, week -4 to week 0), an 8-week treatment (week 1 to week 8), and a 24-week follow-up (week 9 - week 32). Outcome assessments were performed every 4 weeks.

Standard Protocol Approvals, Registrations, and Patient Consents

The study design was approved by the Regional Institutional Review Board of Trials for Traditional Chinese Medicine in Sichuan Province, which was also conformed to the Helsinki declaration (64th World Medical Association General Assembly, October 2013) and registered on clinicaltrials.gov (ID: NCT03133884).[9] Written informed consents were acquired from the participants in the study. The study was reported following the CONSORT guideline.[10]

Participants

Patients with potential TTH were recruited from the outpatient settings of the Teaching Hospital of Chengdu University of Traditional Chinese Medicine, and they were assessed for eligibility by the research team including three neurologists, two research assistants, and three acupuncturists. The neurologists assessed whether the participants had met the diagnostic criteria of CTTH and performed differential diagnosis. The research assistants introduced the trial design to the participants and asked whether they were willing to participate, and the acupuncturists introduced the details of acupuncture treatment.

Participants who met the following criteria were recruited: fulfilled the diagnostic criteria of CTTH in the 3rd edition of International Classification of Headache Disorder (ICHD-3);[11] aged 18-65 years; with a history of CTTH for at least 1 year; with headache attacks for 3 months at a frequency of at least 15 days per month. Participants were excluded for meeting any of the following conditions: being diagnosed with chronic migraine; having headaches that might be caused by other medical disorders (subarachnoid hemorrhage, cerebral hemorrhage, cerebral embolism, cerebral thrombosis, vascular malformation, arthritis, hypertension, or arteriosclerosis); had been taking prophylactic medications in the latest 3 months; concomitant with serious diseases in neurological, cardiovascular, hepatic, and renal systems that might cause inability to receive acupuncture; being pregnant or on lactating. Participants were screened for eligibility by neurologists in the hospital, and the screening process was described elsewhere.[12]

Randomization and blinding

We used the Brightech Clinical Information Management system (Brightech-Magnsoft Inc., Somerset, NJ, USA) to randomly allocate participants to TA or SA group. The randomization sequence was generated through a real-time interactive computer program with a random mix of block sizes (4, 6, and 8), and the sequence could be obtained through the website of the Brightech, text message, or phone call application. Acupuncturists registered in the randomization system would acquire randomization numbers and group assignments before treating an included participant. The participants and outcome assessors were blinded from group assignments and treatment details.

Intervention and control

Participants in the TA group received 20 sessions of acupuncture over 8 weeks, provided for three sessions per week in the first 4 weeks and two sessions per week in the last 4 weeks. Five fixed points were selected—*Fengchi*(GB20), *Baihui*(GV20), *Taiyang*(EX-HN5), *Hegu*(LI4), and *Taichong*(LR3); GB20, GV20, and EX-HN5 were located at the base, the midline and the lateral side of the scull, respectively; LI4 and LR3 were located at the upper and lower extremity, respectively (eTable 1 and eFigure 1). GB20, EX-HN5, LI4 and LR3 were needled bilaterally. No additional points were added during the acupuncture treatment. The acupuncture points were manually stimulated, and achieving *deqi* sensation was required in needling each point. The depth of needling at each point ranged from 12.5 to 20 mm in the TA

group. Participants in the SA group also received 20 sessions of acupuncture at the same acupuncture points, but the acupuncturists controlled the depth of penetration within 2 mm and avoided eliciting *deqi* sensation. One treatment session lasted for 30 minutes. Acupuncture points were manipulated twice every 10 minutes with intermittent stimulation, whereas the needles were retained 30 minutes without any manipulation in the SA group. Acupuncturists qualified for the study had at least 5 years of training and had experience in participating in clinical trials. The participants in both groups were given headache educations in each clinic visits, which included the methods to record headache diaries, avoiding predisposing factors for headaches, and suggestions for the selection of acute drugs.

Outcome measurements

The primary outcome was responder rate at week 16; a responder was defined as a participant with a >50% reduction in monthly headache days after treatment. All participants were asked to record the headache diaries from week -4 to 32, and the number of monthly headache days was calculated from headache diaries. Headache frequency, duration, intensity, accompanying symptoms, and use of acute medications (eg, analgesics) were recorded in the diaries.

Secondary outcomes included the number of headache days (we also calculated the change from baseline after treatment) every 4 weeks, headache intensity, use of acute medication, and safety outcomes. Headache intensity was measured by using a classification system: no headache (scored 0), mild headache (scored 1), moderate headache (scored 2), and severe headache (scored 3). The VAS score—a 10-cm

scale with 0 indicating no pain and 10 indicating the worst pain—was also measured for the evaluation of headache intensity. The use of acute medication was measured by calculating the incidence rate of participants who reported use of acute medication in every 4-week assessment. We suggested the participants to take acute medications that were effective for their headache before attending the trial. Safety outcome was measured as the rate of adverse events.

Statistical analysis

Regarding that the responder rate was 46% for TA and 35% for SA in a previous study,[4] we assumed an odds ratio (OR) of 1.35 in TA-versus-SA comparison in the primary outcome. Assuming a significance level of 0.05, a study power of 0.8, and a correlation coefficient of 0.5 between assessment intervals, we needed to recruit at least 218 participants (considering a drop-out rate of 10%) to reject the hypothesis that the effect of TA is equivalent to SA.

The analysis was performed based on the intention-to-treat principle, and participants who received at least one assessment for the primary outcome after randomization were included in the full analysis set (FAS). Missing values of the FAS were imputed through a multiple imputation method based on a bootstrapping algorithm.[13] Five datasets were imputed and pooled into one for the analysis (Amelia package in R 3.6.0).

The primary analysis of the study was to compare TA with SA in the primary outcome, and the analysis was performed with a logistic regression model that

accounted for the following variables—age, sex, disease duration, and the number of baseline headache days. The effect size of TA versus SA was calculated as odds ratio (OR); the adjusted OR, its corresponding 95% confidence interval (95%CI), and the p-value were calculated for each comparison in the model.

Secondary analyses were performed for secondary outcomes. A linear regression model was used to detect the between-group difference in the number of monthly headache days and mean VAS score, in which the same variables in the primary analysis were adjusted. An ordinal logistic regression model was used for between-group comparison in evaluating headache intensity, and the logistic regression model was used in evaluating the use of acute medication; the aforementioned variables were also adjusted for these two analyses. All analyses were performed in R (3.6.0), and a $p<0.05$ was considered a statistically significant difference.

Considering that the personality of the individual acupuncturist might have significant effects on outcomes[14], we added the covariate—acupuncturist—into the statistical models for the responder rate and the reduction in the monthly headache days, to detect whether there was any difference in treatment effects between the three acupuncturists.

The study protocol and statistical analysis plan are available in eSAP 1, eSAP 2, respectively.

Data availability: The study protocol and anonymized participant data regarding the primary and secondary outcomes will be made available by request from any qualified investigator.

RESULTS

Baseline characteristics

We screened 1230 potential candidates and included 218 of them in the trial; 110 participants were allocated to receive TA, and 108 participants were allocated to receive SA. The screening process and reasons for exclusion were shown in Figure 1. The mean age of the study population was 43.1±12.6 years, and the participants had a median disease duration of 130 months, a mean monthly headache attacks for 21.5 days. The proportion of participants taking acute medication was 33% in total (28.2% in the TA group versus 38% in the SA group, p=0.164). Table 1 shows the baseline characteristics of the participants in each group. The baseline parameters were comparable between groups.

Primary outcome

The primary outcome was the responder rate at week 16, and the results showed that 68.2% of the participants receiving TA responded versus 48.1% of the participants receiving SA (odds ratio, 2.65[95%CI, 1.5 to 4.77]; p<0.001). Table 2 shows that both TA and SA had the responder rate escalated from week 4 (20.1% in TA group versus 13.9% in SA group) to week 32 (68.2% in TA group versus 50% in

SA group). Significant between-group difference was found in all assessment time points except week 4. The largest between-group difference in responder rate was in week 12 (TA versus SA group; odds ratio, 3.33[95%CI 1.87 to 6.05]), and the smallest difference was in week 4 (odds ratio, 1.77[95%CI 0.85 to 3.81]). We found no significant difference in treatment effects between the three acupuncturists, and the results were similar to the main analysis after the covariate acupuncturist was added (week 12, odds ratio 3.3[95%CI 1.84 to 6.02]; week 32, odds ratio 2.48[95%CI 1.4 to 4.46]).

Headache days

The number of monthly headache days was gradually decreased after treatment, both in the TA and SA groups. The mean monthly headache days changed from 20.38±6.36 days at baseline to 7.48±7.97 days at week 32 in the TA group; while it changed from 22.6±6.16 days at baseline to 11.94±9.06 days in the SA group. After adjusting for covariates, we found significant between-group differences in all the assessment time points (Figure 2A). The largest difference was in week 12 (adjusted mean difference, 5.4 days [95%CI 2.8 to 8]), and the smallest difference was found in week 4 (adjusted mean difference, 2.21 days [95%CI 0.24 to 4.18]). We also analyzed the change-from-baseline in the number of monthly headache days and found consistent results with the number of headache days (Figure 2B). The results were still similar to the main analysis after the covariate acupuncturist was added.

Other efficacy outcomes

Table 3 shows the results in headache intensity, VAS score, and proportion of participants with acute medication usage. The proportion of participants reporting no headache intensity increased from 0.91% at week 4 to 30.91% at week 32 in the TA group; while the proportion also increased from 0% at week 4 to 10.2% at week 32 in the SA group. Significant between-group difference was found in weeks 16, 20, 24, 28, and 32 (Table 3).

The mean VAS score decreased from 4.46±1.58 cm at baseline to 2.39±2.27 cm in week 32 in the TA group (change-from-baseline value, -2.04±2.65 cm), while the VAS score decreased from 4.4±1.75 cm at baseline to 3.33±2.07 cm in week 32 (change-from-baseline value, -1.1±2.52 cm). Significant between-group difference was found in weeks 20, 24, 28, and 32, even after covariates were adjusted (Table 3). The proportion of acute medication usage was similar in the two groups, and no significant between-group difference was found (Table 3).

Safety outcome

Four participants reported four adverse events (three in the TA group and one in the SA group); two were subcutaneous hematoma (one in the TA group and the other in the SA group); two had a pain in the acupuncture site (all in the TA group). All the adverse events were mild, and the participants recovered without any required medical management.

Classification of Evidence

This study provides Class I evidence that acupuncture (achieving deqi sensation) reduces mean headache days (per month) in patients with chronic tension-type headache.

DISCUSSION

Main findings

Our study found that both TA and SA had clinically relevant treatment effects for the preventive treatment of CTTH, and TA is superior over SA in the primary outcomes and most of the secondary outcomes. The treatment effect of TA and SA persisted for 32 weeks (8 months) after randomization.

Strength of this study

According to a Cochrane systematic review,[6] previous RCTs had not assessed the effect of acupuncture over 6 months, and our study provided evidence for the acupuncture effect on CTTH with longer-term assessment (nearly 8 months). Secondly, most of the previous studies recruited both episodic and chronic TTH, and our study recruited only CTTH and confirmed the benefit of acupuncture in this population. Third, only one RCT with sufficient study power showed that TA was superior over SA in the preventive treatment for TTH,[5] and our study added new evidence for the superiority of TA over SA in the treatment of CTTH.

Comparison with other studies

The difference between acupuncture and sham acupuncture was debated in the field of chronic pain conditions. Although the Cochrane systematic review showed that acupuncture was superior over sham acupuncture for TTH in both the responder rate and the decrease in the number of headache days, questions are still raised: what does the specific effect of acupuncture depend on? —the selection of acupuncture points or the stimulation process of acupuncture? In an RCT, Endres and colleagues found that *deqi* sensation may be a key factor in the specific effect of acupuncture[5]; their trial found the responder rate significantly higher in acupuncture than in sham acupuncture (66% versus 55%). Our study confirmed this finding, and we further found that *deqi* sensation made difference in clinical effect even when the acupuncture points were the same in both groups, which might indicate that *deqi* sensation might be an independent contributor to the acupuncture effect. The mechanism of how *deqi* sensation affects the effect of acupuncture is unclear.[15,16] It might be the consequence of stronger stimuli at the neuronal sensory, which further leads to a stronger release of endorphins or neurotransmitters.[17,18] It might also be a part of a powerful non-specific effect, which was observed in patients who were given no sensory stimuli.[19] Additionally, since the acupuncture points were manually stimulated for *deqi* sensation, an extra attention of the acupuncturists to the participants might also contribute to the effect. A study from Korean found that *deqi* sensation could spread from the stimulation site to another place distal to the stimulation site.[17] This phenomenon indicates that *deqi* sensation

might spread to the pain site and suppress the pain through gate-control theory. It is worth to point out that in the TA group not only patients had the *deqi* sensation, traditionally linked to an anticipated clinical effect, but there were also additional needle manipulations during procedure twice every 10 minutes, which can also contribute to a significant placebo effect. In our study, we found the responder rate was similar between SA and previously reported sham acupuncture (50% versus 55% in 6-month follow-up), which further confirms that penetration of skin had a physiological effect. However, the mechanism behind it was unelucidated.[20,21] It could also be possible that the effect of sham acupuncture was regression to the mean, since we did not have a waiting-list control. However, the previous study testing the effect of acupuncture on TTH showed that it was unlikely to be only an effect of regression to the mean, in which participants in the waiting-list control group had a response rate of 4%.[4] Previous RCTs of TTH found that the effect of acupuncture persisted for 3-4 months after the treatment stopped[4,5,7,22], and similar findings were also reported in migraine trials.[23] Our study found that, after completion of the 8-week treatment, the acupuncture effect lasted for 24 weeks in the follow-up. The mechanism of the persistent acupuncture effect was unclear. It might be the result of headache education. However, the effect of headache education on CTTH has not been fully examined, the ongoing trial CHESS may provide some evidence in 2021.[24] One recent study showed that headache education reduce 2 migraine days per month, and our study showed a reduction of 14 days per

month indicating that headache education might not be the reason for the reduction of headache days.

It is noteworthy that the proportion of acute medication usage was similar in the two groups. In the TA group, the proportion of acute medication usage was changed from 26.4% at baseline to 14.5% at week 32 (a reduction of 12%); while, it changed from 37% to 21.3% in the SA group (a reduction of 16%). These findings indicated that both TA and SA were effective in decreasing the proportion of acute medication usage, but TA had no advantage in this outcome when compared with SA. However, the number of MHD decreased 14 days in the TA group versus 9.5 days in the SA group at week 32, which might indicate that TA had more advantages in reducing MHD than reducing medication usage.

Implications for clinical practice

The Cochrane systematic review[6] showed that acupuncture for 10-12 sessions over 5-10 weeks was effective for prophylaxis of TTH (the effect persisted for 3-4 months after initiation of treatment), and the review found a significant difference between acupuncture and sham acupuncture (responder rate, pooled RR 1.27, 95%CI[1.09 to 1.48], p=0.003) at 3-4 months after randomization (GRADE moderate quality). Our study confirmed these findings and added the knowledge that 20 sessions of acupuncture over 8 weeks could provide a longer relief of CTTH (lasting nearly 8 months after treatment initiation). Although the promising aspect of acupuncture for CTTH was clear, several clinical questions should be answered. First, the

Cochrane review showed that sham acupuncture was heterogeneity defined, and the effect of sham acupuncture exerts a higher responder rate than placebo pills. Therefore, acupuncture may be underestimated; should it be recommended for first-line treatment for CTTH? As a first-line treatment, it should have a comparative advantage in cost-effective value in comparison with pharmacological treatments. A large sample size RCT showed the benefit of acupuncture when compared with routine care,[25] but the inclusion of patients with migraine in the trial hampered a firm conclusion of whether acupuncture was superior to routine care. Second, is it comparable to other treatment options? The evidence of comparative effectiveness between acupuncture and first-line pharmacological (eg, antidepressants) or non-pharmacologic treatments (eg, physiotherapy, massage, and exercise) were either lacking or with low to very low quality. Third, how many sessions of acupuncture should be applied? The treatment sessions and treatment frequency of acupuncture varied across studies, which might affect the acupuncture effect. Future studies may focus on an individual patient data meta-analysis to determine the impact of the number of treatment sessions on CTTH prophylaxis.

We used a fixed and standardized acupuncture protocol in this trial, regarding that the change in the number of points used might benefit the TA group, since the SA group adopted a standardized protocol and the difference might be caused by the added points. In addition, our previous trial adopted a standardized acupuncture protocol with four points showed a favorable treatment effect for the prophylaxis of migraine.[26] However, adding points according to the headache phenotypes is

common in clinical practice, so future trials might focus on the benefit of adding points to the basic points.

Limitations

Our study is not exempt from limitations. First, the acupuncture points were the same in the two groups. Although this design increased the credibility of blinding, it may underestimate the effect of TA. From another perspective, the study still had the risk of unblinding[27], since acupuncture is common practice in China and we did not assess the credibility of the SA control. However, regarding that the two groups adopted the same number of acupuncture points and pain was also perceived as one of the *deqi* sensations in acupuncture practice[28], we assume that the blinding might be credible. Second, the study was conducted in one center. However, the Teaching Hospital of Chengdu University of TCM is the largest TCM hospital in Sichuan provinces, which attracted participants from the whole Sichuan province—the province has over 100 million residents and 56 ethnics. Therefore, the study results might be generalizable to the Chinese population—having also 56 ethnics. Third, the trial had a low percentage of participation. We assumed that there might be two main reasons. First, we used posters and advertisements on the internet that announced the recruitment of TTH patients, which attracted numerous patients to visit. However, many of them did not record their monthly headache days but felt that they might meet the inclusion criteria. After the 4-week baseline evaluation through headache diaries, we found that many of them had short disease duration

(<12 months) and were subsequently excluded. Second, many participants came from cities that were distant from our teaching hospital, and they refused to participate considering that they had to take an 8-week treatment. Fourth, compared with previous trials, we adopted a more intensive protocol of acupuncture. Although an intensified treatment might increase the effect size of treatment, it decreased the cost-effectiveness of acupuncture. According to previous reviews[29,30], TA seems to have better treatment effect than tricyclic antidepressants through naïve indirect comparisons, but the lack of direct comparison in comparative cost-effectiveness between TA and tricyclic antidepressants was still a limitation and an important question cared by the physicians. Availability and cost-effectiveness of acupuncture remain the main obstacle for acupuncture use in clinical practice, and changing the stimulation methods of acupuncture might be the solution. Fifth, the outcomes were all patient-reported, which is a concern in acupuncture trials—the acupuncturists were not blinded from group assignment.

Conclusions

Acupuncture was efficacious in the prophylaxis of CTTH, and the effect lasted for at least 8 months. However, the longer-term effectiveness of acupuncture and the comparative effectiveness and cost-effectiveness between acupuncture and other treatment options are still needed to be clarified.

Author contributions:

All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: HZ and YL.

Acquisition, analysis, or interpretation of data: TG, Q-HZ, L-YL, T-HH, S-SZ, S-YZ, X-YH

Drafting of the manuscript: HZ, TG, and Q-HZ

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: HZ

Administrative, technical, or material support: LZ and F-RL

Supervision: YL, LZ, and F-RL

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Table 1. Baseline characteristics

Items	**TA Group (n=110)**	**SA Group (n=108)**
Age (year, mean, sd)	43.0 (12.5)	43.2 (12.8)
BMI index (kg/m^2, mean, sd)	22.5 (3.13)	22.3 (2.76)
Headache days (mean, sd)	20.4(6.36)	22.6(6.16)
VAS (cm, mean, sd)	4.46 (1.59)	4.37(1.73)
Total headache hours (hours, mean, sd)	162 (124)	199(161)
Female (n, %)	82(74.5)	75(69.4)
Disease duration (month, mean, sd)	131(131)	129(121)
Headache severity (n, %)		
Mild	57(51.8)	65(60.2)
Moderate to severe	53(48.2)	43(39.8)
Acute medication usage (n, %)		
Yes	29(26.4)	40(37)
No	79(71.8)	67(62)
Unclear	2(1.8)	1(1)

Frequency of acute medications (n, %)		
Almost at every attack	4 (3.6)	2 (1.9)
Occasionally	20 (18.2)	23 (21.3)
Seldom or no use	86 (78.2)	83 (76.8)
Class of acute medications (n, %)		
Not using acute medications	79 (71.8)	67 (62)
NSAIDs	21(19.1)	32(29.6)
NSAIDs + opioids	3(2.7)	1(0.9)
Others	5(4.6)	5(4.6)
Triptans	0(0)	2(1.9)
Unclear	2(1.8)	1(1)
Medication overuse headache (n, %)		
Yes	4 (3.6)	2 (1.9)
No	106 (96.4)	106 (98.1)

Abbreviations: SA, superficial acupuncture. TA, true acupuncture. VAS, visual analog scale.

Annotations: The baseline characteristics were comparable between groups. The headache days and total headache hours were measured in a 4-week period before randomization.

Table 2. The responder rate

Assessment time	TA Group (n, %) (N=110)	SA Group (n, %) (N=108)	TA versus SA [adjusted OR (95%CI)]	P-value*
Week 4	23(20.1)	15(13.9)	1.77(0.85 to 3.8)	0.134
Week 8	59(53.6)	37(34.3)	2.27(1.29 to 4.04)	0.005
Week 12	69(62.7)	39(36.1)	3.33(1.87 to 6.05)	<0.001
Week 16	75(68.2)	52(48.1)	2.65(1.5 to 4.77)	<0.001
Week 20	71(64.5)	48(44.4)	2.46(1.4 to 4.4)	0.002
Week 24	75(68.2)	53(49.1)	2.39(1.35 to 4.29)	0.003
Week 28	72(65.4)	51(47.2)	2.53(1.43 to 4.55)	0.002
Week 32	75(68.2)	54(50)	2.4(1.36 to 4.3)	0.003

Abbreviations: OR, odds ratio. SA, superficial acupuncture. TA, true acupuncture.

Annotations: At the end of acupuncture treatment (week 8), the TA group showed a significant higher responder rate than the SA group, and the significant difference lasted to week 32.

Table 3. Secondary outcomes

Assessment time	**TA group (N=110)**	**SA group (N=108)**	**Difference between groups**	**P-value***
Headache intensity	N (%)	N (%)	Adjusted OR (95%CI)	
Week 4				
No headache	1(0.9)	0(0)	1.13(0.59 to 2.16)	0.716
Mild	84(76.4)	85(78.7)		
Moderate to severe	25(22.7)	23(21.3)		
Week 8				
No headache	5(4.5)	5(4.6)	1.02(0.52 to 2.01)	0.948
Mild	88(80)	87(80.6)		
Moderate to severe	17(15.5)	16(14.8)		
Week 12				
No headache	13(11.8)	12(11.1)	1.17(0.64 to 2.17)	0.608
Mild	79(71.8)	82(75.9)		
Moderate to severe	18(16.4)	14(13)		
Week 16				
No headache	19(17.3)	13(12)	1.74(0.97 to 3.17)	0.065
Mild	71(64.5)	83(76.9)		
Moderate to severe	20(18.2)	13(12)		
Week 20				
No headache	25(22.7)	11(10.2)	1.73(1.01 to 2.99)	0.048
Mild	64(58.2)	74(68.5)		

Moderate to severe	21(19.1)	23(21.3)		
Week 24				
No headache	31(28.2)	14(13)	2.01(1.16 to 3.52)	0.014
Mild	63(57.3)	77(71.3)		
Moderate to severe	16(14.5)	17(15.7)		
Week 28				
No headache	36(32.7)	17(15.7)	1.88(1.12 to 3.17)	0.016
Mild	51(46.4)	64(59.3)		
Moderate to severe	23(20.9)	27(25)		
Week 32				
No headache	34(30.9)	11(10.2)	2.14(1.27 to 3.65)	0.004
Mild	55(50)	69(63.9)		
Moderate to severe	21(19.1)	28(25.9)		
VAS score	Mean (sd)		Adjusted mean difference (95%CI)	
Week 4	3.36(1.5)	3.04(1.42)	0.32(-0.04 to 0.68)	0.08
Week 8	2.99(1.49)	2.66(1.52)	0.33(-0.06 to 0.73)	0.09
Week 12	2.86(1.74)	2.73(1.62)	0.13(-0.32 to 0.58)	0.572
Week 16	2.68(1.89)	2.93(1.84)	-0.25(-0.75 to 0.26)	0.339
Week 20	2.38(1.9)	2.98(1.8)	-0.6(-1.1 to -0.1)	0.019
Week 24	2.36(2.08)	3.06(1.76)	-0.7(-1.22 to -0.19)	0.008
Week 28	2.38(2.23)	3.25(2.07)	-0.88(-1.46 to -0.3)	0.003
Week 32	2.39(2.27)	3.33(2.07)	-0.94(-1.52 to -0.35)	0.002

Use of acute medication	N (%)		Adjusted OR (95%CI)	
Week 4	23(20.9)	26(24.1)	0.99(0.89 to 1.1)	0.851
Week 8	21(19.1)	34(31.5)	0.91(0.81 to 1.01)	0.073
Week 12	24(21.8)	28(25.9)	0.97(0.87 to 1.09)	0.645
Week 16	22(20)	21(19.4)	1.02(0.92 to 1.13)	0.693
Week 20	22(20)	29(26.9)	0.95(0.85 to 1.06)	0.341
Week 24	18(16.4)	20(18.5)	0.99(0.9 to 1.09)	0.848
Week 28	17(15.5)	24(22.2)	0.94(0.84 to 1.04)	0.212
Week 32	16(14.5)	23(21.3)	0.95(0.86 to 1.04)	0.266

Abbreviations: OR, odds ratio. SA, superficial acupuncture. TA, true acupuncture.

Annotations: The proportion of participants with no headache intensity increased after treatment in both groups, and the participants receiving TA had higher proportions of no headache intensity than those receiving SA. The findings were further confirmed in the VAS score. No significant difference was found between groups in the proportion of participants with acute medication usage.

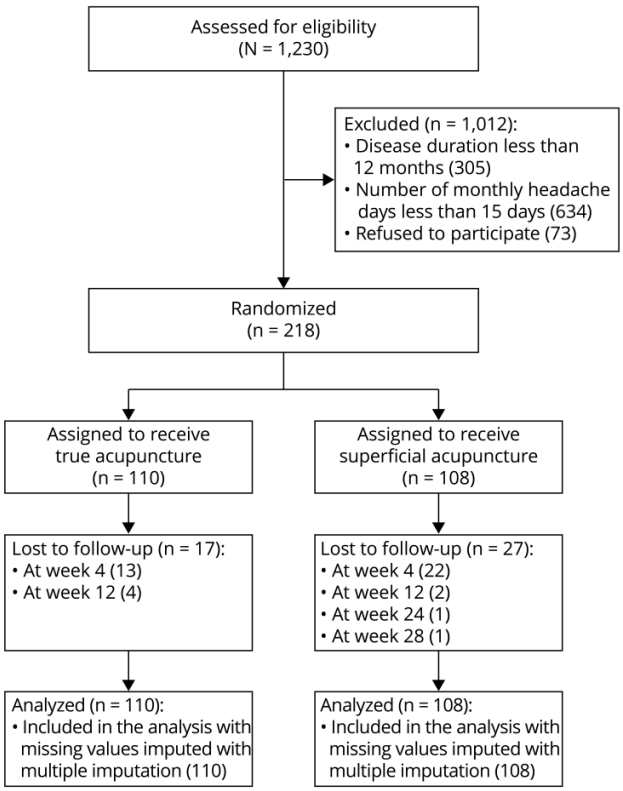
Figure legends

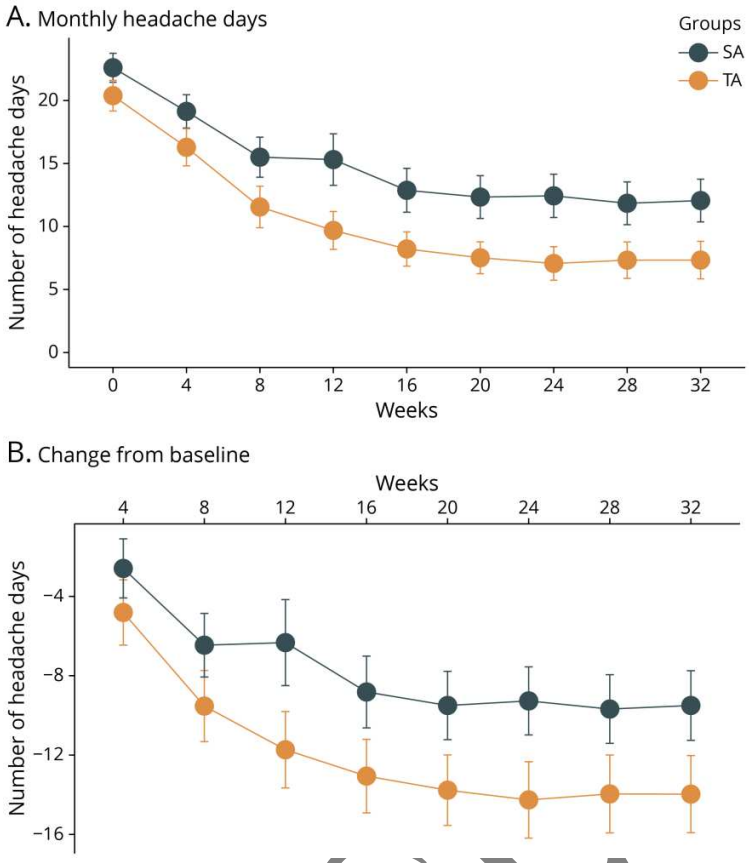
Figure 1. Study flowchart

Figure 2. The number of monthly headache days

Abbreviations: SA, superficial acupuncture. TA, true acupuncture.

Annotations: Figure 2 shows (A)the number of monthly headache days and (B) the change from baseline in the number of headache days. The results showed that the effect of TA lasted for 8 months after initiation of treatment, and the significant difference was found between groups from week 4 to week 32.





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