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Research Submissions

Acupuncture for Treating Acute Attacks of Migraine: A Randomized Controlled Trial

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Objective.—To discuss the results of a multicenter randomized controlled trial of the efficacy of verum acupuncture in treating acute migraine attacks.

Background.—Acupuncture has been used in China for centuries to treat migraine headache. Convincing evidence of its efficacy in alleviating pain, however, has been inadequate to date.

Methods.—A total of 218 patients with migraine were recruited for the study; 180 met the inclusion criteria; 175 completed the callback process and were randomized into 3 groups. One group received verum acupuncture while subjects in the other 2 groups were treated with sham acupuncture. Each patient received 1 session of treatment and was observed over a period of 24 hours. The main outcome measure was the differences in visual analog scale (VAS) scores before treatment and 0.5, 1, 2, and 4 hours after treatment.

Results.—Significant decreases in VAS scores from baseline were observed in the fourth hour after treatment when VAS was measured in the patients who received either verum acupuncture or sham acupunctures ($P < .05$). The VAS scores in the fourth hour after treatment decreased by a median of 1.0 cm, 0.5 cm, and 0.1 cm in the verum acupuncture group, sham acupuncture group 1, and sham acupuncture group 2, respectively. Similarly, there was a significant difference in the change in VAS scores from baseline in the second hour after treatment among the 3 groups ($P = .006$). Moreover, at the second hour after treatment, only patients treated with verum acupuncture showed significant decreases in VAS scores from baseline by a median of 0.7 cm ($P < .001$). Significant differences were observed in pain relief, relapse, or aggravation within 24 hours after treatment as well as in the general evaluations among the 3 groups ($P < .05$). Most patients in the acupuncture group experienced complete pain relief (40.7%) and did not experience recurrence or intensification of pain (79.6%).

Conclusion.—Verum acupuncture treatment is more effective than sham acupuncture based on either Chinese or Western nonacupoints in reducing the discomfort of acute migraine. Verum acupuncture is also clearly effective in relieving pain and preventing migraine relapse or aggravation. These findings support the contention that there are specific physiological effects that distinguish genuine acupoints from nonacupoints.

Key words: acupuncture therapy, acute migraine, acupuncture points, sham acupuncture, traditional Chinese medicine

Abbreviations: CRF case report form, GCP good clinical practice, ITT intent-to-treat, PP per-protocol, TCM traditional Chinese medicine, VAS visual analog scale

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Migraine headache is a common disorder characterized by moderate or severe symptoms aggravated by stressors. The pain is often pulsating and unilateral, and is usually accompanied by nausea or vomiting, phonophobia, or photophobia. Migraine headaches impose significant healthcare, economic, and social costs.[1] Although many migraine patients benefit in some respects from medications,[2] they also continue to experience discomfort, interference with activities of daily life, and other adverse effects from pharmacological treatments. Acupuncture is a traditional Chinese method for treating migraine and other headaches that has been widely used in clinical practice for many years. It has recently gained acceptance in the West as a complementary or alternative treatment for relieving the pain of and preventing migraine attacks. A recent randomized trial showed that acupuncture leads to long-term clinically relevant benefits for patients with chronic headache, particularly migraine.[3] These findings are consistent with much of the previous literature on acupuncture as a treatment for headache.[4-6]

In recent years, however, several randomized controlled trials showed that verum acupuncture is no more effective than sham or minimal acupuncture in reducing the pain of migraine and tension headaches, although it is more effective than no treatment.[7,8] Other researchers have noted that the results of investigations of acupuncture as a treatment for migraine are difficult to interpret,[9] while still others have pointed out that the placebo effect is a confounding factor in evaluating the effectiveness of acupuncture in relieving migraine pain.[10] The present multicenter randomized controlled trial of verum acupuncture in acute migraine treatment was intended to investigate whether verum acupuncture is more effective than sham acupuncture in reducing the pain of migraine headaches.

METHODS

Study Design.—The design and protocol for this trial were developed cooperatively by a group that included acupuncture experts, acupuncture practitioners, neurologists, methodologists, and statisticians. The study was designed as a multicenter single-blind randomized controlled trial.

Settings and Locations.—Seven hospitals participated in the study: First Affiliated Hospital of Chengdu University of Traditional Chinese Medicine (TCM), People's Hospital of Sichuan Province, Number Four People's Hospital of Sichuan Province, First Affiliated Hospital of Hunan University of TCM, Number One People's Hospital of Wuhan City, TCM Hospital of Wuhan City, and Number 452 Hospital of the Liberation Army.

Chinese medical practice differs from the Western model in that patients go directly to a hospital when they are ill. The 7 hospitals involved in this study are not specialized acupuncture facilities; they offer both Western and traditional Chinese therapies. Patients can therefore choose, usually on an outpatient basis, either the neurology department or the acupuncture department of the same hospital when they have a headache.

Sample Size Determination.—A sample size of 52 patients per group was calculated in the original protocol to yield 90% power for detecting a mean change of 2 cm with SD of 1.6 cm on the visual analog scale (VAS) between before and after treatment in a sham acupuncture group.[7] The authors estimated a dropout rate of 15% and therefore aimed to enroll 180 patients.

The intent-to-treat (ITT) population was defined as all randomized patients with a baseline measurement who had at least 1 postbaseline efficacy evaluation. The per-protocol (PP) population was defined as randomized patients who followed procedure throughout the study without major deviations.

Randomization.—Central randomization was used in this trial. The randomization was performed by the National Clinical Trial Center of Chinese Medicine (Chengdu, China), also known as the Good Clinical Practice (GCP) Center of China. Treatment allocation was performed before site initiation. Permuted-block treatment allocation was used to assign participants to each group. A list of sequential numbers was generated using a permuted-block randomization procedure with a block size of 9 in SAS 9.0, with each number randomly assigned to 1 group. Patients meeting the inclusion criteria were randomly assigned in a 1 : 1 : 1 ratio to the verum acupuncture treatment group or to 1 of 2 control groups.

The full randomization process described in the preceding paragraph was preprogrammed and carried out by the main server at the GCP Center. Investigators from the various participating centers would normally send mobile phone messages that included basic demographic information for the test subjects, including name, age, and sex to the main server located within the GCP Center. (All the investigators' mobile phone numbers were preapproved and registered after they had completed a special training course.) A random number and group assignment for each patient were automatically sent back to each investigator by the main server via a reply to the mobile phone message. This procedure assured that randomization would not be influenced by either the acupuncturists or the patients. Each patient was assigned a unique number based on his or her order of enrollment. The investigators received a confirmation email at the same time. This emailed random number, along with the group assignment code, was then attached to the test subject's case report form (CRF).

Blinding.—The sham acupuncture group was divided into 2 subgroups, sham acupuncture group 1 and sham acupuncture group 2, the subgroups defined by different methods for locating the nonacupuncture points. Patients in all acupuncture groups were blinded as to which treatment they received; patients were informed, however, that they would receive either sham acupuncture or acupuncture treatment with different acupoints that had been associated with positive outcomes in clinical studies. Because of the limitations of the clinical facilities available to us, we were unable to ensure the complete blinding of the patients during treatment; we therefore consider this trial single-blind. The researchers who analyzed the data were completely blind to the patients' group and treatment assignments.

Guidelines.—The study was performed according to GCP guidelines for clinical trials and in accordance with the tenets of the Declaration of Helsinki (World Medical Association).

Approval.—The local institutional review board and ethics committee approved the trial protocol, and written informed consent was obtained from all participants before enrollment. All patients were given adequate time for informed consent; they were also given treatment options other than acupuncture if they did not wish to participate.

Patients/Participants.—*Inclusion Criteria.*—Patients included in this study met the diagnosis of migraine with or without aura according to the classification criteria of the International Headache Society,[11] with 1 or more migraine attacks per month during the last 3 months and acute migraine attacks for at least 1 year. Patients had to be having an acute attack at the time of enrollment. All subjects were between 18 and 65 years of age with the age at onset of migraine less than 50 years, and had not taken any medicine for migraine within 24 hours after the beginning of the acute attack. All patients had also provided written informed consent by themselves or through their relatives.

The subjects were asked not to take any medicine during acupuncture treatment. The name of the medication and dosage had to be documented if subjects took medicine because their pain was not alleviated after treatment. Patients were required to sign the informed consent form before enrollment and acknowledge acceptance of one of the needling treatments and related inquiries for 24 hours before and after treatment.

Exclusion Criteria.—Patients with any of the following conditions were excluded: headache caused by such organic disorders as subarachnoid hemorrhage, cerebral hemorrhage, cerebral embolism, cerebral thrombosis, vascular malformation, arteritis, hypertension, or arteriosclerosis. Other conditions of exclusion included psychosis, pregnancy, immunodeficiency, bleeding disorders, allergies, or participation in another trial.

Acupuncture Personnel.—All acupuncturists participating in the study were required to take special training in order to understand the details of this trial. They were trained in the use of the central randomization method and completion of the CRF and electro-CRF as well as the locations of the acupoints and correct manipulation of the needles. All acupuncturists were required to complete all the training and to have passed a special examination to qualify for this trial.

Interventions/Treatment.—The treatment protocol for this study was developed over a 6-month period. Interventions were carried out according to traditional records and contemporary research findings regarding the effectiveness of acupuncture in treating migraine in China or the West. The interventions were formed in consensus with Chinese acupuncturists and acupuncture experts. Both acupuncture and sham acupuncture treatments were administered by specialized acupuncture practitioners.

The treatment for each patient consisted of 1 session of either verum or sham acupuncture followed by observation over a 24-hour period. Filiform needles were used in both the verum acupuncture group and the 2 sham acupuncture groups. Subjects in the verum acupuncture group received needling at genuine acupoints while subjects in the 2 sham acupuncture groups received needling at predesignated nonacupoints. The VAS scores before randomization and 0.5, 1, 2, and 4 hours after randomization were used as the main outcome measure. Subjects were asked to keep a headache diary for recording details of pain during their enrollment in the study.

The verum acupuncture group was given a treatment that used the following acupoints: *Waiguan* (TE 5), *Yanglingquan* (GB 34), *Qiuxu* (GB 40), *Jiaosun* (TE 20), and *Fengchi* (GB 20) used bilaterally. The locations of those points are those defined in 1993 by the World Health Organization, Regional Office for the Western Pacific.[12] The 2 control groups were given sham acupuncture treatment, that is, needling at nonacupuncture points. The nonacupoints used in control group 1 were located halfway between the Triple Energizer and Small Intestine meridians lateral to *Waiguan* (TE 5) horizontally; halfway between the line from *Qiuxu* (GB 40) to *Jiexi* (ST 41); halfway between the Gallbladder and Bladder meridians lateral to *Yanglingquan* (GB 34) horizontally; halfway between the line from *Jiaosun* (TE 20) to *Shuaigu* (GB 8); and halfway between the line from *Fengchi* (GB 20) to *Anmian* (extra point) bilaterally.

The nonacupoints used in control group 2 were located in the medial arm on the anterior border of the insertion of the deltoid muscle at the junction of the deltoid and biceps muscles;[13] the inside of the mid-thigh region 2 cm lateral to half the distance from the anterior superior iliac spine to the lateral superior corner of the patella on the rectus femoris;[13] the edge of the tibia 1 to 2 cm lateral to the *Zusanli* (ST 36) point horizontally;[14] halfway between the tip of the elbow and the axillae;[15] and halfway between the epicondylus medialis of the humerus and ulnar side of the wrist[15] bilaterally.

All acupoints and nonacupoints were stimulated by filiform Huatao needles (Suzhou Medical Supplies Co., Ltd., Suzhou, China). These are sterile single-use acupuncture needles, 25-40 mm in length and 0.30 mm in diameter. Subjects in the treatment group experienced the twinge or tingling sensation (*de qi*) associated with verum acupuncture when the operators inserted or twirled and rotated the needles; subjects in the control groups did not experience *de qi*. Subjects in the verum acupuncture group and both control groups were asked to retain the needles for 30 minutes and then close the acupoint holes with clean cotton balls to prevent bleeding when withdrawing the needle.

Outcome Measurement.—Primary outcome measure was the change in VAS scores from baseline at 0.5, 1, 2, and 4 hours after treatment. Secondary outcome measures included the time point of pain relief, completeness of pain relief, recurrence or intensification of pain, and a general effectiveness evaluation.

The VAS is a common standard for measuring pain syndrome; the scale is graded from 0 to 10 cm, with 0 representing absence of pain and 10 excruciating pain. The intensity of the pain experienced by the subjects was the primary observable outcome measurement. The VAS score was recorded by the subjects after needling treatment. Before treatment, the patients were taught to assess the score by a researcher. The VAS scores were calculated on the basis of the comparison between the baseline figures and the figures after treatment, specifically the lowering of the scores after treatment. For example, the baseline VAS score in 1 instance was 5.5; after treatment it was 4.5; therefore, the VAS reduction score was –1.

All subjects had to complete a VAS score before randomization (baseline), and additional scores 0.5, 1, 2, and 4 hours after treatment. In addition, patients

were asked to keep a headache diary and record the time when the pain started to ease; to note the completeness of pain relief 24 hours after treatment; medication use if any; and recurrence or increased severity of pain 24 hours after treatment. In addition, the subjects provided a general evaluation of acupuncture effectiveness after the treatment was complete.

All adverse events and their outcomes were recorded during or after acupuncture treatments. These adverse events included bleeding, hematoma, fainting, severe pain, and local infection.

Statistical Analysis.—Demographic parameters and other baseline characteristics were analyzed by treatment groups for randomized population. Analysis of the primary outcome measurement was based on the ITT population and analysis of the secondary outcomes was based on the PP population. Comparability among the 3 treatment groups was employed using analysis of variance for continuous variables. Data are presented as mean ± standard deviation (SD); if the normality of those variables could not be assumed, the data are presented as a median (interquartile range) and the Kruskal–Wallis test was used instead.

When there was a significant difference between groups, pairwise multiple comparisons were performed using the Bonferroni procedure with a type I error adjustment ($\alpha = 0.017$). Moreover, a chi-square/Fisher exact test was used for categorical variables; the data are presented as numbers (percentages). The Wilcoxon signed ranks test was used to compare VAS scores before and after treatment in each group.

All statistical assessments were 2-sided and evaluated at the 0.05 level of significant difference. Statistical analyses were performed using SPSS 15.0 statistics software (SPSS Inc., Chicago, IL, USA) and SAS 9.0 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Demographic Data.—A total of 218 patients entered our trial between July and September 2007. Thirty-eight patients were excluded; 11 failed to meet inclusion criteria, 13 were not having a migraine attack at the time they were interviewed, and 14 were afraid of acupuncture. In all, 180 patients participated in randomization. The screening failure rate was 17.4%. Five patients were randomly assigned incorrectly at 1 study center because mobile messaging was blocked during callback. In all, 175 patients (58 in the verum acupuncture group; 60 in the sham acupuncture group 1; and 57 in the sham acupuncture group 2) were randomly assigned. Of the 175 patients, 106 (60.6%) were females.

Among the patients randomized, 12 patients (6.9%) did not complete the study. Figure 1 is a flow chart of the trial that presents the reasons for early termination in detail. In the acupuncture group, 54 of 58 patients (93.1%) completed the study while 4 withdrew early. In the sham acupuncture group 1, 54 of 60 patients (90.0%) completed the study while 6 withdrew early. In the sham acupuncture group 2, 55 out of 57 patients (96.5%) completed the study while 2 patients were terminated early.

According to the definitions of the ITT and PP populations, the ITT population comprised 169 patients and the PP population comprised 163 patients among the 7 hospitals.

Baseline Characteristics.—The groups were comparable in baseline characteristics (Table 1), including the objective parameters of age, sex, diagnosis, location and nature of headache, accompanying symptoms, and VAS scores. Thus there were no statistically significant differences among the treatment group and the 2 control groups ($P > .05$). A significant difference was found only in the duration of disease ($P = .014$). This difference was not considered important because only patients with acute attacks of migraine were enrolled in the study; moreover, the VAS scores before randomization did not show significant differences between the treatment group and the 2 control groups ($P > .05$).

Primary Outcome Measurements.—The differences in the VAS scores among the 3 groups at each time point are shown in Figure 2, indicating significant differences in the VAS scores at the second ($P = .032$) and fourth hours ($P = .028$) after treatment among 3 groups. Moreover, significant differences were found in the VAS scores at the second ($P = .014$) and fourth hours ($P = .007$) after treatment between the verum acupuncture group and the sham acupuncture group 2. The observed median VAS scores for the

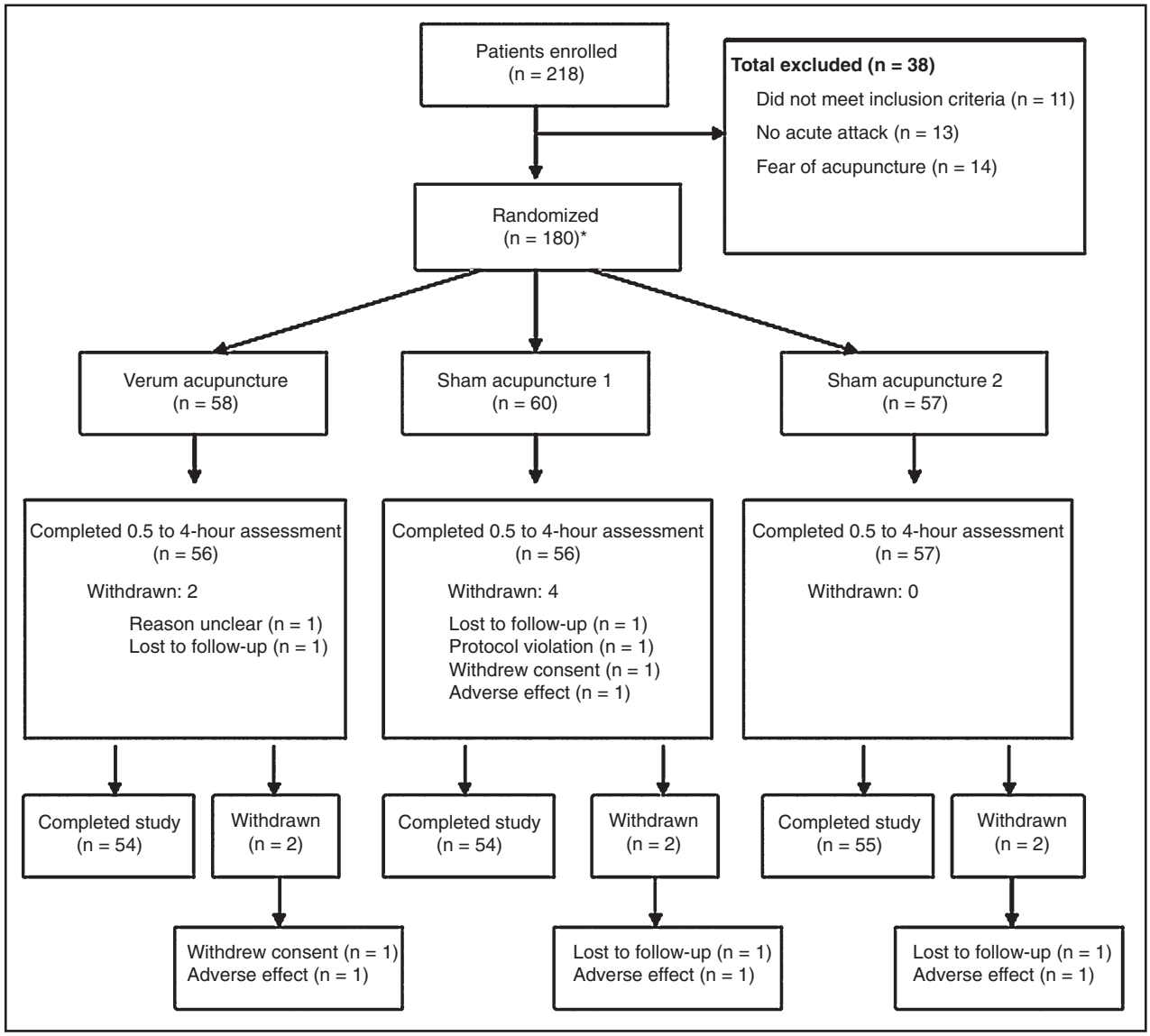

Fig 1.—Trial flow chart. *Five patients were enrolled but not randomized; requests for their random number and group allocation were sent via mobile message; however, replies from the main server failed to return because of temporary blocking of the mobile message system.

individual groups were measured; they are shown in Table 2. Furthermore, the primary outcome measure, the change in VAS scores from baseline at 0.5, 1, 2, and 4 hours after treatment, was examined using the Kruskal–Wallis test with Bonferroni method (pairwise multiple comparisons) with a type I error adjustment ($\alpha = 0.017$). The changes in VAS scores from baseline at each time point in the ITT analyses are shown in Table 2. Significant decreases in VAS scores from baseline were observed in the fourth hour after treatment, when VAS was measured in the patients who received either verum acupuncture or sham acupuncture ($P < .05$). In addition, there was a statistically significant difference among the treatment groups ($P = .012$). No significant difference was found between the 2 sham acupuncture groups ($P = .600$). The VAS scores in the fourth hour after treatment decreased by a median of 1.0 cm, 0.5 cm, and 0.1 cm in the verum acupuncture group, sham acupuncture group 1, and sham acupuncture group 2, respectively.

Similarly, there was a significant difference in the change in VAS scores from baseline in the second

Table 1.—Demographics and Baseline Characteristics of 175 Acute Migraine Patients

Characteristic	All patients (n = 175)	Acupuncture (n = 58)	Sham acupuncture 1 (n = 60)	Sham acupuncture 2 (n = 57)	*P* value
Age, years†	40.33 (12.90)	41.84 (14.21)	39.65 (12.83)	39.49 (11.60)	.550
Female, n (%)‡	106 (60.6)	33 (56.9)	33 (55.0)	40 (70.2)	.191
Migraine diagnosis, n (%)§					
Without aura	162 (93.1)	54 (93.1)	55 (93.2)	53 (93.0)	
With aura	12 (6.9)	4 (6.9)	4 (6.8)	4 (7.0)	1.000
Location of headache, n (%)‡					
Left side	46 (26.3)	16 (27.6)	15 (25.0)	15 (26.3)	
Right side	48 (27.4)	17 (29.3)	16 (26.7)	15 (26.3)	
Both sides	55 (31.4)	14 (24.1)	23 (38.3)	18 (31.6)	
Other	26 (14.9)	11 (19.0)	6 (10.0)	9 (15.8)	.714
Nature of pain, n (%)§					
Pulsating	69 (39.4)	23 (39.7)	23 (38.3)	23 (40.0)	
Stabbing	18 (10.3)	3 (5.2)	11 (18.3)	4 (7.0)	
Dull	23 (13.1)	4 (6.9)	8 (13.3)	11 (19.3)	
Distention	58 (33.1)	26 (44.8)	16 (26.7)	16 (28.1)	
Other	7 (4.0)	2 (3.4)	2 (3.3)	3 (5.3)	.117
Accompanying symptoms, n (%)§					
None	80 (46.2)	22 (37.9)	30 (50.8)	28 (50.0)	
Sensitivity to sound and light	28 (16.2)	11 (19.0)	7 (11.9)	10 (17.9)	
Nausea or vomiting	60 (34.7)	22 (37.9)	20 (33.9)	18 (32.1)	
Other	5 (2.9)	3 (5.2)	2 (3.4)	0 (0.0)	.493
Duration of disease, years¶	3.38 (1.42, 10.00)	2.25 (1.25, 5.00)	3.08 (1.25, 8.50)	5.00 (2.25, 10.67)	.014*
VAS score, cm¶	5.0 (4.0, 5.8)	5.0 (4.0, 5.7)	5.0 (3.0, 5.8)	5.5 (3.5, 6.0)	.348

*Significant difference, $P < .05$.
P values based on †ANOVA, ‡chi-square test, §Fisher exact test, and ¶Kruskal–Wallis test.
Data presented as †mean (SD), ‡§number (percentage), and ¶median (interquartile range).
VAS = visual analog scale.

hour after treatment among the 3 groups ($P = .006$); however, no significant difference was found between the 2 sham acupuncture groups. Moreover, at the second hour after treatment, only patients treated with verum acupuncture showed significant decreases in VAS scores from baseline by a median of 0.7 cm ($P < .001$).

Secondary Outcome Measurements.—Table 3 presents the secondary outcome measurements (time of relief, extent of relief within 24 hours, use of medication, relapse or aggravation within 24 hours, and general evaluation after treatment) in PP analyses. Significant differences were observed in pain relief, relapse, or aggravation within 24 hours after treatment as well as in the general evaluations among the 3 groups ($P < .05$). Most patients in the verum acupuncture group experienced complete pain relief (40.7%) and did not experience recurrence or intensification of pain (79.6%). In addition, a total of 30.2% of the patients in the verum acupuncture group rated the general effectiveness of the treatment at 75% or higher.

Only 9 patients (5.1%) reported adverse effects during the study period. Three patients fainted during the needling, 1 patient suffered nausea and vomiting, 4 patients experienced mild bleeding and hematoma, and 1 patient reported pain and distention. All patients recovered quickly after treatment. No patient experienced a serious adverse event.

DISCUSSION

The study presented in this article comes from the first part of a clinical research project funded by China's National Key Basic Research Program (973 Program), and focused on comparing the efficacy of verum acupoints vs nonacupoints for treating acute

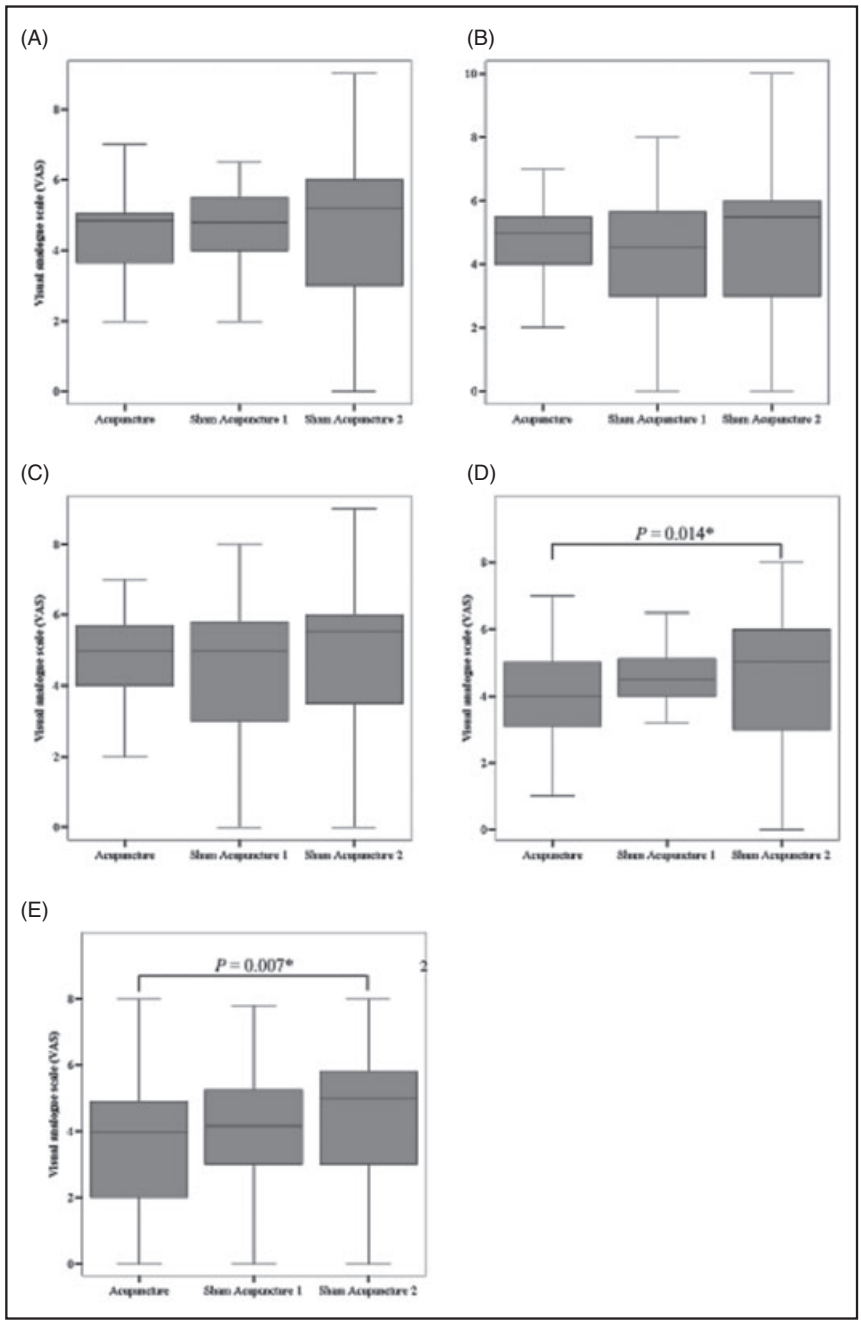

Fig 2.—VAS scores at various time points: baseline (A), 0.5 (B), 1 (C), 2 (D), and 4 (E) hours after treatment. VAS = visual analog scale. *Significant difference, $P < .05$.

migraine pain. Our trial is one of the largest randomized controlled trials outside Germany[16] addressing the effectiveness of acupuncture treatment to date, especially the specific physiological effects of therapeutic acupoints. Our findings from both observed VAS scores and changes in VAS scores from baseline at each time point (by pairwise multiple comparisons between groups determined by a Bonferroni test with $\alpha = 0.017$) demonstrate that verum acupuncture treatment is more effective than sham acupuncture in reducing the pain of acute migraine 2 and 4 hours after treatment, although verum acupuncture is not better than sham treatment at earlier time points, 0.5 and 1 hour after treatment, respectively.

Table 2.—Primary Outcome Measure for Observed VAS Scores and Changes in VAS Scores (cm) From Baseline at Each Time Point in ITT Analyses (n = 169)

Characteristic	Acupuncture (n = 56)	Sham acupuncture 1 (n = 56)	Sham acupuncture 2 (n = 57)	*P* value
Observed VAS scores (cm)				
0.5 hour after treatment	5.0 (4.0, 5.5)	4.6 (3.0, 5.7)	5.5 (3.0, 6.0)	.103
1 hour after treatment	4.9 (6.7, 5.1)	4.8 (4.0, 5.5)	5.2 (3.0, 6.0)	.166
2 hours after treatment	4.0 (3.1, 5.0)	4.5 (4.0, 5.1)	5.0 (3.0, 6.0)†	.032*
4 hours after treatment	4.0 (2.0, 4.9)	4.2 (3.0, 5.3)	5.0 (3.0, 5.8)†	.028*
Changes in VAS scores from baseline (cm)				
0.5 hour after treatment	0.0 (–0.3, 0.0)	0.0 (–0.2, 0.0)	0.0 (–0.1, 0.0)	.471
1 hour after treatment	–0.4 (–1.0, 0.0)†	–0.2 (–0.5, 0.1)	0.0 (–0.5, 0.0)	.063
2 hours after treatment	–0.7 (–1.5, –0.1)†	–0.3 (–0.8, 0.2)†	–0.2 (–0.7, 0.0)†	.006*
4 hours after treatment	–1.0 (–2.1, 0.0)†	–0.5 (–1.2, 0.1)†‡	–0.1 (1.0, 0.0)†‡	.012*

P values based on the Kruskal–Wallis test.
*Significant difference, $P < .05$.
†Indicates a statistically significant difference between each sham acupuncture group and the verum acupuncture group. Pairwise multiple comparisons between groups were determined using a Bonferroni test with $\alpha = 0.017$.
‡Indicates a statistically significant difference before and after treatment in each group using the Wilcoxon signed rank test.
ITT = intent-to-treat; VAS = visual analog scale.

We also found that verum acupuncture treatment is clearly effective in relieving pain and preventing relapse or aggravation, and that such treatment is rated by patients as superior to sham acupuncture in general effectiveness. This finding is consistent with evidence reported in the current literature comparing verum acupuncture with a variety of sham procedures. Although the results from these studies, such as the one published by Melchart et al,[17] also show that verum acupuncture treatment is superior to sham

Table 3.—Secondary Outcomes in PP Analyses (n = 163)

	Acupuncture (n = 54)	Sham acupuncture 1 (n = 54)	Sham acupuncture 2 (n = 55)	*P* value
Time of relief (hours)	0.43 (0.22, 0.50)	0.45 (0.33, 0.52)	0.45 (0.25, 0.50)	.937
Relief within 24 hours, n (%)				
Partial relief	32 (59.3)	45 (83.3)	46 (83.6)	.003*
Complete relief	22 (40.7)	9 (16.7)	9 (16.4)	
Medication, n (%)				
Took medication	33 (61.1)	33 (61.1)	37 (67.3)	.743
Did not take medication	21 (38.9)	21 (38.9)	18 (32.7)	
Relapse or aggravation over 24 hours, n (%)				
No relapse or aggravation	43 (79.6)	36 (66.7)	26 (47.3)	.002*
Relapse or aggravation	11 (20.4)	18 (33.3)	29 (52.7)	
General effectiveness evaluation, n (%)				
0%	3 (5.7)	7 (13.0)	18 (32.8)	<.001*
25%	19 (35.9)	25 (46.2)	27 (49.1)	
50%	15 (28.3)	15 (27.8)	4 (7.3)	
75%	11 (20.8)	5 (9.3)	5 (9.1)	
100%	5 (9.4)	2 (3.7)	1 (1.8)	

PP = per-protocol.

treatments, most of these earlier reports are based primarily on single-center studies with a small sample size. Compared with other recent multicenter trials,[18-20] our study focused on investigating the efficacy of verum acupuncture for alleviating pain in comparison with 2 types of sham acupuncture, and in patients suffering from acute migraine using a larger patient sample from multiple centers. Our study used central randomization to ensure adequate concealment in group assignment.

We took considerable time before the trial to define the control groups because the sham acupuncture procedures that were used are different from those of previous studies published in China and in the West. In most Chinese literature, the locations of nonacupoints selected for use lie beside the therapeutic acupoints and halfway between the lines of 2 acupoints[21,22] while many other reports in Western literature have recorded the locations of nonacupoints as lying at some distance from the meridians and true acupoints.[13,23] Our study took methods reported from the previous literature into serious consideration. In the end, the nonacupoints for the sham acupuncture groups were determined through consensus of the acupuncture experts. Filiform needles were used to stimulate both acupoints and nonacupoints, while the sensation of *de qi* was required only in the verum treatment group; there was no *de qi* elicited in subjects in the control groups. The manipulation of sham acupuncture needles in the present trial was different from that of sham acupuncture interventions in previous work,[7] in which minimal acupuncture was performed by using fine needles to penetrate the skin only superficially. The results of that previous trial, suggesting that verum acupuncture is not more effective than sham acupuncture in reducing migraine headache, are inconsistent with our findings.

The advantages of acupuncture treatment in this study are obvious when comparing these findings with those of other trials comparing the effectiveness of acupuncture to that of drug treatment.[4]

One limitation of the present trial was the lack of comparable baseline values 4 weeks before randomization. This trial had only 1 baseline measurement before randomization. Another limitation was the difference in the duration of disease among the subjects, which was found to differ significantly between the verum treatment group and the 2 control groups, probably because of the sample size.

In conclusion, our study demonstrates the effectiveness of verum acupuncture compared with that of 2 different types of sham acupuncture treatment in reducing the discomfort of acute migraine headache 2 and 4 hours after treatment. The findings presented in the article are consistent with most of the results reported in recent literature, both Chinese and Western. We maintain, however, that there must be different specific physiological effects that distinguish acupoints from nonacupoints, as has been suggested by Cabýoglu et al.[24] We hope to pursue this line of inquiry in future work. The second part of our clinical research project will involve a longer-term treatment of patients with migraine. In that study each patient's treatment will consist of 20 sessions observed over a 16-week period. The design and protocol of that study were published in *Trials* in October 2008.[25]

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