Manual Acupuncture vs Sham Acupuncture and Usual Care for the Prophylaxis of Migraine Without Aura: Protocol for A Randomized Clinical Trial

Clinical sites:

1. Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology

2. Hubei Provincial Hospital of Traditional Chinese Medicine

3. University Hospital of Huangjiahu Campus, affiliated with Hubei University of Chinese Medicine

4. Wuhan No.1 Hospital/Wuhan Hospital of Traditional Chinese and Western Medicine

5. Traditional Chinese Medicine Clinic of Hubei University of Chinese Medicine

6. Xiangyang No.1 People's Hospital, Hubei University of Medicine

7. The Second Hospital of Huangshi

Data Management and Statistical Centers:

Department of Scientific Research Management, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology

Trial registration

The protocol has been registered in ClinicalTrials.gov, with approval number NCT02765581.

Protocol version

Version number: 1.1. Version data: January 22, 2016

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Roles and responsibilities

The protocol was designed by Shabei Xu, Lingling Yu, Xiang Luo, Hua Wang, and Wei Wang. The funder had no role in study design, collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication.

1. Introduction

1.1 Background and rationale

Migraine is a highly prevalent neurological disorder. Epidemiological studies showed that approximately 23 percent of households in the United States contain at least one member suffering from migraine [1]. Migraines impose significant burdens on patients and society due to a high incidence of disability [2] and suicidal behavior [3]. Prophylactic treatment is proposed for migraineurs who suffering from two or more attacks per month [4]. Although prophylactic drugs may be efficacious, but pharmacological therapy usually associated with adverse effects and poor tolerability [5-7].

Current evidence supports the use of Traditional Chinese Medicine (TCM) in the management of migraine [8]. As a major non-pharmacological therapy in TCM, acupuncture found to be at least as effective as, or possibly more effective than, prophylactic drugs for the prevention of migraine attacks [9]. But in terms of demonstrating that patients benefit from acupuncture treatment beyond placebo effects, findings from sham-controlled trials are contradictory [10-13]. A Cochrane review indicates that acupuncture is effective in reducing migraine attacks, despite the efficacy of acupuncture is over sham, but this effect is still small [14]. One challenge in acupuncture research is the use of an appropriate control. It is reported that sham controls involving penetrating needle might have smaller effect sizes than trials that use non-penetrating sham controls [15]. Sham acupuncture involving penetrating needles appear to have important physiologic activity and should to be avoided in acupuncture research [15]. In recent years, non-penetrating sham acupuncture has been increasingly advocated as a sham control in acupuncture research [16,17]. Therefore, high-quality clinical trials are still needed to determine the efficacy of acupuncture for migraine.

1.2 Study Objectives and Hypothesis

We have designed a randomized controlled clinical trial to investigate the efficacy and

safety of manual acupuncture for migraine prophylaxis as compared with non-penetrating sham acupuncture and usual care.

2. Study Design and Methods

2.1 Study Design

This is a multicenter, stratified, single-blinded, randomized, controlled trial. In this study, 150 patients with migraine without aura (MWoA) will be randomized into the three groups through central randomization in a 2:2:1 ratio. The time period of this trial consisted of a 4-week baseline period before randomization, an 8-week treatment period following randomization and a follow-up period of an additional 12 weeks post-treatment. The study flowchart of study procedure was presented in **Figure 1**.

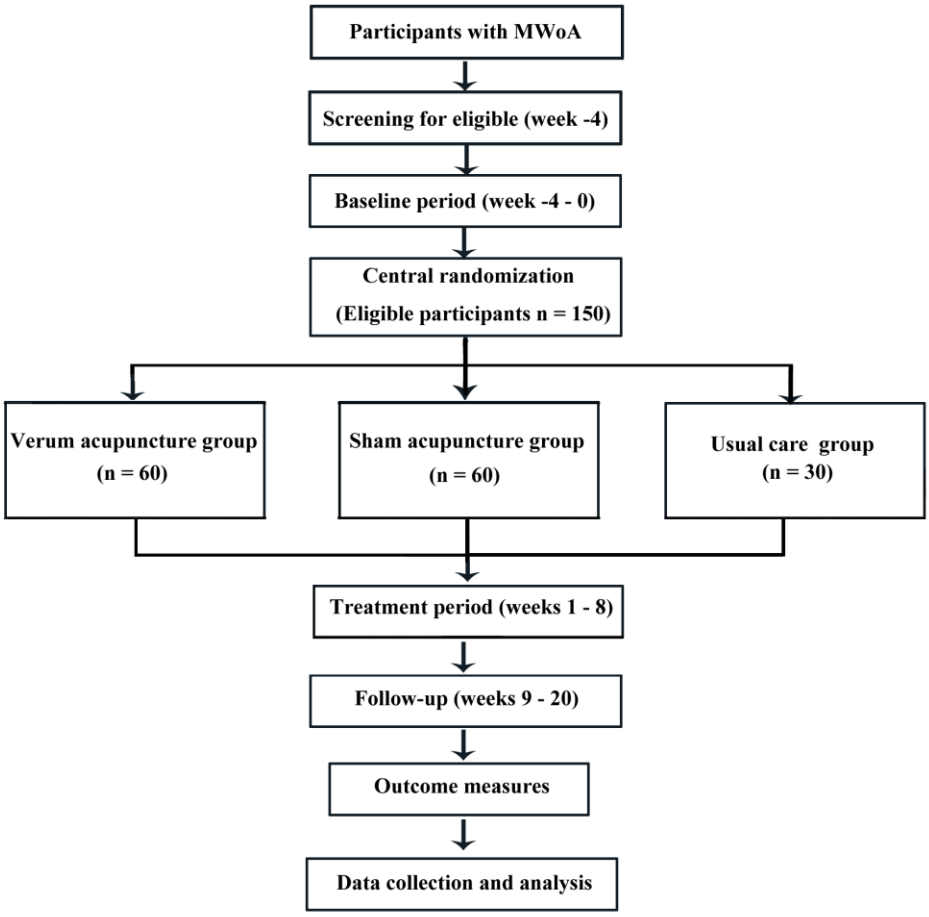

Figure 1. Trial flowchart. MWoA: Migraine Without Aura

2.2 Allocation

Eligible participants will be randomly allocated into manual acupuncture, sham acupuncture, or usual care groups, in a 2:2:1 ratio. The randomization sequence will be generated by a central randomization system (Absolute Clinical Data System Co., Ltd, Beijing, China) according to center-stratified, block randomization with a block size of five. Random numbers and group assignments will be offered to an independent researcher via the website of the central randomization system, who will not participate in any other process of the trial. Acupuncturists will know the group assignment only prior to treatment by telephone or mobile phone from this independent researcher. Central randomization system had strict limits regarding authority; access to the files is restricted to all other investigators. This procedure guarantees adequate that randomization concealment.

2.3 Blinding

Many efforts will be made for maintaining blinding in participants, outcome assessors, and statisticians. First, allocation sequence will be concealed until the end of the study. Second, we will recruit acupuncture-naive patients, using non-penetrating needles as the control, and design the same procedures to perform the same rituals as much as possible in the manual and sham acupuncture groups. Third, participants will receive manual acupuncture or sham acupuncture group in different clinics to prevent any communication in patients between the two groups. However, blinding is not possible for acupuncturists. In this trial, patients will be asked to guess whether they think the needles penetrate the skin at the end of the study.

3. Setting

This study will be conducted in the following hospitals: Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology; Hubei Provincial Hospital of Traditional Chinese Medicine; University Hospital of Huang Jia Lake Campus, affiliated with Hubei University of Chinese Medicine; Wuhan No.1 Hospital / Wuhan Hospital of Traditional Chinese and Western Medicine; Traditional Chinese Medicine Clinic of Hubei University of Chinese Medicine; Xiangyang No.1 People's

Hospital, Hubei University of Medicine; The Second Hospital of Huangshi.

4. Eligibility Criteria

4.1 Inclusion Criteria

Patients will be included if they had:

- Diagnosed as migraine without aura according to the International Classification of Headache Disorders, 3rd edition beta version (ICHD-3β) [18];
- Aged between 15 and 65 years old, with the initial onset of migraines before the age of 50 years;
- Experienced migraine attacks for at least 1 year;
- Experienced migraine attacks with 2-8 times per month during the last 3 months and baseline period, and the duration of migraine attacks lasting 4-72h without the intake of acute drugs or at least 2h with intake of acute drugs;
- Had not taken any acupuncture treatment before study entry;
- Able to complete the baseline headache diary;
- Able to sign an informed consent.

4.2 Exclusion Criteria

Patients will be excluded if they had:

- Tension-type headache, cluster headache, and other primary headache disorders, secondary headache disorders, neuralgia of the face or head;
- Combined with cardiovascular, liver, kidney, gastrointestinal tract, blood system and other serious primary diseases affecting the implementation of treatment programs, or combined with epilepsy, Parkinson or other nervous system diseases;
- Patients with severe mental illness, such as severe anxiety and depression;
- Pregnant women, women in lactation, and those planning to become pregnant;
- Participation in other clinical trials;
- Illiterate, or patients unable to read and understand scales;
- Had experience of acupuncture.

4.3 Recruitment

All patients will be recruited in the outpatient clinics of the participating hospitals by local advertising, hospital website, and hospital Public Accounts.

5. Interventions

The acupuncture treatment protocol was drafted according to Evidence-based Guidelines of Clinical Practice with Acupuncture and Moxibustion for Migraine and based on the consensus of clinical experiences of several acupuncture experts. Acupuncture treatment will be performed by licensed acupuncturists who had at least 5 years of acupuncture experience. All participants will receive 20 sessions of 30-minutes acupuncture and usual care over 8 weeks. In both manual acupuncture and sham acupuncture group, participants will be treated every other day to fulfill a 10-session treatment course, and another course will begin after resting 9 days. We set up the standardized ritual operations and performed them in both manual and sham acupuncture group. In the usual care group, participants were informed to receive acupuncture treatment for free after waiting 24 weeks and completed the whole visit. Usual care included clinical interview, counseling and health education.

5.1 Manual Acupuncture

Manual acupuncture will be applied at obligatory and additional acupuncture points. The obligatory points include bilateral Hegu (L14), Taichong (LR3), Taiyang (EX-HN5), Fengchi (GB20), and Shuaigu (GB8). Additional acupoints are selected based on meridian diagnosis and patient symptoms: bilateral Touwei (ST8) for Yangming meridian headache, Tianzhu (BL10) for Taiyang meridian headache, Baihui (DU20) for Jueying meridian headache. The location and insertion depth of these points was described in **Table 1**. The Streitberger acupuncture needle (size: 0.30mm in diameter and 30mm in length) will be used. After sterilization, the sharp needle will be inserted into the deep tissue layers of acupoint. Acupuncture *de qi* sensations will be obtained through the manipulation of needles (intermittently rotation as well as lift and thrust). In order to induce lasting acupuncture sensations.

Table 1: Acupoints used in the manual acupuncture group

Acupoints	Location	Depth of insertion
Hegu (LI4)	In the midpoint of the radial side of the 2nd metacarpal bone.	0.5 to 1 cun
Taichong (LR3)	Just in the depression distal to the junction of the first and second metatarsal bones.	0.5 to 0.8 cun
Taiyang (EX-HN5)	In the depression behind the tip of eyebrow and outer canthus around a transverse finger's distance.	0.3 to o.5 cun
Shuaigu (GB8)	1.5 cun a directly above the ear apex within the hairline when the ear is folded forward.	0.5 to o.8 cun
Fengchi (GB20)	In the depression between the upper ends of the sternocleidomastoid trapezius muscles.	0.8 to 1.2 cun
Touwei (ST8)	4.5 cun lateral to the midline of head and 0.5 cun directly above the hairline of the forehead.	0.5 to 1 cun
Tianzhu (BL10)	1.3 cun lateral to the midline of head and 0.5 cun directly above the posterior hairline.	0.5 to 0.8 cun
Baihui (DU20)	On the midline of the head, 7 cun directly above the midpoint of the posterior hairline.	0.5 to 0.8 cun

5.2 Sham Acupuncture

Non-penetrating sham acupuncture will be applied at eight non-acupuncture points on the back (**Table 2**). These points are located in different segments from headache, to avoid segmental effects on patients. The Streitberger placebo needle will be used for sham acupuncture. Instead of penetrating the skin, the tip of this needle is blunt and will be retracted up into the shaft when pressed it against the skin.

To maintain blinding in patients, acupuncture ritual is the same in both manual and sham acupuncture group. After sterilization, the acupuncturists will place a small plastic ring over the acupuncture point/non-acupuncture point and fix the ring with plaster, and then inserted the needle through the plaster inside the ring. During a 30-minutes duration, manual manipulation of each needle lasted 10 seconds and repeated a total of 4 times with an interval of 10 minutes. This caused patients unknown whether the treatment is true or sham (**Figure 2**).

Table 2. Sham points will be used in the sham acupuncture group

Non-acupoints	Location	Depth of insertion
Sham point 1-2	Bilateral, at the midpoint between the acupuncture points Jianjin (GB21) and Jugu (LI16).	NA
Sham point 3-4	Bilateral, at a distance of 5 cun from the seventh cervical spine.	NA
Sham point 5-6	Bilateral, at a distance of 5 cun from the eighth thoracic spine.	NA
Sham point 7-8	Bilateral, at a distance of 5 cun from the ninth thoracic spine.	NA

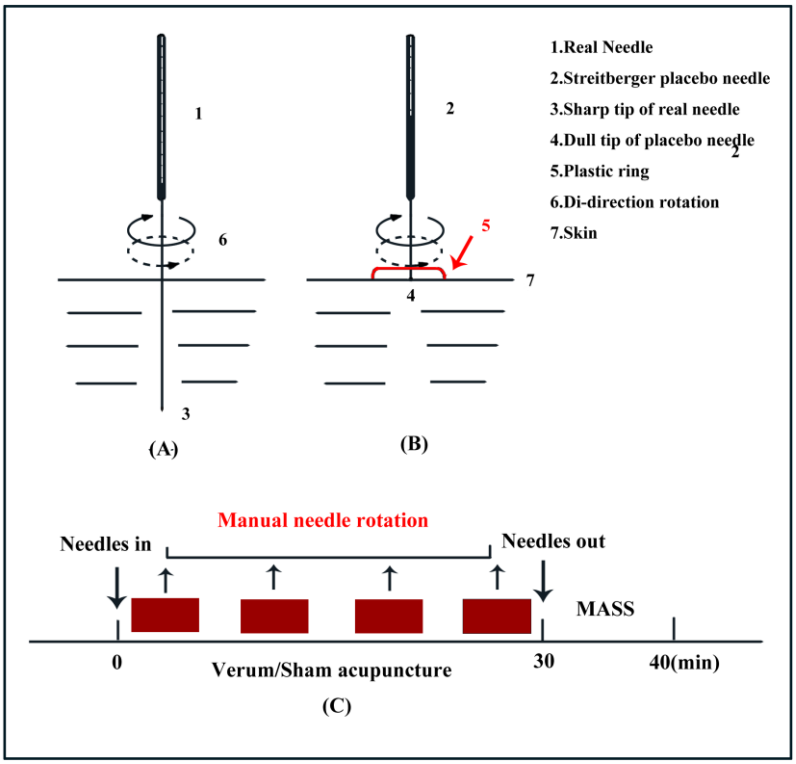

Figure 2. Acupuncture procedure. (A) The acupuncture needle will be inserted in the location of acupoints and be rotated bi-directionally until the patient feels strong acupuncture sensations. (B) The placebo needle will touch the skin of the sham point and will be rotated bi-directionally to blind the patient. (C) During each acupuncture treatment, manual needle rotation will be repeated a total of 4 times. The average acupuncture sensations of each treatment will be assessed by MASS 10 minutes immediately after treatment.

5.3 Co-interventions

For all groups, in case of severe pain (VAS score > 8), diclofenac sodium enteric-coated tablets (25mg / tablet; maximal tolerated dose = 200mg / day) will be allowed as a rescue medication. But in order to avoid confounding factors in the clinical outcomes, participants were instructed not to take any other analgesics and avoid commencing other co-interventions.

5.4 Strategies to Ensure Intervention Protocol Adherence

To improve adherence to intervention protocol, project acupuncturists attended a centralized training during the pilot trial, which included an introduction to intervention protocol and a practical demonstration of the Streitberger needles. The details of each treatment will be recorded on individual Case Report Forms by acupuncturists, which will be kept in a locked cupboard in the clinic and returned to the research team every 4 weeks. Adverse events were documented by both the patients and acupuncturists.

6 Outcomes

6.1 Primary Outcomes

1) The primary outcomes were change in migraine days per four weeks during weeks 1-20 after randomisation compared with baseline (four weeks before randomisation).
2) The primary outcomes were change in migraine attacks per four weeks during weeks 1-20 after randomisation compared with baseline (four weeks before randomisation).

6.2 Secondary Outcomes

1) The proportion of responders which is defined as the proportion of patients with at least a 50% reduction in the number of migraine days and migraine attacks at endpoints;
2) Changes in the intensity of the migraine headaches, which were measured by the VAS and the Short-Form McGill Pain Questionnaire 2(SF-MPQ-2)[19] from

baseline to endpoints;

3) Changes in migraine-related disability, which were measured by the Migraine Disability Assessment Scores (MIDAS)[20] from baseline to endpoints;
4) Changes in health-related quality of life, which will be measured by the Migraine-Specific Quality-of-Life Questionnaire (MSQ) [21] from baseline to endpoints;
5) Changes in sleep-related quality of life, which will be measured by the Pittsburgh Sleep Quality Index (PSQI) [22] from baseline to endpoints;
6) Changes in the intake dose of acute medication from baseline to endpoints;
7) Changes in acupuncture sensations measured by the Massachusetts General Hospital (MGH) Acupuncture Sensation Scale (MASS) [23] between manual acupuncture and sham acupuncture at weeks 1 to 8 after randomization (treatment phase).
8) Changes in anxiety measured by Beck Anxiety Inventory (BAI) [24] from baseline to endpoints;
9) Changes in depression measured by Beck Depression Inventory II (BDI- II) [25] from baseline to endpoints;
10) Personality measured by NEO Personality Inventory-Short Form (NEO-FFI) [26] between three groups at baseline;
11) Changes in Acupuncture Expectancy Scale (AES) [27] from baseline to endpoints (immediately after the third and after the 20th session of acupuncture).
12) Changes in Patient-Doctor Relationship Questionnaire (PDRQ-9) [28] from baseline to endpoints;
13) To test the blinding for group allocation, patients were asked to guess which type of acupuncture they received at the end of the study.
14) Adverse events were recorded after each treatment, including bleeding, subcutaneous hemorrhage, serious pain, palpitation, fainting, and local infection.

7. Participant Timeline

The participant timeline was described in **table 3**.

Table 3. Study design schedule

Period	Baseline		Treatment		Follow-up		
Week	**-4**	**0**	**4**	**8**	**12**	**16**	**20**
Screening	√						
Demography	√						
Informed consent	√						
Eligibility		√					
Randomization		√					
Manual acupuncture			√	√			
Sham acupuncture			√	√			
MASS			√	√			
AES	√		√	√			
Headache diary	√		√	√	√	√	√
Migraine days	√		√	√	√	√	√
Migraine attacks	√		√	√	√	√	√
Proportion of responders	√		√	√	√	√	√
VAS	√		√	√	√	√	√
SF-MPQ-2	√		√	√	√	√	√
MIDAS	√			√			√
MSQ	√		√	√	√	√	√
SF-36	√		√	√	√	√	√
PSQI	√		√	√	√	√	√
BAI	√			√			√
BDI- II	√			√			√
NEO-FFI	√						
PDRQ-9	√			√			√
DDPRQ-10	√			√			√

AES: Acupuncture Expectancy Scale; BAI: Beck Anxiety Inventory; BDI- II: Beck Depression Inventory II; MIDAS: Migraine Disability Assessment Scores; MSQ: Migraine-Specific Quality-of-Life Questionnaire; MASS: Massachusetts General Hospital Acupuncture Sensation Scale; NEO-FFI: NEO Personality Inventory-Short Form; PDRQ-9: Patient-Doctor Relationship Questionnaire; PSQI: Pittsburgh Sleep Quality Index; SF-36: 36-item Short-Form; SF-MPQ-2: Short-Form McGill Pain Questionnaire 2; VAS: Visual analogue scale;

8. Data Collection and Management

Participants will receive a paper-and-pencil headache diary and will be asked to complete from baseline to the end of the follow-up period. The diary will be collected

every four weeks separately from each hospital. All paper-based data will be entered into electronic data capture system hosted at the Translational Medicine Center of Tongji Hospital. The principal investigators (PI) and statisticians have access to the final trial dataset.

9. Sample Size Calculation and Statistical Analyses

9.1 Sample Size Calculation

To drive all the primary hypothesis tests, the sample size was estimated by using the Statistical Analysis System software (version 9.3) (SAS 9.3 Institute Inc., Cary, NC, USA). According to the fixed sequence procedure planned for the primary analyses, sample size required for each individual hypothesis testing was estimated at the two-sided α level 0.05. With other assumptions, the estimated sample sizes were summarized in **table 4**. To ensure adequate power for each individual hypothesis testing, a sample size of 135 were required, which consists of 54 subjects in the manual acupuncture group, 54 subjects in the sham acupuncture group and 27 subjects in the usual care group. To account for up to 10% attrition, the final sample size was 150.

Table 4. Sample sizes required for each individual hypothesis testing

Endpoint	Comparison	Assumptions	Sample Size
First primary endpoint	Verum acupuncture vs. Sham acupuncture	● Two sided α = 0.05 ● 90% power ● 1:1 randomization ratio ● Superiority design ● Expected difference in mean reductions between treatment groups = 1.8 ● Common standard deviation = 2.8	SS_{va} = 52 SS_{sa} = 52
	Verum acupuncture vs. Usual care	● Two sided α = 0.05 ● 90% power ● 2:1 randomization ratio ● Superiority design ● Expected difference in mean reductions between treatment groups = 2.2 ● Common standard deviation = 2.8	SS_{va} = 54 SS_{uc} = 27
Second primary	Verum acupuncture	● Two sided α = 0.05 ● 90% power	SS_{va} = 49 SS_{sa} = 49

endpoint	vs. Sham acupuncture	• 1:1 randomization ratio • Superiority design • Expected difference in mean reductions between treatment groups = 1.2 • Common standard deviation = 1.8	
	Verum acupuncture vs. Usual care	• Two sided $\alpha = 0.05$ • 90% power • 2:1 randomization ratio • Superiority design • Expected difference in mean reductions between treatment groups = 1.5 • Common standard deviation = 1.8	$SS_{va} = 48$ $SS_{uc} = 24$
SS = Sample Size			

9.2 Statistical Hypothesis

To demonstrate the effectiveness of manual acupuncture for migraine, co-primary endpoints will be used in this study. The first primary endpoint is the reduction from baseline in the mean number of migraine days measured during the 4-week cycle of weeks 17-20 compared from baseline. For the primary analyses, manual acupuncture group will be compared against both the sham acupuncture group and usual care group. The formal statistical hypotheses to be tested for the first primary endpoint are:

$H_1: \mu_{1va} \leq \mu_{1sa}$

$K_1: \mu_{1va} > \mu_{1sa}$

And

$H_2: \mu_{1va} \leq \mu_{1uc}$

$K_2: \mu_{1va} > \mu_{1uc}$

Where

H_1 and H_2 are the null hypotheses;

K_1 and K_2 are the corresponding alternative hypotheses;

μ_{va}, $\mu_{sa,}$ and μ_{uc} are mean values of the first primary endpoint in manual acupuncture, sham acupuncture, and usual care groups, respectively.

The second primary endpoint is the reduction from baseline in the mean number of migraine attacks measured during the 4-week cycle of weeks 17-20. The statistical

hypothesis tests will be constructed in the same manner as the first primary endpoint:

H_3: $\mu_{2va} \leq \mu_{2sa}$

K_3: $\mu_{2va} > \mu_{2sa}$

And

H_4: $\mu_{2va} \leq \mu_{2uc}$

K_4: $\mu_{2va} > \mu_{2uc}$

Where

H_3 and H_4 are the null hypotheses;

K_3 and K_4 are the corresponding alternative hypotheses;

μ_{2va}, $\mu_{2sa,}$ and μ_{2uc} are mean values of the second primary endpoint in manual acupuncture, sham acupuncture, and usual care groups, respectively.

9.3 Multiplicity

The superiority of the manual acupuncture over sham acupuncture or usual care can be claimed only when both co-primary endpoints are statistically significant. Therefore, it will not inflate the type I error when testing H_1 and H_3 individually at 0.05 level to demonstrate the superiority of manual acupuncture over sham acupuncture, or testing H_2 and H_4 individually at 0.05 level to demonstrate the superiority of the manual acupuncture over usual care. In addition, to adjust for the multiplicity problem arising from the multiple comparisons among manual acupuncture, sham acupuncture, and usual care group, fixed sequence procedure will be applied so that the family-wise error rate was controlled. The comparison between manual acupuncture and sham acupuncture group (H_1 and H_3) will only be performed when both co-primary endpoints are significant for the comparison between manual acupuncture and usual care (H2 and H4).

9.4 Statistical Analyses

Statistical analysis will be performed by the Translational Medicine Center, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China. The statistician will be blinded to group allocation until final

unblinding. Dummy treatment assignments will be generated by a data manager for the purpose of analysis programming preparation. SAS 9.3 will be utilized for data analysis.

Efficacy analyses will be conducted in the full analysis set (FAS), which will include all randomized subjects of whom the mean number of migraine days and attacks are measured in at least one post-baseline 4-week cycle. Missing data will be imputed by Last-Observation-Carried-Forward (LOCF) method. In addition, multiple imputation method will be considered when deemed necessary. For the primary endpoints, sensitivity analyses will be performed on the Per Protocol Set (PPS) to assess the robustness of the study conclusion to the choice of analysis population. The PPS is a subset of the FAS, which includes all randomized subjects who have no major protocol deviations. List of major protocol deviations will be reviewed and finalized prior to database lock in a blinded manner.

Continuous variables will be summarized by descriptive statistics, which will include the number of subjects, mean, standard deviation, median, minimum, maximum and interquartile range. For the comparison between two groups, unpaired t-test or Wilcoxon rank sum test will be used. When comparisons are made among at least three groups, analysis of variance (ANOVA) or Kruskal-Wallis test will be used. Paired difference will be tested by paired t-test or Wilcoxon signed rank test. Difference between groups will be tested by analysis of covariance (ANCOVA) when there are co-variables (for example baseline value) to be adjusted. The continuous longitudinal data will be analyzed by mixed model for repeated measures with a covariance matrix included.

Categorical variables will be summarized by frequencies and percentages of subjects in each category. Data will be analyzed by Chi-square test or Fisher's exact test when variables are nominal. In the case that a variable is ordinal, Wilcoxon rank sum test or CMH test for row mean score difference will be used. Paired categorical data will be analyzed by McNemar's test. Logistic regression will be used when there are co-variables. For both continuous and categorical variables, 95% confidence intervals will be calculated as appropriate.

Chi-square test, Fisher's exact test or ANOVA will be used for the analysis of baseline characteristics of different groups. Drop-out rates and implementation of protocol intervention will be utilized by Chi-square test or Fisher's exact test. The MASS index, a weighted average of the intensity of acupuncture sensations elicited, was calculated using previously published methods[33]. A one-way ANOVA and post hoc t-tests will be used for analyze of the MASS index across treatment modalities. All the statistical comparisons are two-sided. $P < 0.05$ will be considered significant.

10. Monitoring

All acupuncturists and researchers attended a special training before treatment to ensure their proper understanding of the protocol, and strict adherence to the study guidelines. Only acupuncturists knew the grouping scheme, and no researcher allowed to alter the assignment of a participant. Inspectors from the central structure of the study will check each research center monthly, and report to the investigator. The reasons and details for drop-outs or withdrawals will be documented.

11. Safety

Potential adverse events associated with acupuncture included fainting, hematoma, broken needle, infection, and bleeding. Should any adverse events occur, they will be recorded by the acupuncturist and the treatment will be temporarily stopped. An independent Data and Safety Monitoring Board composed of three experts, from different fields from the Chinese mainland, will monitor the performance and safety of the trial. The board has the right to make the final decision to terminate the trial.

12. Research Ethics Approval and Consent or assent

The trial was designed in accordance with the principles of the Declaration of Helsinki. The trial protocol (version number: 1.1, version data: January 22, 2016) has been approved by the Clinical Trial Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology(Ethics approval numbers: 2016S009) on March 16, 2016, the Ethics Committee of Hubei Province Hospital of Traditional Chinese Medicine (Ethics approval numbers: HBZY2016-C25-01) on May 4, 2016

and the Ethics Committee of Xiangyang No.1 Hospital (Ethics approval numbers: YN20171220) on December 20, 2017. Written informed consent will be obtained from each participant before they enter the trial.

13. Confidentiality

Confidentiality is ensured by storing data in a password-protected database, for which only the research team had the password. Paper-based record forms were identified by numbers and stored in a locked cupboard. Any published patient data were not allowed personal identification, only group data could be published.

14. Dissemination policy

Results of this trial are expected to published in peer-reviewed journals and presented at national and international meetings.

Abbreviations

AES: Acupuncture Expectancy Scale; ANOVA: Analysis of Variance; ANCOVA: Analysis of Covariance; BAI: Beck Anxiety Inventory; BDI- II: Beck Depression Inventory II; FAS: Full Analysis Set; IHS: International Headache Society; LOCF: Last-Observation-Carried-Forward; MIDAS: Migraine Disability Assessment Scores; MSQ: Migraine-Specific Quality-of-Life Questionnaire; MASS: Massachusetts General Hospital Acupuncture Sensation Scale; MWOA: Migraine without aura; NEO-FFI: NEO Personality Inventory-Short Form; PDRQ-9: Patient-Doctor Relationship Questionnaire; PPS: Per Protocol Set; PSQI: Pittsburgh Sleep Quality Index; RCTs: Randomized controlled trials;SF-36: 36-item Short-Form; SF-MPQ-2: Short-Form McGill Pain Questionnaire 2; TCM: Traditional Chinese Medicine; VAS: Visual analogue scale;

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