Informed Consent

Informed Page

Name of Project： Clinical study on the efficacy of women with migraine without aura by opposing needling

Source of project: the National Key R&D Program of China (2019YFC1709700), the Youth Special of Yunnan Province Ten-thousand Plan (YNWR-QNBJ-2019-257), and Science and Technology Innovation Team for Acupuncture, Moxibustion and Tuina Prevention and Treatment of Neurological Diseases in Yunnan Universities (2019YGC04).

Project research organization: College of Acupuncture and Tuina, Chengdu University of Traditional Chinese Medicine, Chengdu, China； School of Second Clinical medicine/The Second Affiliated Hospital, Yunnan University of Chinese Medicine, Kunming, China.

Research leader： Taipin Guo

Dear Mrs,

First of all, thank you for your interest in our clinical research! We will invite you to participate in a randomized controlled clinical trial of acupuncture in women with migraine without aura. This study has been approved by the Ethics Committee of the Sports Trauma Specialist Hospital of Yunnan Province. Before you decide whether to participate in this study, please read the following as much as possible to help you understand the research, the purpose, the research process and deadlines, and what may be brought after you participate in this study, which might be benefits, risks or discomfort. If you prefer, you can also discuss it with your family, friends, or ask your doctor for an explanation to help you make a decision.

Research introduction

I. Research background and research purposes

1. Research background

Migraine is a common clinical condition and is the second most disabling disease worldwide, affecting professional, academic, social, family and personal life. Migraine can also affect cardiovascular disease, psychiatric disorders and sleep disorders, and the disability-adjusted life years (DALYs) and economic burden of disease caused by migraine are increasing each year. The

prevalence of migraine is relatively similar across countries and is about two to three times higher in women than in men. In China, where there have been no large scale flow studies, the prevalence of migraine among medical students is about 10.8% (13.1% for women and 7.2% for men).

Acupuncture is safe and effective on migraine, and its efficacy has been recognized internationally in recent years. A study published in the BMJ showed that acupuncture was more effective in the prevention of migraine without aura attacks than sham acupuncture and conventional treatment, significantly reducing the number of headache days and the number of attacks. Another study published in JAMA Internal Medicine showed that long-term acupuncture for migraine significantly reduced the number of migraine attacks, number of days of headache, headache intensity and reduced medication use compared to sham acupuncture and waiting for treatment. Another study showed acupuncture to be as effective as the best available medication and superior to medication in terms of adherence and side effects.

The opposing needling (Jùcì) is an ancient classical acupuncture technique introduced in classical Chinese literature on acupuncture (*Huang Di Nei Jing*) that is more than 2000 years old. It refers to the acupoints on the right side (healthy side) are selected for diseases on the left (affected side) and vice versa. The opposing needling is now widely used for painful disorders of various causes and has good clinical efficacy. Migraine is mostly a unilateral headache, which is an indication for the left and right acupoints of the opposing needling, and the current treatment also shows a trend towards better efficacy. However, the available evidence is insufficient and a high quality RCT is necessary to demonstrate the efficacy of the opposing needling for migraine.

2. Research purposes

The purpose of this study was to evaluate the efficacy of opposing needling in women with unilateral migraine without aura.

3. Study expected number of participants

The study is expected to include 243 women with unilateral migraine without aura.

II. Who can participate in this study?

(1) Unilateral migraine, women, age is between 18-60 years old (the starting age is less than 50 years old);

(2) Meet the ICHD-3 diagnostic criteria for MwoA;

(3) In the past 3 months, the number of monthly migraine attacks is greater than or equal to 2 times, and the number of migraine days is less than 15 days per month;

(4) The severity of migraine attacks in the past 4 weeks (baseline period) is moderate to severe (average VAS score 4-9);

(5) Have a history of migraine for more than one year;

(6) Have not received acupuncture treatment within 1 month;

(7) Volunteer to participate and sign the informed consent.

(8) No other trials were taken within three months.

III. Who is not suitable for research?

(1) Patients with bilateral or alternating unilateral migraine;

(2) People with a history of head trauma, other primary headaches and headaches of unknown

diagnosis;

(3) People with a history of head trauma, other primary headaches and headaches of unknown diagnosis, or cervicogenic headache;

(4) Combined with severe anxiety, depression, insomnia, and another psychiatric disease or intellectual disabilities who cannot cooperate with the questionnaire, or infection, bleeding tendency, allergies and skin diseases;

(5) Pregnancy, lactation, or those who have fertility requirements in the next 6 months;

(6) Having the habit of taking analgesic and psychotropic drugs for a long time;

(7) Cannot understand or record the headache diary;

(8) Those who have participated in similar researches within 3 months.

IV. What will be done if you participate in the research?

If you meet the inclusion criteria and agree to participate, you will first need to undergo relevant tests to check that you meet all the requirements to participate in the study.

1. Before you are included in the study, you will undergo the following tests to determine if you can participate in the study.

(1) Your medical history, clinical signs and symptoms, current and past medications, physical examination and blood biochemistry will be interviewed and recorded. All these tests are free of charge and will have no adverse effect on your health or condition.

2. If you meet the inclusion criteria through the above screening, the study will be conducted according to the following steps:

(1) The trial will be divided into 3 groups. At the beginning of the study, your doctor will decide which group you will receive based on the random numbers provided by the computer.

(2) After enrollment in the group, you will be treated once every two days, approximately 3 times a week for 8 weeks, for a total of 24 treatments, with a follow-up of 8 weeks, and the whole process will last for 4 months.

(3) The acupuncture needles used in this study were Huatuo brand sterile single-use acupuncture needles made by Suzhou Medical Supplies Factory Limited, which had passed the inspection and obtained the production license (manufacturer's license: Su Food and Drug Supervision Production License No. 2001-0020, registration certificate No.: Su Food and Drug Supervision Machinery License No. 2004 No. 2270202).

(4) On the day of treatment, at the 4th week and 8 weeks after treatment, you should follow your doctor's instructions to visit the hospital and report truthfully to your doctor, who will ask questions to record changes in your condition and carry out physical and physical and chemical examinations. The doctor will also carry out relevant laboratory tests depending on the clinical situation.

3. Other matters requiring your cooperation

You must visit the doctor at the time appointed with you. Feedback on your condition is very important as your doctor will be able to determine whether the treatment you are receiving is working and provide timely guidance. It is also your responsibility to report to your doctor any changes in your body and mind during the trial, whether you think they are related to the study or not.

During the study period, you are asked to avoid the use of other medications for migraine without aura, and to take the non-steroidal anti-inflammatory drug fenpropathrin extended-release

capsules for pain relief if the headache is unbearable, and to take any previously effective pain medication. Record in detail the name, size, dose and duration of the medication taken and the duration of pain relief after taking it. Preventive medication for migraine is prohibited. Please contact your doctor in advance if another treatment is required. You are required to bring any other medication you are taking to each follow-up visit, including any medication you continue to take for other co-morbidities.

V. Possible benefits of participating in the study

You may benefit from this study, including the possibility of improvement in your condition, and if you participate in this study, you will receive relevant free screening and treatment and health education on migraine prevention during the study period.

VI. Adverse reactions, risks and protective measures for participating in the study

You may have soreness, numbness, heaviness and swelling during the acupuncture process, which are all normal reactions to acupuncture. There may be adverse reactions after needling, but they are rare and mild. You may feel dizzy during needling due to your physical condition or emotional stress, which can be relieved after stopping needling and taking proper rest; bleeding and haematoma may occur after needling, which will disappear after local pressure; however, if infection occurs at the site of needling, your doctor will deal with it promptly.

If you experience any discomfort, new changes in your condition, or any unforeseen circumstances during the study period, whether or not they are related to the acupuncture treatment, you should inform your doctor promptly and he/she will make a judgement and give appropriate medical treatment.

You will need to attend regular follow-up visits to the doctor during the study period for tests that may cause you trouble or inconvenience.

VII. Treatment options available to you other than participating in this study

Your doctor will discuss with you the other treatment options currently available for your condition, including the corresponding risks and benefits. For migraine, there are currently anti-inflammatory and analgesic drugs, mainly non-steroidal anti-inflammatory drugs (NSAIDs), which are effective and have side effects such as gastrointestinal bleeding, gastric ulcers and cerebrovascular accidents.

VIII. The relevant costs

During the study period, relevant free physical and laboratory tests (including blood tests, liver and kidney work, etc.), and acupuncture treatment will be provided. The doctor will make every effort to prevent and treat any possible harm caused by this study. If an adverse event occurs during the clinical trial, a committee of medical experts will identify whether it is related to the acupuncture treatment or the study procedure. The sponsor will provide the cost of treatment and appropriate financial compensation for damage related to the trial process in accordance with the provisions of our Code of Practice for the Quality Management of Pharmaceutical Clinical Trials.

Treatment and tests required for other medical conditions during the treatment period will not be covered free of charge

IX.The confidentiality of clinical data

Your medical records (research charts/CRFs, laboratory tests, etc.) will be kept intact at the hospital where you have been visiting. The doctor will record the results of the laboratory tests in your medical record. The investigator, ethics committee and drug regulatory authorities will be given access to your medical records. Any public reports of the results of this study will not disclose your identity. We will make every effort to protect the privacy of your personal medical information to the extent permitted by law.

X. You can voluntarily choose to participate in research and withdraw from the study

Whether or not to participate in the research is entirely up to you. You may decline to participate in the study or withdraw from the study at any time during the study, which will not affect your relationship with the doctor and will not affect your medical or other benefits.

In your best interest, your doctor or researcher may discontinue your participation in this study at any time during your research. If you withdraw from the study for any reason, you may be asked about your use of the trial drug. You may also be asked to undergo laboratory tests and a physical examination if your doctor deems it necessary.

XI. What should I do now?

Participation in this clinical study is based on a completely voluntary principle and needs to be carried out with your consent and signed informed consent. Whether or not you participate in this clinical study depends entirely on your wishes. You have the right to suspend and withdraw from this research treatment at any time. Exiting this study will not affect your medical treatment.

Your physician may suspend your participation in this study in advance if: Your health condition is not suitable for continued participation, or you may not comply with the research program requirements.

The doctor will promptly notify you or your legal representative if there is medical information that may affect your willingness to continue your research during the study. Before you decide to participate in this study, please ask your life as much as possible until you fully understand this test study.

If you have any questions, suggestions or complaints about this study, please do not hesitate to discuss them with the research team, whose contact details can be found on the signature page. If you feel uncomfortable communicating with the research team, you can make inquiries or complaints to the Ethics Committee of the Yunnan Specialist Hospital for Sports and Trauma. The contact number of the Ethics Committee: 0871-63126166.

Thank you for reading the above material. If you decide to take part in this study, please let your doctor know and he/she will make all the arrangements for you to study.

Informed Consent

Signature Page

1. I have carefully read the contents of the informed consent form, and the researchers have answered my questions.

2. Having fully understood the purpose, methods, possible therapeutic benefits and risks to be encountered and other terms of this clinical study as mentioned in the informed consent form, I voluntarily participate in this study and promise to cooperate fully with the investigators.

3. I understand that I can withdraw from the study at any time and I do not need any reason. The medical services I receive and the legal rights I enjoy are not affected at all.

Finally, I decided to agree to participate in this study and to ensure compliance with my doctor's advice.

Subject Signature: _____ Date: _____

Contact Number: _____

I have explained fully detail to the subjects, including the potential risks.

Doctor/Researcher Signature: _____ Date: _____

Contact Number: _____

知情同意书

告知页

项目名称：巨刺法治疗女性无先兆性偏头痛的临床研究

项目来源：国家重点研发计划（2019YFC11709701）；云南省万人计划青年拔尖人才项目（YNWR-QNBJ-2019-257）；云南省高校针灸推拿防治脑病重点实验室 (2019YGC04)

课题研究单位：成都中医药大学针灸推拿康复学院；云南中医药大学针灸推拿康复学院/第二附属医院

项目负责人：郭太品

亲爱的女士:

首先，感谢您对我们这项临床研究的关注！我们将邀请您参加一项“巨刺法治疗女性无先兆性偏头痛的临床研究”。本研究已通过云南省体育运动创伤专科医院伦理委员会审核。在您决定是否参加这项研究之前，请尽可能仔细阅读以下内容。它可以帮助您了解该项研究以及为何要进行这项研究，研究的程序和期限，参加研究后可能给您带来的益处、风险和不适。如果您愿意，您也可以和您的亲属、朋友一起讨论，或者请医生给予解释，帮助您做出决定。

研究介绍

一、研究背景和目的

1. 研究背景

偏头痛为临床常见疾病，是世界范围内第二大致残性疾病，可影响职业、学术、社会、家庭和个人生活等领域。偏头痛还可影响心血管疾病、精神疾病和睡眠障碍等疾病，并且因偏头痛所导致的致残调整年（disability-adjusted life years，DALYs）及疾病经济负担都在呈逐年加重趋势。各国偏头痛发病率较为接近，且女性发病率约为男性的 2-3 倍左右。在中国尚未有大范围流调研究结果，医学生中的偏头痛患病率约 10.8%（女性 13.1%，男性 7.2%）。

针灸治疗偏头痛安全有效，近几年来其疗效在国际上均得到认可。一项发表在《BMJ》杂志的研究显示相对于假针灸和常规治疗，针灸对无先兆发作性偏头痛的预防具有较好的疗效，可以明显减少头痛天数和发作次数。另一项发表在《JAMA Internal Medicine》杂志的研究显示偏头痛的长期针刺与假针刺、等待治疗相比，可以明显减少偏头痛的发作次数、疼痛天数、疼痛强度和减少药物使用。另一项研究显示针灸与目前最佳药物治疗具有同等疗效，

且在依从性和副作用方面优于药物。

巨刺法是中国古代《黄帝内经》中介绍的一种古老的古典针灸技术，距今有 2000 多年的历史。巨刺者，左取右，右取左”。巨刺法目前被广泛应用于各种原因所致的疼痛类疾病，具有较好的临床疗效。偏头痛大多为单侧头痛，属于巨刺的左右取穴治疗的适应病种，目前的治疗也显示较好疗效的趋势，但现有的证据不足，有必要开展高质量的 RCT 试验来证明巨刺法治疗偏头痛的疗效。

2. 研究目的

这项研究的目的是评价巨刺法治疗女性单侧无先兆性偏头痛的疗效。

3. 研究预计纳入参试者例数

本研究预计纳入 243 名女性单侧无先兆性偏头痛患者。

二、哪些人能参加这项研究？

1.符合以下条件的人，将会被邀请参加这项研究：

（1）单侧偏头痛，女性，年龄在 18-60 岁之间（发病年龄小于 50 岁）；

（2）符合 ICHD-3 中无先兆性偏头痛的诊断标准；

（3）近 3 个月头痛发作每月大于或等于 2 次，且头痛天数每月小于 15 天；

（4）近 4 周（基线期）头痛发作程度为中度至重度（VAS 4-9 分）；

（5）超过 1 年以上偏头痛病史；

（6）1 个月内未接受过针灸治疗；

（7）自愿参加并签署知情同意书者；

（8）三个月内未参加其他试验。

三、哪些人不宜参加本研究

（1）双侧或交替单侧偏头痛患者 ；

（2）头部有任何外伤史、伴有其他类型头痛或者诊断不明的头痛者，或者是颈源性头痛；

（3）合并心脑血管、肝、肾、造血系统等严重原发性疾病及其他器质性疾病;；

（4）合并有严重的焦虑、抑郁、失眠和其他精神疾病或智力障碍，不能配合问卷调查，或有感染、出血倾向、过敏和皮肤病的人；

（5）妊娠和哺乳期妇女，近 6 个月内有生育要求者；

（6）长期或目前正服用镇痛药物及精神类药物依赖症者；

（7）不能理解或填写头痛日记；

（8）在过去 3 个月内参加过类似的研究

四、如果参加研究将要做什么？

如果您符合入选标准并同意参加，您首先需要接受相关的检查以检验您是否符合参加这项研究的所有条件。

1. 在您入选研究前，您将接受以下检查以确定您是否可以参加研究：

（1）医生将询问并记录您的病史、临床症状和体征、正在使用及过去使用过的药物，并进行体格检查及血液生化等检查。检查治疗前后及随访结束时各检测一次，以上所有检测均免费，而且不会对您的健康和病情产生不良影响。

2. 若您通过以上筛查符合纳入标准，将按以下步骤进行研究:

（1）试验分为 3 组，研究开始，医生将根据计算机提供的随机数字，决定您接受哪组治疗。

（2）入组后每两天治疗 1 次，每周治疗约 3 次，治疗 8 周，共 24 次，随访 8 周，整个过程将持续 4 个月。

（3）本研究中使用的针灸针为苏州医疗用品厂有限公司生产的华佗牌一次性使用无菌针灸针，已经过检查合格，获得生产许可证（生产企业许可证：苏食药监生产许 2001-0020 号，注册证号：苏食药监械准字 2004 第 2270202）。

（4）治疗当日，治疗后第 4 周，8 周，您应该按照医生嘱咐到医院就诊，并如实向医生反映情况，医生将询问记录您的病情变化，并进行体格检查、理化检查。医生还将根据临床具体情况，进行相关实验室检查。

3. 需要您配合的其他事项

您必须按医生和您约定的时间来医院就诊。您的病情反馈非常重要，因为医生将判断您接受的治疗是否真正起作用，并及时进行指导。同时，您还有责任向医生报告试验过程中您身体和精神方面的任何改变，无论您认为这种改变是否与这项研究有关。

在研究期间，请您尽量不要使用治疗无先兆性偏头痛的其他药物，如果头痛难忍时，可以服用非甾体抗炎药物芬必得缓释胶囊止痛，可以服用既往有效的止痛药物。使用药物后续详细记录下来服用药物的名称、规格、剂量、服用时间，服用后疼痛缓解时间等。禁止服用偏头痛的预防性药物。如需要进行其他治疗，请事先与您的医生取得联系。您在每次随访时都必须将正在服用的其它药物带来，包括您有其它合并疾病须继续服用的药物。

五、参加研究可能的受益

您将可能从本项研究中受益。此种受益包括您的病情有可能获得改善，如果您参加本研究，研究期间，将得到相关的免费检查和治疗以及对您进行预防偏头痛发生的健康教育。

六、参加研究可能的不良反应、风险和不适、不方便

针刺过程中您可能会有酸、麻、重、胀的感觉，这均为针刺的正常反应。针刺后可能存在不良反应，但较少而轻微，针刺时可能因为您的体质问题或情绪紧张出现晕针现象，停止针刺和适当休息后可缓解；针刺后可能出现出血、血肿等现象，经局部按压后可消失；但如果针刺部位出现感染，您的医生会及时处理。

如果在研究期间您出现任何不适，或病情发生新的变化，或任何意外情况，不管是否与针刺治疗有关，均应及时通知您的医生，他/她将对此作出判断并给与适当的医疗处理。

您在研究期间需要按时到医院随访，做一些检查，这些都可能给您造成麻烦或带来不方便。

七、除参加本研究外，您可选的其他治疗

您的医生将与您讨论目前针对您的病情可选择的其他治疗方案，包括相应的风险和益处。针对偏头痛的患者，目前可以选择非甾体类抗炎药(NSAIDS) 为主的消炎镇痛药进行治疗，作用效果较好，主要存在胃肠道出血、胃溃疡、脑血管意外等副作用。

八、有关费用

在研究期间，将得到相关的免费理化检查（包括血常规、肝肾功等），和针灸治疗。医生将尽全力预防和治疗本研究可能带来的伤害。如果在临床试验中出现不良事件，医学专家委员会将会鉴定其是否与针刺治疗或研究过程有关。申办者将按照我国《药物临床试验质量管理规范》的规定对与试验过程中相关的损害提供治疗的费用及相应的经济补偿。

在治疗期间，如果您同时合并其他疾病所需的治疗和检查，将不在免费的范围之内。

九、个人信息是保密的吗？

您的医疗记录（研究病历/CRF、化验单等）将完整地保存在您所就诊的医院。医生会将化验检查结果记录在您的病历上。研究者、伦理委员会和药品监督管理部门将被允许查阅您的医疗记录。任何有关本项研究结果的公开报告将不会披露您的个人身份。我们将在法律

允许的范围内，尽一切努力保护您个人医疗资料的隐私。

十、可以自愿选择参加研究和中途退出研究

是否参加研究完全取决于您的意愿。您可以拒绝参加此项研究，或在研究过程中的任何时间退出本研究，这都不会影响您和医生间的关系，都不会影响您的医疗待遇与权益，或有其他方面利益的损失。

出于对您的最大利益考虑，医生或研究者可能会在研究过程中随时中止您继续参加本项研究。如果您因为任何原因从研究中退出，您可能被询问有关您使用试验药物的情况。如果医生认为需要，您也可能被要求进行实验室检查和体格检查。

十一、怎样获得更多的信息?

参加本项临床研究，本着完全自愿的原则，需要在您同意并签署知情同意书的前提下进行。是否参加本项临床研究，完全取决于您本人的意愿，您有权在任何时候选择中止和退出本项研究性治疗，退出本研究并不会影响您的医疗待遇。

您的医师可以在下列情况下提前中止您继续参加本项研究：您的健康状况不适合继续参加，或者您不能遵守研究方案的要求。

如在研究过程中出现可能影响您继续参加研究意愿的医学信息，医生将及时通知您或者您的法定代表。在您做出参加本研究的决定前，请尽可能向您的医生询问有关问题，直至您对本项试验研究完全理解。

如您对这项研究存在任何疑问、建议或投诉，请及时与研究团队讨论，联系方式见签字页。如您感觉不便与研究团队沟通，可向云南省体育运动创伤专科医院伦理委员会进行咨询或投诉。伦理委员会联系电话: 0871-63126166。

感谢您阅读以上材料。如果您决定参加本项研究，请告诉您的医生， 他/她会为您安排切有关研究的事务。

知情同意书

签字页

1. 我已经仔细阅读了知情同意书告知页的内容，研究者已解答了我提出的疑问。

2. 我在充分理解了知情同意书提及的本项临床研究的目的、方法、可能获得的治疗利益和可能遇到的风险以及其他条款后，自愿参加此项研究，并承诺与研究者充分合作。

3. 我明白我可在任何时候退出研究，并且不需要任何理由，我得到的医疗服务和享有的法律权利不受任何影响。

最后，我决定同意参加本项研究，并保证遵从医嘱。

受试者签名:_____ 日期：_____年_____月_____

联系电话:_____

我确认已向患者解释了本研究的详细情况，包括其权力及可能的受益和风险。

医生/研究者签名:_____ 日期：_____年_____月_____

联系电话:_____