Patient informed consent form

Project name： Efficacy and safety of acupuncture in the treatment of osteoarthritis of the knee: study protocol for a randomized controlled trial

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Research unit： Affiliated Hospital of Jiangxi University of Traditional Chinese Medicine

Informed consent version number： 2.0

Informed consent version date： January 6, 2025

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You will be invited to participate in a scientific research project called "acupuncture" to treat the efficacy and safety of knee osteoarthritis in the treatment of knee osteoarthritis in the research project of the affiliated hospital of jiangxi university of traditional Chinese medicine and jiangxi university of Chinese medicine. In this case, we will explain to you in detail:

1. Background and purpose of the test

Knee osteoarthritis (KOA) is a common chronic degenerative joint disease that severely affects patients' quality of life and function. With the intensification of global population aging, the incidence of KOA has shown a significant upward trend, and has become one of the main causes of disability in middle-aged and elderly people. Epidemiological studies have shown that about 40% of people over the age of 50 have symptomatic KOA, and the proportion is as high as 60% in people over the age of 65. It is worth noting that KOA not only affects the elderly population, in recent years due to obesity, sports injuries and other factors, the incidence of KOA in the younger population is also on the rise. KOA not only causes constant pain and dysfunction for patients, but also imposes a huge burden on the society and economy. Studies show that KOA is associated with $136 billion in direct and indirect medical costs annually in the United States. In China, the annual economic burden caused by KOA is about 88 billion yuan. In addition, KOA is associated with multiple complications, such as depression, anxiety, and cardiovascular disease, further increasing the health burden of patients. The effective treatment of knee osteoarthritis is becoming more and more important. The objective of this study was to evaluate the efficacy and safety of acupuncture in patients with knee osteoarthritis.

2. Acupoint sensitization acupuncture

Acupoint sensitization acupuncture means that the appropriate stimulation needle acts on the acupoint, so as to play the function of dredging meridians, harmonizing Yin and Yang, promoting the right and driving away evil, and can prevent and treat a variety of diseases. Acupoint sensitizing acupuncture technology has been widely used in the treatment of cervical spondylosis, scapulohumeral periarthritis, lumbar disc herniation, knee joint osteoarthritis, stroke (and its sequelae), migraine, trigeminal neuralgia, peripheral facial inflammation, irritable bowel syndrome, functional dyspepsia, functional constipation, benign prostatic hyperplasia and other diseases, led by the Affiliated Hospital of Jiangxi University of Traditional Chinese Medicine. A multi-center clinical study was carried out, a total of 5217 patients with 22 different diseases were observed, and it was found that the clinical effect was significant, and the cure rate was increased by 24.17% on average compared with the traditional needle push therapy. In the past 5 years, 27961 patients were treated with acupoint sensitization acupuncture in the affiliated hospital of Jiangxi University of Traditional Chinese Medicine, with a total effective rate of 96.3%.

3. Requirements for participation in this study

The team member responsible for the study will discuss with you the requirements for participating in the study. You will need to fully explain your knee pain and past history to the team members. If you meet the following criteria, you may, in the judgment of the Study Group members, be eligible to participate in the study if you meet all of the following criteria:

Inclusion criteria：(1) aged 18-70 years old, regardless of gender; (2) meeting the diagnostic

criteria of the American College of Rheumatology (ACR) of KOA [40] ; (3) patients with an NRS score of at least greater than 4 for knee pain, and the pain has lasted for at least 3 months; (4) diagnosed with osteoarthritis of the knee by magnetic resonance imaging (MRI) or x-ray in the last 3 years; (5) volunteering to participate in this trial and signing informed consent. Exclusion criteria included the following: (1) patients with a history of knee surgery; (2) patients who had received any physical therapy related to osteoarthritis of the knee, such as corticosteroid injections, acupuncture, or moxibustion, within the past 3 months; (3) patients who had a disease that could lead to pain in the knee, such as a fracture, a synovial cyst, or rheumatoid arthritis; (4) a severe degenerative disease that causes disability of the knee, or any significant nerve injury (e.g., a neuropathy); or (5) patients who had a history of knee surgery. or any significant neurological injury; (5) Prior serious mental illness, organ failure, or malignancy; (6) Planned knee surgery within the next 3 months; (7) Pregnancy or breastfeeding.

4.Research stage

The whole study period was 24 weeks, and there were 4 visits after enrollment, including the visit at enrollment and the visit at 4, 8, 16 and 24 weeks afterwards. We will collect the following information: General information (sex, age, medical examination, lifestyle, education), diagnosis/treatment records (comorbidities, medication, medical costs, outpatient and hospitalization records), treatment outcomes records (pain intensity, dysfunction, disability, depression, anxiety, sleep quality, fear of exercise, disaster, pain self-efficacy, oral analgesics), and Security.

4. Treatment grouping

We will randomly assign you to the acupuncture group or the control group.

（1）Control group

Participants in the sham acupuncture group will receive sham acupuncture treatments at real acupuncture points. A Takakura acupuncture simulation device (Figure 2)was used , which illustrates a sham acupuncture device used to implement a control between the acupuncture group and the sham acupuncture group in a randomized controlled trial (RCT), thus ensuring that patients are blinded to the treatment of the intervention. The construction of the device consists of a hollow needle handle, retractable cannula, connecting ring, Park tube (telescope-like structure), plastic ring and double-sided adhesive. The entire device is secured to the surface of the patient's skin by double-sided adhesive, forming a stable base. The hollow needle handle is designed with a retractable cannula that allows for what appears to be a needling motion without actually piercing the patient's skin, thus simulating the look and feel of a real needle puncture, and the Park Tube further ensures the stability of the device, preventing the needle from accidentally slipping out or piercing the skin.

The device's sham needling operation mimics real needling through appearance and tactile sensation, making it difficult for patients to distinguish, meeting the requirement of blinding and effectively controlling the patients' cognitive bias towards the type of intervention. Patients in the sham acupuncture group received this sham acupuncture intervention, which was designed to ensure that only the actual biological effects of acupuncture differed between the experimental group and the control group, and to exclude the psychological implication effects caused by the patients' expectation effects or the operation itself, so as to enhance the scientific validity and reliability of the research results. At the same time, a special fake acupuncture needle is used, which has the same appearance as

the real acupuncture needle, but the tip of the needle is passivated, and the fake needle is placed at the acupuncture point, without piercing the skin, and only the tip of the needle contacts the skin surface.To simulate the sensation of a real needle prick, the surrounding skin was gently pressed while placing the sham needles. The duration of needle retention was the same as that of the real acupuncture group. The treatment points (Figure 3), treatment frequency, duration and follow-up period of the sham acupuncture group were kept the same as those of the real acupuncture group. The Standards for Reporting Interventions in Clinical Trials of Acupuncture and Moxibustion (STRICTA)〔35〕 will be followed throughout the trial to ensure the standardization and reproducibility of the study.

（2）Treatment group

The intervention was performed by two licensed acupuncturists with at least 10 years of clinical experience who received two weeks of training in standardized intervention methods prior to the trial. Acupoints location refers to the WHO Standard Acupuncture Point Locations in the Western Pacific Region (WHO Standard)〔41〕.The acupuncture group will receive the following acupoints (Figure 3, Table 2): the affected side of Chize(LU5), Quchi (LI11), Dubi (ST35), Fengshi (GB31), and Xiyangguan (GB33).

Needling was performed with 0.30mm x 40mm disposable Huatuo brand sterile acupuncture needles.After the needles were inserted, needle manipulation was performed at all acupuncture points to achieve the sensations of soreness, numbness, distension, and heaviness.Each acupoint was manipulated for about 30 seconds, and the acupuncture treatment was performed for one 30-minute session. During the period of needle retention, the manipulation stimulation was repeated every 10 minutes, and the stimulation intensity was as strong as the patient could tolerate and did not cause significant discomfort. Participants received 3 acupuncture treatments per week for 8 weeks, for a total of 24 treatments. A 24-week follow-up observation was performed at the end of treatment.

6. Suspension and exit criteria

(1) When the pain of the experimental group was not alleviated, they were required to withdraw from the study because they did not meet the conditions;

(2) Take the initiative to quit during the test;

(3) Poor compliance, lost visitors;

(4) Withdrawal from the trial due to serious adverse reactions (such as hospitalization, disability, life-threatening).

7. Possible benefits of participating in the study

If patients choose or are randomized to the trial group, they will receive 8 weeks of electroacupuncture free of charge during the follow-up period. If they choose or are randomized to the control group, they will receive free acupuncture treatment at the end of the follow-up visit. In addition, patients will receive a more comprehensive evaluation of their disease condition at each follow-up visit and will be given treatment instructions by their physician.

8. Risks and prevention and treatment plans in the trial

The risks for patients in the trial group of this study are possible hematoma, needle fainting, needle breakage, needle stagnation, pneumothorax, etc., which may occur in patients due to improper operation. The control group does not have any additional risks. We will provide comprehensive safety

training to patients before the start of the study to try to avoid adverse reactions caused by improper needle manipulation. In case of hematoma, a small localized hemorrhagic hematoma will disappear after a period of time as long as attention is paid to disinfection and infection is avoided; in case of a larger hematoma or more bleeding, medical attention should be sought in time, and the project team will be responsible for further treatment and bear the cost of treatment. A small number of patients may have a dizzy reaction during the needling process, if so, the needling treatment should be discontinued. There are risks, discomforts and inconveniences in any scientific study, so you should consider carefully before agreeing to participate in this study.

9. Participation/withdrawal/termination of the study

Participation in this study is entirely voluntary. You may refuse to participate in this study, or you may withdraw from this study at any time during the study, without affecting your relationship with your doctor or causing you to lose medical or other benefits.

10. Confidentiality

Any of your personal data will be anonymized and kept strictly confidential for research purposes only. Any researcher who needs to use the database of your data will be required to sign a confidentiality agreement and use and analyze the data under strict supervision and management. Although your data may be subject to monitoring by relevant authorities (e.g. ethics committees, data safety monitoring committees), we ensure that the data will not be disclosed to the public.

11. Other Matters

The analgesic medication you are taking and the treatment and investigations required for comorbidities will not be reimbursed.

This consent form is in duplicate, one for the research unit and one for the subject. If there is any violation of the study protocol, you can directly complain to the Ethics Committee.

Subject signature：

Investigator signature：

Time：