Subject informed consent

Project name: Study on the effect of Tongyuan acupuncture on consciousness disorder after stroke

Solution version number and version date: V2.0/2023.10.8

Informed Consent Version number and version date: V2.0/2023.10.8

Dear family members of the subject:

We invite your family members (subjects) to participate in a study that has been reviewed and approved by the Medical Ethics Committee of Nanfang Hospital, Southern Medical University. Before you make a decision, we want you to understand the reasons for doing this study and what it requires of your family (subjects).Your participation in this study is voluntary, which means you can choose to participate or not.The research team will explain this information sheet to you and answer any questions you may have.

If you have any questions, please ask us. You are welcome to discuss this study and the information contained in this document with those close to you, such as your partner, family, friends, and doctor.

After you have considered all the information related to this study and all your questions have been answered, if you agree to allow your family to participate, the research team will ask you to sign and date an informed consent form (at the end of this document) before proceeding with any study-related procedures.

I. Research background

Stroke is a common and frequently-occurring disease in China. At present, there are about 13 million stroke patients in China, and stroke has become the biggest disease burden of Chinese residents. Patients with cerebral apoplexy often have sequelae and dysfunction of different degrees, and consciousness disturbance is the most influential one on prognosis and quality of life. At present, drug therapy, neurosurgical interventional therapy and modern physical therapy are mainly used for post-stroke consciousness disorder in foreign countries. China mainly combines

modern Western medicine treatment with traditional Chinese medicine treatment, such as Chinese medicine and acupuncture to treat the sequelae of stroke. The above therapies to improve the patient's state of consciousness (" awakening ") are not supported by sufficient evidence-based evidence, and the second is that they have disadvantages, such as invasive, expensive, and strict indications.

2.purpose of research

The purpose of this study is to investigate whether Tongyuan acupuncture can improve the consciousness disorder after stroke, and to provide a new safe, effective, feasible and easy to popularize treatment method.

3.Research product (or diagnostic technology) introduction

Acupuncture has been used for the treatment of sequelae of stroke for thousands of years. Tongyuan acupuncture method is a set of traditional Chinese medicine therapy initiated by Professor Lai Xinsheng, whose meaning is "Tongdu nourishing the spirit, Qi returning to Yuan". A large number of previous studies have confirmed that Tongyuan acupuncture has a unique effect on the cardiovascular system, gynecology, ent, neurology and other functional disorders. In this study, Tongyuan acupuncture was used in patients with post-stroke consciousness disorder to observe its efficacy and explore the mechanism of action.

The acupuncture needles used in this study were disposable sterile acupuncture needles produced by Suzhou Tianxie Acupuncture Instruments Co., LTD. Medical device Registration Certificate No. / Product Technical Requirement No. : Su Yi Registration Permit 20162200894.Manufacturer license No. : Su Drug Regulatory Machinery production Permit No. 20070037.The medical device has been listed for many years, is our hospital official unified procurement of acupuncture treatment equipment, for our hospital acupuncture treatment routine use of equipment.

4.research process

Approximately 174 people will participate in the study at the medical facility.

5. stages of research

■Before the study:

In order to check whether your family members (subjects) are suitable to participate

in this screening, the following procedures will be carried out:

• Obtain the demographic characteristics and vital signs of your family (subjects)

• Medical examination of your family member (subject)

• Ask your family members (subjects) for information about their medical history and accompanying medications

• Collect blood from your family member (subject) for laboratory testing

• If your family (subject) is a woman with a potential to give birth, a pregnancy test will be performed. Subjects must have negative pregnancy test results to participate in the study.

• Conduct a scale assessment of your family's (subject's) state of consciousness.

The results of the screening tests and/or the results of related questions will help the researcher decide if your family can continue with the study. If these tests indicate that your family is suitable for participation in the study, the investigator will notify your family of a visit as soon as possible. If your family does not meet the relevant criteria, they will not be able to continue to participate in the study, and the researchers will notify you of the results as soon as possible.

■Baseline period：

If the investigator confirms that your family is eligible to join the trial, your family is confirmed to be included in the study and to receive treatment in the trial or control group for a total of 4 weeks in a random assignment (similar to a lottery).This visit will carry out the following procedures:

• Double check if your family is eligible to participate in this study

• Access to randomized study treatment assignment (pass Yuan acupuncture)

• Assign your family members a specific identification number to participate in this study

• Assigned to test group or control group based on randomization results

• Perform a physical examination and collect vital signs data

• State of consciousness scale assessment

• Electroencephalogram (EEG), brainstem evoked potential (BSP), and brain fluctuation chart were examined

■Treatment period：

Your family (subject) will be randomized to either the trial or control group (random like flipping a coin), during which the researchers will observe the actual effects of your family (subject) using the Tongyuan acupuncture method or the control group's fake acupoint method. To ensure that the effects of your family (subject) using the Tongyuan acupuncture method are accurately recorded and evaluated, Your family members (subjects) are required to cooperate during this period to complete the following procedures:

- Receiving acupuncture treatment from the therapist, the test group selected points: Baihui, Zhongwan, Guanyuan, Qihai, Tianshu (double).Point selection criteria: the national standard "Name and Location of points" (GB/T12346-2006).The patient was supine, the acupuncture points were disinfected with 75% ethanol, and the acupuncture points on the head and neck were first acupuncture, and then the acupuncture points on the abdomen and limbs. Baihui: When the 1.5 inch millimeter needle is needled, the tip of the needle and the acupoint are at a 15-30 °Angle, and the needle is about 1 inch flat along the subcutaneous area. The twisting speed is about 200 times per minute, and the stitches are once every 15 minutes, and each stitch is about 30 seconds. Zhongwan, Tianshu: 1.5 inch needle straight puncture 1 inch, small amplitude lifting and twisting. Guan Yuan, Qi Hai: 1.5 inch millimeter needle downward oblique puncture 1 inch, small amplitude lifting and twisting. The above acupoints were measured by obtaining qi, and the needles were retained for 30min, once a day. Point selection of the control group: acupuncture treatment was performed 1cm beside the point selection of the experimental group. The piercing Angle is the same as the test group, only piercing, not twisting.
- Duration of intervention: once a day, 5 days a week for 4 consecutive weeks. Twenty days in total.
- Perform a physical examination of your family members (subjects) and collect vital signs data.
- Before the intervention, the treatment course was 1 week, the treatment course was 2 weeks, the treatment course was 3 weeks, the treatment course was 4 weeks (after the end), and the follow-up: 4 weeks after discharge, the state of consciousness scale was assessed: GCS score, NIHSS score, CRS-R scale (the Coma Recovery

Scale–Revised Scale), and FOUR scale score (Full Outline of Unresponsiveness Scale).

• Electroencephalogram (EEG), brainstem evoked potential (BEPP), and brain fluctuation map were examined before intervention and 4 weeks after treatment.

■Follow-up period (4 weeks after discharge)：

After the patient completes this stage of the visit, it is usually assumed that your family (the subject) has completed the entire study, during which the researcher will perform the following procedures:

Assess your family members (subjects) on a scale of state of consciousness.

6．What tests and evaluations will the study carry out?

After providing written informed consent, your family (subject) will undergo a number of tests, examinations and procedures during the study. If you have any concerns about any of these tests, discuss them with the study doctor.

Regarding the testing and procedures of this study, we would like to explain to you the following:

• Medical history: The study doctor will ask you questions about any current or past illnesses in your family (subject) and what waking treatments (including medication and physical therapy, surgery) have been undertaken.

• Demographic data: The study physician will collect information about your family (subject) individuals, such as date of birth and ethnic background.

• Physical examination: The study physician will perform a medical examination of the body of your family member (subject) to evaluate all or some of the following human systems: head, eyes, ear, nose and throat, chest, lungs, heart, abdomen, bones, skin, neck, and nervous system.

Height and weight: The height and weight of your family members (subjects) will be measured.

• Vital signs: The study doctor will measure your family member's (the subject's) blood pressure, heart rate, temperature, and respiratory rate.

• Blood draw: Your family members (subjects) will have their blood drawn twice during the study period, each group of about 2ml.Blood samples will be collected for the following items: interleukin-6, neuron-specific enolase, to assess the inflammation and neurological function status of your family (subject).

Electroencephalogram, brainstem evoked potential, fluctuation chart: Used to

assess the state of consciousness and hormone levels of your family members (subjects).

7．How long will the study last?

The clinical study lasted about 4 weeks (1 visit), which was divided into 4 weeks of acupuncture treatment and 4 weeks of follow-up visit. During the study period, your family members (subjects) must complete 1 visit after discharge (Telephone video).

You may opt out of the study at any time without penalty or forfeiture of any benefits that your family (subject) would otherwise have received. However, if during the study you decide to withdraw from the study, we encourage you to consult with your family (subject) physician first. In consideration of the safety of your family (subject), it is possible that a relevant examination will be conducted after the exit.

8. Risk and/or discomfort

The main goal of the research team is to keep your family (subjects) safe at all times.However, Tongyuan acupuncture treatment may cause side effects, including rare or currently unknown side effects. During this study, we will use blood and urine tests, physical examinations, and ECG to closely monitor the heart, kidney, liver function, and other body systems of your family members (subjects).

If you feel any deterioration in the health of your family member (subject), or if your family member (subject) has unexpected or unusual symptoms, you should contact the study team immediately, even if you believe that these problems are not caused by the study procedure or the acupuncture procedure.

1) Risk of therapy: It may cause bleeding at the acupuncture point or subcutaneous hematoma. If this happens, the operator will immediately withdraw the needle and apply pressure to stop bleeding;

2) Risks and discomfort associated with the research procedure, such as:

• Blood collection: A blood sample will be collected via a small needle inserted into a vein in the arm or hand of your family member (subject).Your family (the subject) may feel discomfort and/or soreness during the insertion and removal of the needle, and there may be small bruising. In rare cases, the vein may become blocked, or small nerve damage may occur, causing numbness and pain. If this happens, it will subside after a while;

Electroencephalogram (EEG) : When an EEG is done, small sticky patches are placed on the heads of your family members (subjects).Wires connected to the patch will send information about electrical activity back to the instrument for recording and measuring. This test takes only a few minutes and is painless, however, adhesive is used on the patch placed on the head, so it is possible to slightly irritate the skin of your family member (subject).

9. What are the benefits of participating in the study?

Your family member's (subject's) participation in this study may result in your family member's (subject's) disease being controlled or alleviated. But there are no guarantees. We hope that the information obtained from the participation of your family (subjects) in this study will help to develop new therapies for patients with this disease in the future.

10. Alternative treatment options

In addition to participating in this study, your family (subject) has the following options:

• General acupuncture treatment: according to the traditional point selection: may also have a wakefulness effect, may not, there is no evidence-based basis; The risks are the same as in this study.

• Hyperbaric oxygen therapy: This protocol is not suitable for patients with skull base fracture, which may improve patients' consciousness, but there is still insufficient evidence-based evidence;

• Naloxone drugs: Adverse effects include hypotension, hypertension, ventricular tachycardia, ventricular fibrillation, dyspnea, pulmonary edema, cardiac arrest, and withdrawal syndrome in patients with opioid dependence. It is possible to improve patient awareness.

At any time, you can discuss your family member's (subject's) disease and its possible consequences with the study physician and determine which treatment option is best for your family member (subject's).

11. Use of research results and confidentiality of personal information

At the end of the study, we write a report and send it to government regulators.The

results of this study may also be published in a journal, may be reported at a conference, but will not contain any information that could identify your family member (subject).

To ensure privacy, records or samples released for research purposes will not include the names of your family members (subjects) or other identifying information. Instead, your family (subject) information will only be identified by a code. Only the study physician and authorized personnel will be able to link this code to the names of your family members (subjects) through a checklist that will be kept securely at the study center.

In order to ensure that the research is conducted correctly at the research Center, the sponsor, the ethics review committee and the government administration may have access to the data of your family (subject) as required, and they are bound by confidentiality obligations and will not violate the privacy of your family (subject).

You have the right to control the use and disclosure of personal information about your family members (subjects).Where permitted by national law, you can request to see the medical information of your family member (subject) at any time. You have the right to see all information collected about your family member (subject) through the study physician and to request correction (if applicable).

12. Research relevant new information

During the study period, if there are changes in study procedures, newly identified side effects, or significant circumstances that may affect the health of your family (subject) or willingness to participate, the study team will notify you. The study physician will inform you immediately and discuss with you whether your family (subject) wishes to continue to participate in the study. If your family member (subject) decides not to continue to participate in the study, the study physician will make arrangements for your family member (subject) to continue their medical care. If your family (subject) decides to remain in the study, the study physician may ask you to sign a new informed consent form.

13. Regarding research costs, compensation and damages

1) Drugs used in the research and related examination expenses

The treatment and procedures required by the study protocol were provided free of charge by the sponsor, including acupuncture therapy and consciousness scale assessment, electroencephalogram, brainstem evoked potential, and fluctuation map examination.

Routine drug treatment and rehabilitation training, blood routine and blood biochemical examination must be paid by oneself.

2) Compensation for participating in the study

Your family members (subjects) will not receive any financial compensation for participating in this study.

3) Damages

If your family members (subjects) are harmed by participating in the study, they can receive free treatment provided by the sponsor, Nanfang Hospital of Southern Medical University, and will pay compensation according to law.

14. Subjects' rights and responsibilities

1) Your rights

Throughout your participation in the study, you do so voluntarily. If your family (subject) decides not to participate in this study, it will not affect any other treatment your family (subject) should receive. If your family (subject) decides to participate, you will be asked to sign this written informed consent form. You have the right to withdraw from the trial at any time at any stage of the trial without discrimination or unfair treatment, and your family members (subjects) will not be affected by the corresponding medical treatment and rights.

2）Your responsibility

Provide truthful information about your family's (subject's) own medical history and current physical condition; Inform the study physician of any discomfort experienced by your family (subject) during the study; In any experimental treatment, there may be risks to your family (subject) or your family (subject) fetus, so your family (subject) and your family (subject) partner should avoid any activities that may lead to pregnancy during the study period. If a member of your family (subject) becomes pregnant during the study, please notify your study physician immediately.

15. Relevant contact information

If you have any questions related to this study, please contact us at 18588528868.

- If your family members (subjects) have any questions related to their rights/interests, or if you would like to report difficulties, grievances or concerns encountered during participation in this study, or if you would like to provide comments and suggestions related to this study, please contact the Medical Ethics Committee of Nanfang Hospital, Southern Medical University at 020-62787238 or E-mail:nfyyec@163.com

Subject signature page

Informed consent statement

I have been informed of the purpose, background, process, risks and benefits of the study.I had plenty of time and opportunity to ask questions, and I was satisfied with the answers.

I was also told who to contact when I had questions, difficulties, concerns, suggestions for research, or wanted further information or help with research.

I understand that I may choose not to participate in the study or withdraw from the study at any time during the study without any reason. In addition, the researcher did not use deception, inducement, coercion and other means to force me to agree to participate in the study.

I already know that if I get worse, or if I have a serious adverse reaction, or if my study doctor feels that continuing to participate in the study is not in my best interest, he or she will decide to withdraw me from the study. The sponsor or regulatory authority may also terminate the study during the study period without my consent. If this happens, the doctor will notify me promptly, and the study doctor will also discuss my other options with me.

I have read this informed consent form and agree to participate in this study.

I will get a copy of this informed consent with my signature and that of the investigator.

Signature of legal representative:_____ date：_____

phone:

(Note: If the subject is incapacitated or has limited capacity, such as the inclusion of vulnerable groups such as mental disorders/confusion, the legal representative shall sign at the signature of the legal representative below)

I have accurately informed the subject of this document, that he/she accurately read the informed consent form, and certify that the subject was given an opportunity to ask questions and that he/she consented voluntarily.

Investigator Signature:_____ date：_____

phone：