Traditional Chinese medicine diagnosis and treatment of major and difficult diseases

Key technology research-Evidence-based evaluation and effect mechanism of Shenhuang granules in sepsis: randomized, double-blind, placebo-controlled, effective clinical trial

Informed Consent Form · Informed Notification Page

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Dear patient:

Your doctor has confirmed that you have sepsis.

We will invite you to participate in a pilot study of "Key Technology of TCM Diagnosis and Treatment of Major and Difficult Diseases-Evidence-based Evaluation and Effect Mechanism of Shenhuang granules: Randomized, Double-blind, placebo-controlled, Effective Clinical Trial" to evaluate the effectiveness and safety of Shenhuang granules on sepsis.

Before you decide whether to participate in the study, read the following as carefully as possible. It will help you understand the study and why the study was conducted, the procedures and duration of the study, the benefits, risks and discomfort you may have after participating in the study. If you wish, you can also discuss with your relatives and friends, or ask your doctor to give an explanation to help you make a decision.

Research introduction

1. Research background and study objectives

Sepsis is a life-threatening organ dysfunction due to the disordered response to infection. Most patients need treatment in the ICU, and it is the leading cause of death worldwide. For many years, the development of new drugs for sepsis treatment has not failed to reduce the significant mortality rate, and there is no effective drug treatment method. Therefore, sepsis is a serious disease that seriously threatens the life and health of patients, and causes a huge burden to the society, and is a

major problem in the medical community.

The pathogenesis of sepsis is complicated, and the immune imbalance is the key mechanism. The hibition of host immune function may be the fundamental cause of the increased long-term mortality in sepsis, and immune bidirectional modulation may be an important treatment option to improve the survival rate and quality of life of patients with sepsis. In recent years, the contribution of TCM to sepsis has been highly valued both at home and abroad. The treatment of sepsis mainly plays the role of bidirectional immune regulation by removing evil and strengthening upright. Our team has achieved some results in the use of traditional Chinese medicine in the diagnosis and treatment of sepsis. Supported by the National Natural Science Foundation of China (81774070). The team also found that magnolol could inhibit the inflammatory reaction of septic intestinal mucosa, and was also supported by the National Natural Science Foundation of China (82174178). This team qi huang scholars inherit the academic experience of Zhu Liangchun Chinese medical master, warm disease does not have to be confined to the health, gas, camp, blood transmission law, that is, the disease at the beginning of the double solution, the idea of the "not only seize the real, more emphasis on the Yin, not only can not only reduce the invisible evil heat, but also in addition to the physical" academic theory. On the basis of inheriting the academic theory of Master Zhu Liangchun, the early treatment rule of "truncation reversal" was proposed. In the early stage of sepsis, the evil of "poison" and "urgent Yin" were adopted to quickly cut off the malignant development trend of sepsis. Developed "jin red soup", undertake the national key research and development project "based on the truncation torsion strategy of TCM sepsis evidence-based evaluation and effect mechanism research (2018YFC1705900)", and in more than half a century of research found that jin red soup can improve systemic inflammatory response syndrome [28], effective protection of early myocardial injury in patients with sepsis, improve heart function. In the COVID-19 epidemic, we found that the "acute deficiency" clinical syndrome existed in COVID-19 sepsis patients in the early stage, which is an important factor leading to death. Further research is needed to investigate the clinical efficacy of "Shenhuang granules" in non-novel coronavirus infection caused by sepsis.

The purpose of the study: To conduct a multicenter, randomized, double-blind, placebo-controlled, effective clinical trial to evaluate the efficacy, safety, and effect mechanism of Shenhuang granules on sepsis.

The ethics committee has considered that the study complies with the principles of the

Declaration of Helsinki.

二、 Who should not take part in the study

(1) Patients with liver and kidney dysfunction of 3 in the individual SOFA score of liver or kidney;

(2) Expected death within 48 hours, or SOFA 15, or APACHE Ⅱ 30, or patients refused active treatment;

(3) Patients with allergic reactions;

(4) Patients treated with chemotherapy or radiotherapy or high-dose immunosuppressants in the last 1 month;

(5) At the same time or have participated in other clinical trials within 30 days;

(6) Women of pregnancy and lactation;

(7) Patients with severe gastrointestinal bleeding, intestinal obstruction, or severe increase in intra-abdominal pressure (IAP 20mmHg).

3. What will you need to do if participating in the study

1. Prior to your inclusion in the study, you will undergo the following checks to determine if you can participate in the study:

Your doctor will ask, record your medical history, and have a physical examination.

2. If you have completed the above examinations, the study will be performed as below (specify the treatment and the examinations according to the follow-up points)

The investigator was randomized into either the trial group or the control group.

Test group: septic cluster therapy + ginseng huang granules for 5 days. The ization of sepsis was according to the 2021 International Guidelines for Severe Sepsis and Septic Shock. Shenhuang granules (Tianjin Hongri Pharmaceutical Co., LTD.): twice a day, 1 pack, 100ml warm boiled water (temperature about 40 ° C) after dissolution, oral or nasal feeding (gastric or intestinal feeding).

Control group: sepsis cluster therapy + placebo for 5 days. The ization of sepsis was according to the 2021 International Guidelines for Severe Sepsis and Septic Shock. Placebo (Tianjin Hongri Pharmaceutical Co., LTD.): 1 pack per day, 100ml warm water (about 40 ° C), oral or nasal feeding (gastric or intestinal feeding).

(1) Baseline data: patient's name, gender, age, enrollment diagnosis, time of sepsis diagnosis, underlying disease, allergy history, personal history, temperature, respiration, heart rate, blood

pressure, oxygen saturation and other vital signs.

(2) Main outcome measures: the 28-day mortality rate

(3) Secondary outcome measures:

A. Total hospital stay and ICU stay

B. Total hospitalization costs and ICU admission costs

C. Overall mortality rates and ICU mortality rates

D.28 days of accumulated no mechanical ventilation time

E. Tongue and pulse syndrome information on days 0 and 5-7

F. TCM symptom points on days 0 and 5-7

G. SOFA score and APACHE II score on days 0 and days 5-7.

(4) Other observation indicators (Days 0 and 7):

A. Inflammatory indicators: WBC, percentage of neutrophils, CRP, PCT, tumor necrosis factor (TNF- α), interleukin-6 (IL-6), interleukin-10 (IL-10);

B. Main organ function indicators: BNP, TnI, creatinine, urea nitrogen, total bilirubin, direct bilirubin, indirect bilirubin, AST, ALT, arterial lactic acid;

C. Coagulation condition index: PT, APTT;

D. Immune function: absolute number of lymphocytes, $CD4^+$T cell number, and $CD8^+$Number of T cells, B cells, and NK cells.

(5) Safety indicators: adverse reaction symptoms or adverse events (such as allergies).

If you need to take stool and blood samples, you also need to observe the following indicators. If not, please ignore them.

(6) Metabolomics study: serum samples from days 0 and 5-7 were kept for the main efficacy components of ginseng granules and metabolomics analysis;

(7) Intestinal microecology study: fecal samples from day 0 and 5-7 days were kept for intestinal microecology study.

4. Possible benefits of participation in the study

In order to compensate for the inconvenience you may bring to you in this study, you will get free tongue, pulse and other TCM syndrome information evaluation twice, free yellow granule treatment.

If you take stool and serum samples, you will also get two more metabolomics and intestinal

flora microecological tests.

You and the society will likely benefit from this study. Such benefits include the potential for improvement in your condition and the possibility that this study may help develop a new treatment for other patients with similar conditions.

5. Possible adverse reactions, risks and discomfort, and inconvenience of participating in the study

Side effects of traditional Chinese medicine: some patients occasionally see gastrointestinal discomfort reaction after taking it.

Although no adverse effects of the study method have been found so far, if you experience any discomfort, new changes or any unexpected conditions, regardless of the drug, inform your doctor and he / she will make a judgment and medical treatment.

The physician and the research group will do their best to prevent and treat possible injuries due to this study. If an adverse event occurs in the clinical study, the investigator will determine if it is related to the study. The investigator / research group will provide the cost of treatment and the corresponding financial compensation for the damage related to the study.

In addition, the (study intervention) may be ineffective, and the disease continues to develop due to ineffective treatment or other diseases. During the study, if the study is ineffective, the physician will discontinue the study and switch to other treatments that may be effective.

Is personal information confidential?

Your medical records (study medical records / CRFs, laboratory test sheets, etc.) will be kept intact in the hospital, and your doctor will record the laboratory test results on your outpatient medical records. The investigator or research team members, the ethics committee and the government department of the project will be allowed to access your medical records. No public report on the results of this study will disclose your personal identity. We will make every effort to protect the privacy of your personal medical information as permitted by law.

Beyond this study, it is possible that your medical records and pathology examination specimens will be used again in future studies. You may also now declare denying other studies than this study to utilize your medical records and pathology specimens.

7. How do you get more information?

You can ask any questions about this study at any time. Your doctor will leave you his / her

phone number so you can answer your questions.

If you have any complaints about participating in the study, please contact the hospital ethics committee office.

Your doctor will promptly notify you if there is any important new information during the study that may affect your willingness to continue participating in the study.

8. You can voluntarily choose to participate in the study and withdraw from the study midway

Participation in the study depends entirely on your willingness. You may refuse to participate in the study or withdraw from the study at any time during the study, which will not affect your relationship with your doctor or the loss of your medical or other benefits.

Your doctor or investigator may suspend your participation in this study at any time for your best interest.

You may not participate in this study, or you may opt out of the study.

If you withdraw from the study for any reason, you may be asked about your use of the trial drug. You may also be required to have a laboratory examination and a physical examination if your doctor thinks it is necessary. This is very good for protecting your health.

9. What should I do now?

You will decide whether to participate in this study. You can discuss it with your family or friends before making a decision.

Before you make your decision to participate in the study, please ask your doctor any questions until you fully understand the study.

Thank you for reading the above materials.

If you decide to participate in this study, please tell your doctor or research assistant that he / she will arrange everything for you about the study.

Please keep this information.

Informed Consent Form · Consent signature page

Clinical Research Project Name: Research on key technology of TCM diagnosis and treatment of major and difficult diseases-Evidence-based evaluation and effect mechanism study of Shenhuang granules: randomized, double-blind, placebo-controlled, effective clinical trial

Clinical research unit: The First Affiliated Hospital of Zhejiang Traditional Chinese Medicine University

EC Approval No.: Upper right corner of EC Approval

Consent statement

I have read the above introduction to this study and have the opportunity to discuss and ask questions about this study. All the questions I have raised have been answered satisfactorily.

I am aware of the risks and benefits that may arise from participating in this study. I know that the study is voluntary, I confirm I have enough time to consider this and understand:

I I can consult my doctor for more information.

I can withdraw from this study at any time without discrimination or retaliation, and my medical treatment and interests will not be affected.

I am also aware that if I withdraw from the study, especially due to drug reasons, if I tell the doctor about the changes in my condition and complete the corresponding physical examination and physical and chemical examination, it will be very beneficial to me and the whole study.

If I need to take any other medication due to the change in my condition, I will ask my doctor for his advice in advance or tell him the truth afterwards.

I agree with the ethics committee or the sponsor representative and the study quality supervisor.

I agree with ☐ or reject ☐ for studies other than this study utilizing my medical records and pathology examination specimens.

I will obtain a copy of the signed and dated informed consent form.

Finally, I decided to consent to participate in this study.

Subjects signed:_____ _ _ _ _ _ _ _ month _ _ _ _ _ _ _ _ _ _

Subject Contact Number:_____cell-phone number:_____

Signature of the legal agent (if any):_____date:_____year___moon_ sun

I confirm that the patient has explained the details of the study, including its rights and possible benefits and risks, and gave him a copy of the signed informed consent form.

Investigator Signature: Date:____year _____moon _ _ sun

Investigator working telephone number: 13777571598 Mobile Phone number: 13777571598

Ethics Committee Office of the First Affiliated Hospital of Zhejiang Traditional Chinese Medicine University

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