Trial name: Effects of coenzyme Q10 on endothelial and cardiac function in patients undergoing hemodialysis: a pilot randomized controlled trial
Version 03

Consent form

（Version 03, November 5, 2018）

Name of subject： _____

Binding address： _____

Telephone number： _____

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Dear Mr. / Madam_____**:**

We sincerely invite you to participate in the clinical trial of "Effects of coenzyme Q10 on endothelial and cardiac function in patients undergoing hemodialysis". This study is conducted in the hemodialysis center of the 306th Hospital of Chinese PLA. Before you agree to participate in this study, please read this consent form carefully. The consent form will provide you with the research background, purpose, method, benefits, the possible risk, and your rights and interests protection during the trial. The information provided in this consent form can help you decide whether to participate in this study or not. If you have any questions, please consult the researchers of the project to ensure that you fully understand the content. If you agree to participate in this study, please sign the consent form and keep a consent form signed by the two sides. This research program has been approved by the ethics committee of the 306th Hospital.

1. Why participate in this study?

Cardiovascular events are highly prevalent. Endothelial and cardiac dysfunction are frequent occurrences in dialysis patients, which are related to higher cardiovascular morbidity and mortality among dialysis patients. Excessive oxidative stress is highly prevalent and also correlated with cardiovascular morbidity and mortality for hemodialysis patients. The excessive oxidative stress might result from due to loss of antioxidants during dialysis and activation of white blood cells triggering the production of reactive oxygen species.

Coenzyme Q10 (CoQ10) is an important in vivo antioxidant. Supplementation with CoQ10 may be of benefit to the general population. Previous studies have demonstrated that oral CoQ10 supplementation improved endothelial dysfunction in the general population. Meanwhile, treatment with CoQ10 can result in improvement in the left ventricular ejection fraction, heart failure, and reducing cardiovascular events and mortality.

Increasing evidence has indicated that CoQ10 supplementation can effectively decrease oxidative stress in dialysis patients. One randomized controlled trial has explored the efficacy of CoQ10 supplementation on cardiac function and found that CoQ10 supplementation decreased left ventricular mass and left ventricular posterior wall as well as interventricular septum thickness, and did not improve diastolic heart function in this special population. Another small sample study indicated that no significant effect of CoQ10 treatment on N-terminal pro-B-type natriuretic peptide (NT-proBNP) was found. However, in the per-protocol analysis, significantly lower levels of NT-proBNP among patients assigned to 1200 mg CoQ10 compared to placebo were found.

Thus, we will conduct this pilot randomized controlled study to evaluate the efficacy and safety of CoQ10 in hemodialysis patients.

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This study has been approved by the ethics committee of the 306th Hospital of Chinese PLA. This study complies with the relevant Chinese laws and regulations, the Helsinki declaration and other ethical principles to protect the rights and interests of subjects.

2. Who can take part in the study?

（1）Inclusion criteria

The inclusion criteria are as follows: undergo thrice-weekly hemodialysis for at least 3 months; aged more than 18 and less than 85 years; life expectancy greater than 1 year.

（2）Exclusion criteria

Patients will be excluded if they have any of the following: poor adherence of dialysis or medications; severe systemic or local infection; malignancy; planning to receive kidney transplant within 12 months; hospitalization within 30 days; history of a major atherosclerotic event within 3 months; pregnancy or lactation; current use antioxidant other than vitamin C; use of hemodialysis catheter.

3. How many people participated in the study?

The study is expected to recruit 60 eligible patients. The allocation ratio is 1:1. Participants will be randomized to CoQ10 or placebo group. Both the CoQ10 and placebo will be indistinguishable from each other in shape, size, color and packaging. You may be randomly assigned to the CoQ10 group or placebo group (the probability of being assigned to each group is 50%), but you can only enter only one group for treatment and evaluation. No matter which group you will be assigned, you will be given the appropriate basis and symptomatic treatment for your condition.

4. What is the research procedure?

We will first screen the hemodialysis patients, select the population with inclusion and exclusion criteria, and sign consent form with the patients. After agreeing to be the subject of our study, you will be followed up clinically every 3 months until the end of the study at 12 months. Biochemical data will be collected at baseline and every 3 months including hemoglobin, urea, creatinine, albumin, calcium, phosphate, intact parathyroid hormone, brain natriuretic peptide, and high-sensitivity C-reactive protein measured by standard methods. Kt/V values will be also calculated and collected. FMD test and echocardiographic examinations will be performed at baseline, 6 and 12 months. You will be followed up regularly for 12 months.

5. Possible risks and adverse reactions associated with participation in this study.

(1) The possible side effects and adverse reactions of study drugs

This study will provide you with CoQ10 or placebo. For hemodialysis patients, daily CoQ10 supplementation at doses as high as 1800 mg was safe and well-tolerated according

previous studies. Potential adverse events include gastrointestinal discomfort, loss of appetite, nausea, diarrhea, and rash. If you have any discomfort, new changes in your condition or any unexpected circumstances whether or not related to the drug, you should inform the research doctor in time, and the research doctor will make judgment and medical treatment.

(2) Blood drawing risks: including transient, mild pain, local bruises, mild dizziness in a few people, or extremely rare needle infections.

(3) Other risks: there may also be some other risks, discomfort, drug interactions or adverse reactions that are currently unknown.

6. What are the benefits of participating in this study?

One possible scenario is that you may not directly benefit from this study. Another possible scenario is that your endothelial function or cardiac function will be improved if you are allocated to treatment group if the effects of CoQ10 do exist. But we cannot guarantee this. Although participating in this study may not bring you immediate benefits, your participation may bring benefits to future dialysis patients.

7. If you don't participate in this study, is there any alternative treatment?

If you decide not to participate in this study, you will receive and undergo all usual clinical care activities including thrice-weekly dialysis, regularly monitor cliniacal and laboratory parameters and so on. Your researcher will suggest a treatment plan that suits you. Your researcher will also be happy to explain the possible benefits and risks of other treatments for your disease.

8. The cost of participating in the study

If you participate in this study, you can get free access to CoQ10 or placebo, free measurement for brachial artery flow-mediated dilation, and free echocardiography examination for three times. The above tests and inspection fees shall be borne by this study. However, the medication for the basic treatment and the examination or test items beyond the above instructions shall be at your expense.

9. Management of the occurrence of research-related injuries

If you suffer any adverse events related to this study or cause you any injury during the study period, the researcher will positively treat you and assume relevant responsibilities according to law. The sponsor (investigator) will not be responsible for your medical expenses if you do not comply with the requirements set forth by the investigator under this clinical trial protocol.

10. Voluntary participation and withdrawal from the test

You may choose not to participate in the study, or withdraw consent form from the study after being notified by the researchers at any time without discrimination or retaliation. Your medical treatment and rights will not be affected.

If you cannot make decision immediately, you have enough time to consider, if necessary, you can consult with relatives, friends and other people you trust before making decision.

The investigator may terminate your participation in the study if you require additional diagnosis/treatment, or if you do not follow the study plan, or for any other reasonable reason.

If you decide to withdraw early from a study, it is important that you consult the researchers about what other procedures to follow. During the study period, you may keep in touch with the information related to you in the study.

11. Your personal information will be strictly protected

If you decide to participate in the study, your personal information in and about the study will be kept confidential. Responsible for research physicians and other researchers will use your medical information for research. This information may include your name, address, telephone number, medical history, and information obtained during your study visit. To ensure that the research is conducted in accordance with the regulations, the sponsor, the pharmaceutical administration or the members of the ethics review committee are required to have access to your personal data at the research institute when necessary. Your personal information will not be disclosed when the results of this study are published.

12. Other items

1. For the sake of your health, the researcher may withdraw you from this study without your consent if:

If you continue to participate in this study, the risks may outweigh the benefits;

You do not participate in the study according to the study protocol instructed by the researcher;

The test is terminated prematurely.

2. We still recommend that you take necessary contraceptive measures during the trial if you or your partner during the trial become pregnant, tell the researcher or your physician immediately.

13. Who should you contact if you have any questions or difficulties?

If you have any questions about this study or if you have any discomfort or injury in the course of this study, please contact your research physician: _____。
Telephone:_____。

If you have any questions about your rights and interests during the research, please contact the biomedical ethics committee of our hospital at:_____。

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Consent form·Signature page

Subject consent form statement

I have read this consent form and fully understand all the contents.

I have the opportunity to ask questions and all questions have been answered.

I understand that participation in this study is voluntary.

I can choose not to participate in this study, and my medical treatment and benefits will not be affected.

If I need additional treatment, or if I do not follow the study plan, or if there is a research-related injury or for any other reason, the study physician may terminate my continued participation in the study.

I will receive a signed copy of the informed consent.

Name of subject: _____ Signed by legal agent: _____
Signature of the subject: _____ Relationship with subjects: _____
Telephone of subject: _____ Legal representative telephone: _____

Date: Year Month Day Date: Year Month Day
(Note: legal representative's signature is required if subject is incapacitated)

Investigator notification statement

I have informed the subject or his/her legal representative of the purpose, methods, procedures, risks and benefits of the study in detail; Give him/her enough time to read the informed consent form, discuss with others, and answer all questions he/she raises; I have informed the subject of the contact information when encountering problems; I have informed the subject or his/her legal representative that he/she does not need any reason to withdraw from the study at any time during the study.

Name of the investigator: _____

The investigator's signature: _____

Researcher telephone: _____

Date: Year Month Day