The Role of Fatty Acids in Vaccine Efficacy: A Randomized Controlled Clinical Trial

Informed Consent Form

NCT ID: Not yet assigned

Date: May 20 2023

Informed Consent Form

Dear Sir/Madam:

Hello! You are invited to participate in the "Study on the Effect of Nutritional Supplements on the Action of Rabies Vaccine" project, which is supported by Vanke School of Public Health, Tsinghua University, and has been reviewed by the Institutional Ethics Committee. This informed consent form provides you with detailed information to help you decide whether to participate in this project. Participation in the study is entirely your own choice and we encourage you to discuss it with your family and friends before making a decision to participate in this study. The basic information about this research project, the research process and other important information are as follows:

I. Introduction to the research project

1. Project name: Study on the effect of nutritional supplements on the effect of rabies vaccine

Sponsor: Vanke School of Public Health, Tsinghua University

Investigator: Vanke School of Public Health, Tsinghua University (Contact: Assistant Professor Ai Zhao)

2. Study background

Rabies, also known as hydrophobia, is an acute zoonotic disease caused by the invasion of the central nervous system by rabies virus. There is no effective treatment for rabies, and once clinical symptoms appear, rabies is almost 100% fatal. *Law of the PRC on the Prevention and Treatment of Infectious Diseases* classifies it as a B Class infectious disease. However, rabies is a vaccine-preventable disease. Vaccination of dogs is the most cost-effective way to prevent rabies in humans. More than 29 million people worldwide receive post-bite immunizations each year, a practice that is estimated to save thousands of lives each year. Pre-exposure prophylaxis is equally effective, and the current recommended bite free vaccination protocol in China is: 0 days (same day),

7 days, 21 days; a booster can be given after 1 year, and then every 1 to 3 years thereafter. The health of human body cannot be achieved without various nutrients, but some of them cannot be synthesized directly by human body and need to be consumed or supplemented through diet or nutritional supplements. Different nutrients have their own specific functions, and there have been some studies suggesting the immunomodulatory effects of many nutritional supplements, but there is still limited evidence on their effect on vaccine efficacy. Therefore, we chose a safe and cost-effective rabies vaccine to study the effect of nutritional supplements on its efficacy.

3. Research aim

To clarify the effect of nutritional supplements on serum metabolic indices, immunological markers and inflammatory markers after rabies vaccination and to assess the effect of nutritional supplements on the effectiveness of rabies vaccination.

II. Research content:

1.Study size and follow-up period

This study is intended to be a randomized controlled trial (RCT) design in which 42 participants will be vaccinated against rabies and followed up with a nutritional supplement intervention during the vaccination period.

You will be visited once prior to the start of the study, which will include a visit to introduce you to the contents of this informed consent form and to answer your questions. If you agree to sign the informed consent form, a nutritional questionnaire will be administered by the investigator and the necessary physical examinations, biospecimen collection and physiological and biochemical tests will be performed. You will be given brief dietary instructions prior to the start of the trial, you will be required to eat as directed for the first 3 days of the trial, you will be given a nutritional supplement intervention on days 3-19 of the trial, and you will be given a rabies vaccination on days 6, 20, and 34 of the trial. Your health and diet will be dynamically analyzed during this period.

a. Inclusion criteria:

(1) 18-45 years of age;

(2) BMI 18.5-24.9 kg/m2;

(3) Those who have never received rabies vaccination;

b. Exclusion criteria:

(1) Severe abnormal lipid metabolism disease;

(2) Those who have used lipid-lowering drugs, weight-loss drugs, or insulin drugs within the last three months;

(3) Those who have received other vaccines in the last three months;

(4) Those who have used probiotics or prebiotics in the last three months;

(5) Those who have used steroids and immunosuppressive drugs, other hormonal drugs in the last year

(6) Those with immunodeficiency diseases;

(7) A history of severe vaccine allergy;

(8) Hepatic and renal metabolic disorders;

(9) Those who have had fever, cold, severe diarrhea, etc. in the past month.

2. Research process

2.1 Randomized grouping

There are three experimental groups in this study: dietary supplement group A, supplement group B, and placebo group. After you agree to join this survey, you will be randomly assigned to either group by drawing the random numbers in the envelope. Your grouping information will be concealed and you will be informed of your assigned group at the end of the study.

2.2 Research procedure

The study was divided into four main phases (some phases were crossed) from days 0 to days 34 of the study.

Phase 1: Pretreatment period (Day 0-Day 2): all four groups adopted the healthy diet recommended in this study through dietary instructions. And a 3-day dietary survey was conducted.

Phase 2: Intervention period (Day 3-Day 19): Groups 1 and 2 were given placebo control and low-dose dietary supplements on Day 3-Day 19, respectively, and group 4 was supplemented with low-dose dietary supplements on Day 6-Day 19. dietary surveys were conducted on Day 3-Day 5, Day 13-Day 15. 6 blood and stool samples were collected on Day 3-Day 26.

Phase 3: Vaccination period (Day 6-Day 34): one dose each of rabies Vero vaccine was administered on Day 6, Day 20, and Day 34, respectively.

No changes in lifestyle such as nutrition and exercise were made in Phases 2 and 3.

Number of samples taken:

Test Day 3: 18 ml of blood collected intravenously on an empty stomach; 9 g of stool;

Trial Day 6 (Vaccination Day 0): 8 ml of blood collected intravenously; 9 g of stool;

Trial Day 13 (vaccination Day 7): 8 ml of blood collected intravenously; 9 g of feces;

Trial Day 16 (vaccination Day 9): 8 ml of blood collected intravenously; 9 g of stool;

Trial Day 19 (Vaccination Day 11): 8 ml of blood collected intravenously; 9 g of stool;

Trial Day 26 (Vaccination Day 13): 18 ml of blood collected intravenously; 9 g of feces.

Sampling requirements:

Test Day 3, Day 6, Day 13, Day 16, Day 19, Day 26: morning test, of which Day 3, Day 19, Day 26 must be fasting (no water), no alcohol the night before, no spicy and oily food.

The duration of this study was 34 days, and a total of 3 visits to Haidian Hospital to complete vaccination and 6 visits to Tsinghua University Hospital to complete blood collection were required.

III. Possible benefits of participating in this study

1. After participating in this study, you will be able to detect abnormal indicators through biochemical examination in time and get timely medical guidance.

2. We will give you professional dietary advice and scientific guidance on nutritional supplements.

3. You will receive a free rabies vaccination.

IV. Compensation received for participating in this study

After participating and completing all aspects of this study, you will receive a total of 2800 RMB. Those who do not complete the nutritional supplement intake, vaccination, and blood and stool collection on time will be terminated from the study and will be paid according to the number of blood collection (200 RMB per collection).

V. Possible discomfort and risks associated with participation in this study and precautions

1. Blood collection side effects:

Pain, bruising or other discomfort may occur at the site of the blood collection. It is very unlikely that fainting or infection at the site of the blood collection may occur. If you feel dizzy, lie down and rest immediately and notify the study doctor. The study physician will carefully monitor all possible side effects.

Precautions: If you experience varying degrees of nervousness and fear and anxiety

during the blood collection, the investigator will listen patiently to your complaints and provide proper psychological support until you are stable. If you experience nausea, the blood collection will be stopped immediately, and you will be helped to lie flat on the bed with your head on one side and given low-flow oxygen. Notify the doctor and measure blood pressure, pulse and respiration, observe your mental state, and provide psychological care.

2. Adverse reactions to rabies vaccine:

After 2011, the rate of adverse reactions to rabies vaccine in China has decreased significantly. However, a very small percentage of people still have adverse reactions after vaccination, such as mild local reactions (pain, redness, swelling or hard knots at the injection site, etc.) and mild systemic reactions (fever, headache, dizziness, gastrointestinal symptoms, etc.). The overall incidence of adverse reactions to rabies vaccine in China is 5.6%. Smoking, drinking and staying up late during vaccination should be avoided as much as possible.

In addition, the psychological and physical health of the survey respondents will be tested, and any unknown risks that occur will be promptly identified and actively addressed with the professional medical team.

VI. Confidentiality of the research

1. This study uses coding for your information entry instead of your real name, you are given an individual number after enrollment, and all information and data other than online survey information is kept in a storage cabinet exclusively by enrollment number, and non-study team members have no right to view it. By signing this informed consent form, you consent to our use of your information;

2. user data can be destroyed promptly when the user deletes or terminates use of the data collection to ensure that user data is not compromised;

3. All biological samples collected in this study will be stored in specialized laboratories. The storage, transportation and analysis of biological samples are

managed in a standardized manner to ensure the identification and traceability of biological samples, and the managers of the biological sample repository are qualified for the study and trained in their operation to ensure that dedicated personnel conduct quality control checks on the facilities and equipment where biological samples are stored in a timely manner. The biological samples collected in this study are for the use of this research project only. After the end of this study, the remaining biological samples will be stored in the biological sample bank.

4. The identity of the subjects in the published results of this study remains confidential and your personal information will not be independently disclosed in any research reports and publications about this project.

VII. Rights of participants

1.The right to voluntary participation

This study will be conducted under the supervision and guidance of the relevant state authorities, in accordance with the relevant laws and administrative regulations and in compliance with the relevant ethical guidelines, and the ethics committee will be responsible for the review, guidance and supervision of this study. In the event of changes in the study procedures or conditions, you have the right to informed consent, which will be explained to you by a dedicated researcher, and your written consent will be reobtained. You have the right to refuse to participate in or withdraw from the study at any time without discrimination, unfair treatment, or retaliation as a result. The investigator has the right to terminate you during the course of the study if:

Termination of the study is the best medical option for you;

You do not comply with medical advice;

The study is cancelled.

2. Research-Related Injuries and Compensation

In the event that you suffer a study-related injury, we will provide the necessary medical treatment and cover the appropriate medical costs and compensation in accordance with the relevant laws and regulations of China.

VIII. Contact information

If you have questions about this study, please feel free to consult a member of the research team.

Or consult with the contact person for this project at

Name: Ai Zhao, contact address: Tsinghua Vanke School of Public Health and Wellness, contact number: 010-627996447.

If you have any questions related to your rights/interests, or if you would like to reflect any difficulties or dissatisfaction encountered in participating in this study, or would like to provide comments and suggestions related to this study, please contact the Ethics Committee of Tsinghua University School of Medicine.

Informed Consent Form (Signature Page)

If you fully understand the content of this research project and agree to participate in this study, you will sign this informed consent form in duplicate, one copy to be retained by the investigator and one copy by the subject himself/herself or by the principal.

I. Signed by the subject himself/herself or his/her delegate:

1. I have carefully read the informed consent form and have fully understood the purpose and procedure of this study and the possible benefits and risks of participating in this study, and all questions I have asked have been answered to my satisfaction.
2. I have had sufficient time to consider and make a decision.
3. I voluntarily participate in this study, and I understand that I may refuse to participate in the study or discontinue and withdraw from the study at any time and under any circumstances, without penalty, and my rights to which I am entitled will not be affected.
4. I agree to have my study data accessed by national regulatory inspectors, members of the ethics review committee when needed.
5. I will be provided with a signed and dated copy of the informed consent form

Participant (Signature) :
Date: (Y) (M) (D)
Contact number:

II. Signed by the investigator performing the informed consent process:

I declare that I have explained in detail to the above participant the content, steps, possible dangers and benefits of this study, given him/her sufficient time to read the informed consent form, discuss it with others, and given adequate answers to any questions raised by the participant, and that the other person has received satisfactory answers and expressed understanding. I have informed the subject that he/she can contact the researcher at any time when he/she encounters a study-related problem, and that he/she can contact the Ethics Committee of Tsinghua University School of Medicine at any time when he/she encounters a problem related to his/her rights/interests, and have provided accurate contact information. I have informed the subject that he/she can withdraw from this study at any time. I have informed the subject that he/she will be given a copy of this informed consent form, which contains my signature and his/her signature.

Researcher (Signature) :
Date: (Y) (M) (D)
Contact number: