Effect of Oral Supplement Intervention on Influenza Vaccine Efficacy: A Randomized Controlled Clinical Trial

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Vanke School of Public Health
Tsinghua University

Informed Consent Form

Effect of Oral Supplement Intervention on Influenza Vaccine Efficacy: A Randomized Controlled Clinical Trial

Dear Sir/Madam:

You are being invited to participate in a clinical research study. Before deciding whether to participate, you need to understand why we are conducting this research and what it involves. This informed consent form provides detailed information to help you decide whether to participate in this study. Please read it carefully and make a thoughtful decision about your participation. When the research staff discusses this informed consent form with you, you can ask them to explain any unclear parts. The research staff can answer any questions you may have during the study. Participation is entirely voluntary, and we encourage you to consider opinions and suggestions from your family and friends before making your decision to participate. If you are currently participating in other studies, please inform the research staff. The basic information about this research project, research process, and other important information are as follows:

I. Research Project Introduction

1. Project Information

- Project Title: Effect of Oral Supplement Intervention on Influenza Vaccine Efficacy: A Randomized Controlled Clinical Trial
- Sponsor: Vanke School of Public Health, Tsinghua University
- Researcher: Vanke School of Public Health, Tsinghua University (Contact: Associate Professor Ai Zhao)

2. Research Background

Influenza is an acute respiratory infectious disease caused by influenza viruses, with particularly high morbidity and mortality rates among older adults. As people age, immune function gradually declines, making older adults more susceptible to influenza virus infection. Currently, influenza vaccination is the most effective means of preventing influenza and its related complications. According to literature, after influenza vaccination, the body produces an initial immune response, with hemagglutination inhibition antibody titers peaking around day 14, along with the production of neutralizing antibodies and other specific antibodies. As immune memory establishes, antibody levels gradually decrease and stabilize at post-response baseline levels.

Human health depends on various nutrients, but some nutrients cannot be directly synthesized by the body, and dietary intake may not meet requirements, necessitating supplementation. Current research suggests that certain fatty acid supplements have immunomodulatory effects, although evidence regarding their impact on vaccine efficacy is limited. Studies have shown that fatty acid supplements can effectively enhance immune response to vaccination in young populations while maintaining safety. However, due to immune senescence in older adults, their vaccine responsiveness is reduced, making them a key target population for improving vaccine protection.

3. Research Objective

This study employs a randomized controlled trial design to administer influenza vaccine to all participants while providing nutritional supplement intervention during the vaccination period, to evaluate the effectiveness, safety, and gut microbiota changes across different groups.

II. Research Process Description

1. Research Scale and Follow-up Period

Prior to study initiation, you will have an initial visit where this informed consent form will be explained, and your questions will be answered. If you agree to sign the informed consent form, research staff will conduct nutritional questionnaires, necessary physical examinations, surveys, and biological sample collection. Before the trial begins, we will provide simple dietary guidance, and throughout the trial, we will implement nutritional supplement intervention, with influenza vaccination administered on day 4. Your health status and dietary conditions will be monitored dynamically.

Inclusion Criteria:

1. Age 60-65 years
2. BMI 18.5-26.9 kg/m²
3. No influenza vaccination within the past year
4. Able to understand and sign informed consent, and complete all follow-up visits

Exclusion Criteria:

1. Severe lipid metabolism disorders
2. Use of lipid-lowering drugs, weight loss medications, or insulin within the past three months
3. Other vaccinations within the past three months
4. Use of probiotics or prebiotics within the past three months
5. Use of corticosteroids, immunosuppressants, or other hormonal medications within the past year

6. Immunodeficiency diseases
7. History of severe vaccine allergies
8. Liver or kidney metabolic disorders
9. Fever, cold, or severe diarrhea within the past month
10. Poorly controlled chronic diseases (e.g.,high blood pressure, blood sugar)
11. Use of influenza antiviral drugs within two weeks
12. Cognitive impairment
13. Planned surgery in the near future

Withdrawal Criteria:

1. Use of other nutritional supplements during intervention
2. Non-compliance with supplement intake instructions
3. Occurrence of major illness
4. Severe vaccine allergic reaction
5. Voluntary withdrawal

2. Research Process

The study requires 25 days, divided into three main phases:

Phase One: Adaptation Period (Day 0-Day 2)

Starting Day 0, participants will be given either placebo (1000 mg/day), fatty acid supplement (1000 mg/day), or TUDCA (1000 mg/day) for dietary supplement adaptation, with the following sample collection:

Day 0 (All participants):

- Blood collection and survey
- Fasting blood draw (10mL, 2 non-anticoagulant tubes) for liver/kidney function, blood lipids, and coagulation time tests; samples stored at -80°C
- Baseline survey and 24h dietary recall

Phase Two: Vaccination Period (Day 3)

All participants receive one dose of quadrivalent influenza vaccine.

Phase Three: Follow-up Period (Day 3-Day 24)

Experimental group 1 continues fatty acid supplementation, experimental group 2 continues TUDCA supplementation, and control group continues placebo, with the following sample collection:

Day 13:

- Blood and stool collection
    - Fasting blood draw (10mL, 2 non-anticoagulant tubes) for neutralizing antibodies, specific antibodies, and non-targeted metabolomics; samples stored at -80°C
    - Stool sample collection (10g) for gut microbiota and metabolome analysis

Day 24:

- Blood collection, stool collection, and survey
    - Fasting blood draw (10mL, 2 non-anticoagulant tubes) for neutralizing antibodies, specific antibodies, non-targeted metabolomics, complete blood count, blood chemistry, inflammatory markers (IL-1, 2, 6, 8, 10, 17), blood lipids, and coagulation time; samples stored at -80°C
    - Stool sample collection (10g)
- Post-intervention survey and 24h dietary recall

Important Notes:

- Please maintain your usual nutrition, exercise, and lifestyle habits during the trial
- Use the provided sterile containers for stool collection, avoid urine contamination, and ensure each sample is larger than five peanuts in size
- Must be fasting before sample collection (no water), no alcohol the night before, avoid spicy and greasy foods

III. Potential Benefits

By participating in this research, you will receive professional dietary advice and scientific nutritional supplement guidance. Additionally, you will receive free influenza vaccination.

IV. Compensation

Upon completing all study requirements, you will receive 300 RMB.

V. Potential Discomfort, Risks, and Precautions

This study involves nutritional supplement intervention, vaccination, and biological sampling, with potential risks as follows:

1. Supplement Intervention Risks The placebo, fatty acids, and TUDCA are common dietary supplements with proven safety in previous research. At recommended doses, potential adverse reactions include mild gastrointestinal discomfort (diarrhea, bloating), nausea, or decreased appetite, with low occurrence probability. Some sensitive individuals may experience mild allergic reactions such as rash or itching.

2. Vaccination Risks Quadrivalent influenza vaccination may cause local and systemic reactions, including injection site redness, pain, induration, and mild fever, fatigue, or muscle pain. These reactions are typically temporary, resolving within 1-3 days. Rarely, allergic reactions (hives, breathing difficulties) may occur.

3. Biological Sample Collection Risks

- Blood draws: May cause temporary pain, dizziness, bruising, or minor infection, though probability is low. Professional medical staff will perform blood draws using sterile techniques.
- Stool collection: No direct physical risks, though may cause mild psychological discomfort.

All intervention measures are based on components with established safety profiles and standardized procedures, with controllable potential risks.

VI. Confidentiality

1. Your information will be coded to replace real names, with all materials stored securely and accessible only to research team members.
2. Data will be destroyed upon user deletion or termination of data collection.
3. Biological samples will be stored in specialized laboratories with standardized management procedures.
4. Your identity will remain confidential in any research publications.

VII. Participant Rights

1. Voluntary Participation This research follows relevant laws and ethical guidelines, with oversight from the ethics committee. You have the right to:

- Be informed of any changes in research procedures

- Refuse participation or withdraw at any time without discrimination
- Be removed from the study if it's in your best medical interest
- Be removed for non-compliance with instructions
- Be informed if the study is cancelled

2. Research-Related Injury and Compensation If you experience research-related harm, we will provide necessary medical care and compensation according to relevant regulations.

VIII. Contact Information

For questions about this research, contact: Name: Ai Zhao Address: Vanke School of Public Health, Tsinghua University Phone: 010-627996447

For questions about your rights/interests or to report concerns, contact the Ethics Committee of Tsinghua University School of Medicine.

Consent Signature Page

If you fully understand this research project's content and agree to participate, please sign this informed consent form in duplicate, with copies retained by both the researcher and participant/proxy.

I. Participant or Proxy Signature:

1. I have carefully read this informed consent form and fully understand the purpose, process, potential benefits, and risks of participating in this research. All my questions have been satisfactorily answered.
2. I have had sufficient time to consider and make my decision.
3. I voluntarily participate in this research, understanding I can refuse or withdraw at any time without penalty or loss of rights.
4. I agree to allow inspection of my research records by national regulatory personnel and ethics committee members when needed.
5. I will receive a signed and dated copy of this informed consent form.

Participant Signature: _____ Date: ____/____/____ Contact Phone: _____

II. Research Staff Signature:

I declare that I have explained in detail the content, procedures, potential risks, and benefits of this research to the above participant, allowing sufficient time for reading the informed consent form and discussion. I have fully answered all questions to their satisfaction and understanding. I have informed the participant they can contact research staff anytime for study-related questions and the Ethics Committee of Tsinghua University School of Medicine for rights/interests-related issues, providing accurate contact information. I have informed the participant they can withdraw from this study at any time. I have informed the participant they will receive a copy of this informed consent form containing both our signatures.

Researcher Signature: _____ Date: ____/____/____ Contact Phone: _____