Title

The efficacy and safety of metformin intervention in elderly overweight or obesity with mild cognitive impairment

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Clinical Research Department: Endocrine Department

Sponsor: none

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Informed consent form of subject

The efficacy and safety of metformin intervention in elderly overweight or obesity with mild cognitive impairment

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Version number and date of informed consent form: 01 2025.08.07

Dear Subject:

You will be invited to participate in a clinical study. This instruction provides you with information to help you decide whether to participate in this clinical study. Please read it carefully and ask the researcher in charge of the study if you have any questions. We will communicate with you or your family in detail to introduce the relevant situation of the study. If you agree to participate in the study, please also provide the information related to the disease, including the onset, family history, previous visit and some test results. We will number you and establish a medical record.

You volunteer for this study. This study was reviewed by the Ethics Committee of this institution.

一、 Research background

The elderly patients with obesity have a high prevalence of cognitive impairment and there is a heavy family and social burden, so early intervention for patients with mild cognitive impairment (MCI) is of great value. Central nervous insulin resistance plays a role in the pathogenesis of cognitive dysfunction, which can be assessed by functional magnetic resonance imaging by observing central insulin resistance. Large-scale database studies of some type 2 diabetic patients have shown that the use of metformin is associated with a significant reduction in the risk of dementia, but some studies have reached different conclusions, and the related studies in elderly patients with obesity are rare. We speculate that metformin may improve cognitive dysfunction by improving central insulin resistance in elderly patients with obesity.

A total of 54 elderly obese patients with mild cognitive impairment were screened for a prospective, randomized controlled single-center clinical cohort study. One group was treated with metformin plus lifestyle intervention, and the control group was treated with simple lifestyle intervention. All the subjects were followed up for 26 weeks. History collection, physical examination and laboratory tests, Montreal Cognitive Assessment, and central insulin resistance assessment using nasal insulin inhalation combined with functional magnetic resonance imaging, serving as the objective basis for cognitive function assessment were performed before and after intervention. The main purpose of the study is to provide more accurate clinical research evidence for the prevention and treatment of mild cognitive impairment in elderly obese patients, so as to reduce the risk of developing into dementia and reduce the burden on families and society.

二、Research purposes

To explore the efficacy and safety of metformin in sufficient amount in elderly overweight or obese patients with MCI. To provide reliable evidence for the elderly overweight or obesity patients with MCI to delay and reverse the cognitive dysfunction.

三、Research process

The number of subjects expected to be enrolled in the study was 54, and based on the numbers generated in the randomization table, you have a 50% chance of entering either the trial group or the control group, 27 in each group.

Experimental group: Patients were treated with metformin sustained-release tablets (1500mg once a day, oral administration) and received lifestyle intervention guidance.

Control group: simple lifestyle intervention guidance.

The study lasted 26 weeks, and subjects were interviewed by telephone every 1 month during the follow-up period, with the focus on adverse events. Safety visits were conducted 4 weeks after the 26-week treatment period. All subjects were required to complete the following items twice in total during the enrollment phase and at the end of the follow-up phase:

1) Subject signs informed consent form;

2) A medical history (including education, smoking, drinking, and medication) was collected;

3) Obtain demographic data (gender and date of birth);

4) Carry out a comprehensive physical examination, obtain vital sign data (height, weight, temperature, respiration, heart rate, systolic/diastolic blood pressure, waist circumference, hip circumference, and body composition), and fill in disease baseline data;

5) Detection of fasting blood glucose (FBG), fasting insulin, fasting C-peptide, glycated hemoglobin (HbA1c), and blood lipids (CHO, TG, HDL-C, and LDL-C);

6) Safety examinations: routine blood tests (WBC, RBC, HGB, PLT), urine routine (WBC-M, RBC-M, PRO, KET, GLU), liver function (ALT, AST, TBIL, ALP, GGT), kidney function (BUN, Cr), feces routine, routine 12-lead ECG;

7) record concomitant medication;

8) Cognition scale evaluation: Montreal Cognitive Assessment (MoCA);

9) Nasal insulin inhalation combined with fMRI imaging examination.

Demographic data, blood withdrawal test and cognitive scale assessment were routine items for clinical diagnosis and treatment, while nasal insulin inhalation combined with fMRI examination was non-routine.

四、Alternative treatment

1)GLP-1RA: It is an ideal drug for the treatment of cognitive decline, but it needs injection, causing serious gastrointestinal adverse reactions and it needs high economic cost.

2)SGLT-2 inhibitors: It has been reported that it is effective in improving cognitive function but may cause adverse reactions in the genitourinary system.

五、Risks and discomforts

Your blood sample collection will be conducted strictly in accordance with aseptic requirements, and there may be some very small risks, including transient pain, local cyanosis, mild dizziness in a few people, or extremely rare needle infection. Gastrointestinal discomfort may occur with the use of metformin sustained release tablets.

六、Expected benefits

Both the experimental group and the control group in this study may improve your cognitive dysfunction. Test group's metformin is a first-line medication for diabetes and may improve your glycemic control. In the control group, lifestyle intervention may also improve blood glucose control.

七、Expenses and compensation

Expenses: Metformin provided free of charge; The expenses for blood drawing and fMRI were also borne by the researchers.

Compensation: Subjects received a transportation subsidy of 150 yuan per visit and a blood draw nutrition subsidy of 100 yuan per visit.

八、Compensation

You will be entitled to free treatment and/or appropriate compensation in the event of damage related to this clinical study.

九、Precautions before, during and after the study

The subjects cooperated with doctors for regular follow-up during the study to avoid missing or taking wrong drugs, and timely reported any possible adverse events.

十、Confidentiality

If you decide to participate in this study, your participation in the study and your personal data during the study will be kept confidential. Your biological sample will be identified with the study number instead of your name. Information that identifies you will not be disclosed to members outside of the study group unless your permission is obtained. All study members and the Sponsor are required to keep your identity confidential. Your files will be kept in a locked cabinet for researchers only. To ensure that the study is conducted in accordance with the regulations, members of government departments or ethics committees are required to have access to your personal data at the study unit when necessary. No personal information will be disclosed when the results of this study are published.

十一、 Handling of biological samples

At the end of the study, biological samples were not processed.

十二、 Re-obtaining informed consent

According to regulatory requirements, the investigator was required to obtain informed consent from the subject if:

1. changes in the research plan, scope and content;
2. The research is conducted with ID samples used for diagnosis and treatment in the past;
3. The human biological samples with identity or relevant clinical history materials in the biological sample database are used for research again;
4. other changes occur in the process of study.

十三、 Voluntary

You may choose not to participate in the study or to notify the investigator at any time to withdraw from the study and your data will not be included the results without affecting any of your medical treatment or rights.

The investigator may terminate your participation in the study if you require additional treatment, or if you do not follow the study plan, or if you have study-related injury occurs, or for any other reason.

You will be kept informed of the information and progress of the study and will be informed of any new safety information relevant to the study.

十四、Subject obligations

As a study subject, your responsibilities are to: Provide facts about your medical history and your current physical condition; Inform study physicians of any discomfort experienced during the study; Do not take restricted medications (such as steroid hormones, hypoglycemic drugs outside of this study); Tell study physicians if you have recently participated in other studies or are currently participating in other studies.

十五、 Contact information

If you have questions related to this study, or if you have suffered any discomfort or injury during the study, or have questions about the rights and interests of participants in this study, you can contact Dr. Tao Xiaoming at 18121223958 or Dr. Jiang Cuiping at 18964612712.

If you have any questions or concerns regarding your rights, interests, and health related to participating in this study, you can contact our Ethics Committee at 02162483180-720408.

Subject Signature Page

Subject consent statement:

□ I have read the above introduction about this study, and the study doctor has explained the study content to me in detail. I do not have any more doubts about this study to consult before signing the informed consent form. On this basis, I volunteered to participate in the clinical studies presented herein, and my decision was based on an adequate understanding of the risks and benefits that may arise from participating in this study. In addition, the investigator did not forcibly obtain my consent to participate in the study by using deception, inducement, or coercion, and I knew that I could unconditionally withdraw from the study at any stage.

□ This informed consent was signed by the guardian or legal agent of the subject due to incapacity and restricted capacity.

Subject Signature: Signature of legal representative:

Date: Date:

Subject contact information: Legal representative contact information:

Signature of guardian:

Date:

Signature of guardian:

Investigator's statement:

I confirm that the patient has been explained in detail about this study, in particular the risks and benefits that may arise from participating in this study.

Investigator signature:

Date:

Contact information of researcher:

Note: This is the subject's signature page where the study contents and related information were explained in detail by the study doctor to the subject, and the informed consent was signed by the subject himself/herself/his/her guardian/legal representative and the study doctor who explained it to the subject. If a subject has questions about the content of the study, the investigator should immediately recall in person. An original copy was retained by both the investigator and the subject after the signing.