Informed consent

Research Proposal Name: Application of atorvastatin in the treatment of intracranial vertebrobasilar artery dissecting aneurysm

Department: Beijing neurosurgical Institute

Version: V1.0

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Dear patients:

We invite you to participate in the research project "The Application of Atorvastatin in the Treatment of Patients with Intracranial Vertebral Basilar Aneurysm" under the Youth Innovation Fund Project of Beijing Institute of Neurosurgery. The study will be conducted at Beijing Tiantan Hospital, and an estimated 40 subjects will volunteer to participate. This study has been reviewed and approved by the Ethics Committee of Beijing Tiantan Hospital.

1. Why conduct this research?

Endovascular treatment and surgical treatment are commonly used treatments for unruptured intracranial aneurysms. However, some patients temporarily choose conservative treatment and regular imaging follow-up because the risk of aneurysm rupture is low or the risk of treatment is greater than the risk of rupture. Conservative treatment of unruptured aneurysms The risk of aneurysm development and rupture is generally reduced by controlling risk factors such as hypertension and hyperlipidemia.

Studies have shown that the inflammatory response of the aneurysm wall, especially oxidative stress, plays a crucial role in the occurrence, development, and rupture of aneurysms. High-resolution magnetic resonance imaging can determine the occurrence and degree of inflammation by observing the enhancement of the blood vessel wall. Atorvastatin has been found in other diseases to be effective in reducing the inflammatory response in the body. Therefore, the subjects of this study were patients with unruptured intracranial aneurysms who were treated conservatively and showed signal enhancement in the aneurysm wall by MRI.

Therefore, in this study, we evaluated whether atorvastatin can effectively inhibit the vascular wall of the intracranial aneurysm by comparing the MRI images of patients without intracranial aneurysm taking atorvastatin at the time of enrollment and after six months of follow-up. Inflammation, as well as slowing the development of aneurysms and reducing the probability of aneurysm rupture and bleeding.

Through the implementation of this study, it is expected to provide a new treatment model for the conservative treatment of intracranial unruptured aneurysms.

2. How many people will participate in this study?

All patients with unruptured intracranial aneurysms who underwent conservative treatment in the Neurointerventional Department of Beijing Tiantan Hospital and showed signal enhancement in the aneurysm wall by MRI will be invited to this study. About 40 people were invited to participate in this study by the Neurointerventional Department of Beijing Tiantan Hospital.

3. How long will this study last?

The primary endpoint of this study was the changes in the enhancement of the aneurysm wall at the time of patient enrollment and 6 months after taking the drug, and the secondary endpoint was ① morphological indicators of the aneurysm (size, size, Aneurysm neck width, tumor area, tumor volume, etc.); ② Probability of aneurysm rupture and hemorrhage 6 months after operation; ③ Changes of serum inflammatory indexes (CRP, TNF-α, IL-1β, and IL-6) at 6 months after the operation. Therefore, this study is expected to last for 18 months.

You may opt-out of the study at any time without forfeiting any of the benefits you should have received. However, if you decide to withdraw from the study during the study, we encourage you to discuss this with your doctor first. Considering your security issues, there may be a related check after you log out.

4. What does this study include?

If you agree to participate in this study, first, we will ask you about your medical history and review all the medicines you are currently taking. Secondly, record the results of routine laboratory tests and auxiliary

examinations during your hospitalization, including blood tests, blood biochemical examinations, coagulation examinations, and other laboratory examinations, as well as auxiliary examinations such as electrocardiogram and head magnetic resonance (MRI). In addition to routine laboratory tests, we will draw about 10ml of blood from your arm vein and store it in this research specimen bank for etiology and other related research. We can perform a urine test for you (for women of childbearing age only), women who are pregnant cannot participate in this study. Finally, if we believe you are suitable to participate in this research, we will proceed with the following research procedures with your consent.

According to the plan, we randomly divided the participants into groups, one group received oral atorvastatin and the other group received no atorvastatin. Regardless of which group you're assigned to, we'll control for aneurysm-related risk factors, such as high blood pressure, high blood lipids, and more. This study is a "double-blind" study, which means neither you nor your study doctor knows which drug you are taking. Subjects randomized to atorvastatin will receive oral atorvastatin, and patients randomized to no atorvastatin will receive a placebo in the same form as atorvastatin. A placebo is a tablet that looks identical to the study drug but does not contain the active ingredient. We use placebos in our studies to understand whether the beneficial or detrimental effects observed in subjects are actually from the study drug. All study drugs will be blinded, meaning neither you nor your study doctor can tell which drug you are taking. However, in an urgent and necessary situation, your doctor will be able to know which medicines you are taking.

On days 1-7, you will receive atorvastatin 20mg orally once a day. All study medication will be provided to you in a box. The study doctor will record in writing how many pills you take from which box at a time. The daily dose must be following the study requirements under the guidance of the study doctor. The study doctor will give you enough of the study drug to last until the next visit; at the follow-up visit, you will return the entire kit and any unused study drug to the doctor. If you decide to participate in this study, you must agree to take the medicine as directed by the study doctor and not to give the study medicine to anyone else. Do not take any other medicines or receive other treatments, whether prescribed or purchased from a pharmacy or supermarket, until approved by your study doctor. In addition, any special diet must be determined after discussion with the study physician.

During this period, we will plan to request the collection of basic information and imaging information of patients and relevant information during follow-up. You need to assist the doctor to complete the items required in the questionnaire, and you also need to leave reliable contact information (including phone number and address) so that the doctor can arrange a follow-up for your disease after surgery.

5. Do I have other treatment options?

Participation in this study may or may not inhibit the inflammatory response of the aneurysm, thereby inhibiting the progression and rupture of the aneurysm. If you do not participate in this study, you can choose other treatment options, and your doctor will give you the best treatment according to your condition.

6. Who was selected for the study?

(1) Aged over 18 years old;

(2) Patients with intracranial unruptured vertebrobasilar artery dissection aneurysm with a diameter of ≥3mm;

(3) Aneurysm patients without clinical indications for surgery and conservative treatment: asymptomatic aneurysm; Aneurysm diameter < 7mm; no aneurysm morphological risk factors (such as ascus, lobulated aneurysm);

(4) High-resolution MRI showed aneurysm wall enhancement;

(5) All subjects or their proxies People need to sign informed consent.

Whether you can participate in the study will be decided after a doctor's examination.

7. Who should not participate in research?

(1) Aneurysms whose pathological mechanisms are inconsistent with dissecting aneurysms, such as cystic and fusiform;

(2) No contraindications to MRI (such as contrast agent allergy, claustrophobia, or implantation of metal foreign bodies, etc.);

(3) Diagnosis Patients with other serious diseases or Hunt-Hess grade ≥3 will significantly affect the follow-up;

(4) patients with recurrent aneurysm and retreatment;

(5) pregnant women;

(6) combined with other serious systemic diseases, expected survival Patients with a time less than 1 year;

(7) Abnormal liver and kidney function;

(8) Patients with other immune diseases

If you are one of the conditions, it is not within the scope of this study.

8. What are the risks of participating in research?

The use of all drugs carries risks and may lead to adverse effects, whether or not it was part of this study. During the study, we will promptly notify you of any new findings related to atorvastatin that may affect your participation or continued participation in this study. You will also be notified promptly of any drug-related information that may negatively affect your health. If you wish to withdraw from the study because of new findings, your doctor will arrange for other treatment for you.

Risks of using atorvastatin:

1) Allergic reaction and angioedema;

2) Progressive multifocal leukoencephalopathy;

3) Lymphocyte decrease, increasing the risk of infection;

4) Liver damage;

5) Other adverse reactions: facial flushing, abdominal pain, diarrhea, nausea, etc.

9. What are the benefits of participating in research?

Since the safety and efficacy of atorvastatin in patients with multiple sclerosis have been confirmed, its mechanism of action is related to the inhibition of inflammatory response in the human body, and the development and rupture of the intracranial aneurysm have been confirmed to be related to the inflammatory response in vivo. Closely related, therefore, participating in this study may potentially control aneurysm growth and reduce the risk of aneurysm rupture, although no guarantee participating in this study may improve your health for the better. At the same time, during the research process, the research doctor will pay close attention to your physical condition and make corresponding assessments promptly.

10. Do I need to pay for the study?

You will receive the study drug for free.

You will not be paid for participating in this research.

11. What happens if I am harmed while participating in the study?

Any research has implications for patients, and any treatment is risky rather than completely safe. In addition, any treatment may be ineffective, and the disease may continue to develop due to ineffective treatment or due to other diseases. Our hospital and the centers are all Grade III A hospitals, and the hospital personnel and medical

equipment are qualified to rescue patients. If your health does suffer from study-related damage as a result of your participation in this study, please notify the study physician immediately and they will be responsible for appropriate treatment for you. Beijing Tiantan Hospital will bear the cost of treatment and give you corresponding financial compensation following relevant national regulations.

For patients taking atorvastatin, we regularly test liver and kidney functions. Once adverse drug reactions occur, the drug should be stopped immediately and relevant symptomatic treatment will be given. If the patient has changed in the shape of the aneurysm during the follow-up period, the patient should be comprehensively evaluated and conservative or surgical treatment should be decided. If the aneurysm ruptures and hemorrhages in the patient, we will open the green channel and carry out surgical treatment as soon as possible. After the treatment, we will transfer the patient to the intensive care unit to closely monitor and treat the patient.

Even if you have signed this informed consent form, you still retain all your legal rights.

12. Is my personal information confidential?

Your medical records will be kept in the hospital, and investigators, research authorities, and ethics committees will have access to your medical records. Any public reporting of the results of this study will not disclose your identity. We will make every effort to protect the privacy of your personal medical information to the extent permitted by law.

13. Do I have to participate in research?

Participation in this study is entirely voluntary, and you may refuse to participate in the study, or withdraw from the study at any time during the study without any reason. This decision will not affect how your doctor treats you.

If you decide to withdraw from this study, please contact your doctor in advance.

14. How will participate in this study affect my life?

During the study period, in addition to the treatment and follow-up visits during your normal medical visits, we will only contact you when arranging follow-up visits, the purpose of which is to arrange your follow-up matters (review time, bed arrangements, etc.), you may feel that these arrangements will cause inconvenience.

You can ask your study doctor if you have any questions about the tests and procedures in the study.

You cannot participate in any other clinical studies of drugs or medical devices during the entire study period.

15. Related consultation.

If you have any questions related to this research, please contact Yisen Zhang and Mirzat Turton, landline and mobile phone 01059975936, 15001232615, 18699158800.

If you have any questions related to your rights, or if you would like to express your dissatisfaction and concerns during your participation in this research, please contact the Ethics Committee Office of Beijing Tiantan Hospital at 010-59978555.

Patient Statement:

I have read the above description of this study and am fully aware of the possible risks and benefits of participating in this study. I volunteered to participate in this study.

I agree□ or disagree.□ Studies other than this study utilized my medical records and examination specimens.

Patient signature：_____ Date：_____

Patient name：_____ Contact number：_____

Signature of legal representative：_____ Date：_____

Legal representative name：_____ Contact number：_____

Physician's Statement: I confirm that the details of this study have been explained to the patient, particularly the possible risks and benefits of participating in this study.

Doctor's signature.：_____ Date：_____

Doctor's name：_____ Contact number：_____