Safety and Efficacy Evaluation of Remimazolam for Endoscopic Ultrasound-guided Fine Needle Aspiration/Biopsy

Unique protocol ID:EUS-FNA-2022-01

Date:2022-05-10

Informed Consent Form

We cordially invite you to participate in a clinical study on sedation protocols during Endoscopic ultrasound-guided fine needle aspiration/biopsy (EUS-FNA/FNB). Your participation in this study is entirely voluntary, and you may choose not to. If you decide not to participate, it will not affect your relationship with your doctor. In order for you to decide whether or not to participate, it is important to understand the details of this study. Please read the following information carefully and discuss it with your family, friends and doctor. If there is something you don't understand, or if you want to learn more about this study, please feel free to ask your doctor.

Aims and brief summary of this study

In this study, patients who receive EUS-FNA/FNB would be invited as participants, and propofol would be used as the control sedative and remimazolam would be used as experimental sedative during EUS-FNA/FNB operation. The main purpose of the study is to compare the performance of two sedation regimens in EUS-FNA/FNB, and to evaluate the safety and efficacy of the two anesthesia regimens for EUS-FNA/FNB.

This project has been approved by the Ethics Committee of the Third Xiangya Hospital of Central South University, and a total of about 264 patients who are going to undergo EUS-FNA/FNB would participated in this study. All participating patients have a 1 in 2 chance of being randomly assigned to either remimazolam or propofol, as do you. Which group you fall into is completely random. If you choose not to participate in this study, it will not affect your current and future treatment at all, and you can use other sedation regimens, such as propofol intravenous anesthesia, etc.

Medicine in this study

The sedative in experiment group is remimazolam, which is a new type of short-acting sedative-hypnotic drug. It mainly acts by combining with GABAa, with fast onset, short half-life, rapid recovery, no accumulation in long-term infusion, and less impact on hemodynamics. Its respiratory and circulatory inhibition is small, and the sedative effect can be quickly reversed by flumazenil.

The sedative in control group is propofol. Propofol is a short-acting intravenous anesthetic with rapid onset of action and stable induction. Due to its high lipophilicity, it can quickly pass through the human blood-brain barrier and achieve a deep degree of sedation in a short time. Propofol is currently the most commonly used intravenous anesthetic, widely used in EUS-FNA/FNB, and its sedative effect is generally recognized.

Oxycodone, a semi-synthetic pure opioid receptor agonist, will also be used in the trial and

is widely used in clinical practice.

At present, other optional sedation methods include propofol intravenous anesthesia and so on. You can use this protocol for sedation if you do not wish to participate in this study.

Study process

This study is divided into the following steps:

1. Informed consent and participant recruitment
2. Information collection and participant screening
3. Randomization
4. EUS-FNA/FNB information collection and preoperative preparation
5. Sedation induction and maintenance
6. EUS-FNA/FNB operation
7. Follow-up of patients 1-3 days after operation
8. Statistics and analysis

The duration of this study is roughly 7 days for screening period, 1 day for treatment period, and 3 days for safety follow-up period. You will be required to visit the hospital 4 times during the screening and safety follow-up periods throughout the study period. During the study, you will have routine blood tests, liver and kidney function, blood biochemistry, coagulation function and imaging tests.

Possible risk and inconvenience

In general, all sedative drugs usually have side effects, and no matter which sedation regimen you take, there are other risks that come with them. If you have any discomfort, please tell your doctor promptly.

Previous clinical studies have shown that remimazolam may cause dizziness, headache and other adverse reactions, most of which are temporary. The sedative in control group is propofol, and adverse reactions such as hypotension, respiratory depression, tachycardia and bradycardia may also occur.

The adverse reactions and risks you may experience during the study period include but are not limited to the above-mentioned items. Any study drug may have other unforeseen or even serious adverse reactions. If new adverse reaction information is discovered during the period, the study doctor will also inform you in time. At the same time, the study doctor will closely observe your condition and determine whether you have any adverse reactions. If necessary, other drugs will be used to treat you to reduce the adverse reactions or discomfort. If you are breastfeeding, you will not be able to participate in this program.

Possible benefits

Through the strictly controlled anesthesia process and more comprehensive vital signs monitoring in this study, you may obtain a more comfortable anesthesia experience and higher life safety assurance; a good anesthesia state during operation will also provide convenience for the operator, so as to obtain better quality the best endoscopic images; in addition, due to good

anesthesia, you have the opportunity to complete the EUS-FNA/FNB in a shorter time; finally, you will be followed up 1-3 days after the operation, and the relevant evaluation will help guarantee your postoperative safety. In general, you will be able to get a more thorough examination during the study and be able to discuss your treatment with the study doctor. You may have immediate medical benefits, remimazolam, propofol and oxycodone Hydrochloride are all marketed drugs and you will benefit from the role of the drugs in EUS-FNA/FNB.

Because of individual differences, we cannot predict whether or not an anesthesia regimen will have side effects for you, and the magnitude of these side effects, so you may not benefit from this clinical trial.

If you are reluctant to participate in the program, the routine sedation regimen (propofol) would be used. This program is relatively widely used and has good safety, but there may still be side effects such as hypotension, respiratory depression, and bradycardia.

Compensation and treatment

When you have serious adverse reactions due to sedation during the operation of EUS-FNA/FNB, the trial will be terminated immediately, and we will take all necessary measures to rescue. This study will not increase the risk of your endoscopic procedure. If you experience any discomfort during this study, or new changes in your condition, or any unexpected circumstances, whether or not related to the operation, please inform your study doctor promptly, and they will make serious judgments and rigorous medical care. When a subject suffers damage related to the test, it will be identified and dealt with in accordance with the routine medical procedures, and the specific amount of compensation will be determined by the appraisal results of the relevant departments and the negotiation results between the two parties (participant and hospital).

Individual privacy policy

Your medical information will be kept confidential at all times. In addition to your research doctor, the sponsors, monitors, auditors, ethics committees, and health regulators of this study may review your original medical data related to the study to ensure that the study is standardized and the data is true and reliable. But all information will be kept confidential and the results of this study may be published in a medical journal without revealing your identity.

Points for attention

Before participating in this study, please read the inclusion and exclusion criteria of the study carefully to make sure that you meet the inclusion criteria and that there are no problems mentioned in the exclusion criteria; during the research, if you have any physical discomfort, please inform your doctor, the doctor will make corresponding treatment according to your situation; when you need to follow up, please cooperate with the follow-up doctor as much as possible, so as to make a more accurate and timely diagnosis, which is beneficial to your treatment; finally, during the research process, if you have any questions about this research, you can contact your research doctor, who will answer you in detail.

The rights of yours

If you are unwilling to participate in the program, our hospital's routine sedation regimen (propofol intravenous anesthesia) would be used. This will not affect your EUS-FNA/FNB procedure. If there is any important new information about the study drug during the study that may affect your willingness to continue participating in the study, we will notify you and discuss with you whether you should continue the study. You can request to withdraw from this study at any time for any reason. To ensure your safety, please complete the last visit so that the doctor can complete all the inspection items required by the last inspection and discover possible adverse reactions. Whether you participate in or refuse to participate in this research, or withdraw from the research, you will not be discriminated against or retaliate, and your medical treatment and rights will not be affected.If the informed consent is updated during the study, you will need to sign the new version of the informed consent form again. After the study, if you need specific information about your medication, you can consult your study doctor. During the research process, we will provide you with a comprehensive evaluation of relevant indicators, monitoring of vital signs, and evaluation of the side effects of EUS-FNA/FNB for you; after the end of the research, if you still have medical questions related to this project, you can consult us. Contact your doctor and we will do our best to answer it for you.

Contact information

If you have any concerns or questions about the study, or in the event of any emergency, please contact your doctor promptly. Please save this information.

Doctor's name: _____

Telephone number: _____

If you have any questions about your rights, you can contact:

Ethics Committee of the Third Xiangya Hospital of Central South University

Tel: 0731-88618938

Informed consent

I have read the above and understand the aim of the study, its purpose, and the possible adverse effects of this drug, and have had the opportunity to discuss and ask questions about this study with my doctor. All my questions have been answered satisfactorily. I agree to visit the doctor on time during the study and receive the appropriate examinations related to this study. I will comply with the subject instructions and fully cooperate with the researcher to truthfully and objectively provide the researcher with the health status and related conditions before participating in this study, during the study and during each follow-up period. I understand that participation in the study is voluntary, I acknowledge that I have had sufficient time to consider this, and I understand that I can withdraw from the study at any time without my subsequent treatment being adversely affected, and I understand that physicians have the right to at any time in accordance with my circumstances suspend the study. I hereby express my consent to participate in this clinical study and I will receive a signed and dated copy of the informed consent form.

Participant's sign: **Telephone number:**

Date:

I have explained the details of the study to the above study participant and have provided the participant with a signed informed consent form.

Researcher's sign: **Telephone number:**

Date: