

INFORMED CONSENT

version: 2.0, Date: 2024-1-2

INFORMED CONSENT

Effect of esketamine on postoperative sleep disturbance in patients undergoing spinal surgery: a randomized, double-blinded, placebo-controlled clinical trial

Project entrust organization: Beijing Tiantan Hospital

Contract Research Organization: N/A

Version: 2.0

2nd, January, 2024

INFORMATION SHEET

You will receive *spinal surgery*. We would like to invite you to participate our study, which is “*Effect of esketamine on postoperative sleep disturbance in patients undergoing spinal surgery: a randomized, double-blinded, placebo-controlled clinical trial*”, to evaluate the effect of esketamine on the PSD of patients undergoing spinal surgery. This study is approved by Ethics Committee of Beijing Tiantan Hospital of Capital Medical University. During our study, we will follow the Declaration of Helsinki.

Before you decide whether participate this clinical trial, please take time to review this information carefully. This form describes the purpose, procedure, study duration, risks, and possible benefits of participating the study. You may also wish to talk to others, including your friends, family, or discuss with your anesthesiologist about your participation in this study.

1. PURPOSE of THIS STUDY

Postoperative sleep disturbance (PSD), which can result in sleep fragmentation, deprivation, and a reduction in slow-wave sleep (SWS) and rapid eye movement (REM) sleep, is one of the most common complications after major surgery, and its incidence varies from 30-80%. The incidence of PSD after spinal surgery is approximately 61.4%. Previous investigations have reported that continued PSD can cause chronic pain or increased pain sensitivity, heightened stress levels, delirium, gastrointestinal dysfunction, increased risk of cardiovascular events and decreased immune responses. Therefore, sleep promotion is one of the most important ways to help surgical patients recover by reducing delirium, pain, fatigue, and cognitive dysfunction.

Esketamine is a right-handed monomer of ketamine that retains all the advantages of ketamine and has a stronger affinity for NMDA receptors. Recently, there has been increasing interest in its ability to improve sleep disturbance because of its anti-inflammatory, powerful analgesic and antidepressant effects. Since research on the effect of esketamine on PSD in patients undergoing major spinal surgery is scarce and objective measures of sleep are lacking, we conducted this randomized, double-blinded, placebo-controlled clinical trial.

2. NUMBER of PARTICIPANTS

In total, 156 patients will be included in the study.

3. WHO WILL PARTICIPANT IN THIS STUDY

- Age range from 18 to 65 years old
- American Society of Anaesthesiologists (ASA) physical status I to III
- The patient underwent elective spinal surgery under general anaesthesia.

4. WHO SHOULD NOT PARTICIPATE in the STUDY

If you have following condition, you should not participate in the study:

- Body mass index (BMI) ≥ 35 kg/m².
- Severe lesions of important organs.
- The patient underwent tracheal intubation or was admitted to the intensive care unit (ICU) postoperatively.

INFORMED CONSENT

version: 2.0, Date: 2024-1-2

- History of adverse reactions or contraindications to ketamine or esketamine.
- Cognitive dysfunction, communication disorders.
- Patients who refused to participate in this study.

5. DURATION OF THIS STUDY

This study will only be conducted during your hospital stay. You will be followed up at 24h, 48h, 72h after surgery for any adverse reactions, and your sleep quality will be assessed.

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

6. PROCESS OF THIS STUDY

If you are willing to participate in this study, your doctor will learn about your medical history, ask about your current disease, and current treatment medications to further confirm whether you are suitable for participating in this study.

If you are willing to participate in this study, during the general anesthesia of the operation, you have a half chance of using esketamine. There is also a one-half possibility of using saline. The incidence of post operative sleep disturbance will be assessed.

The day before your scheduled surgery, the researcher will determine whether you meet the inclusion-exclusion criteria of this study based on your disease and current status. If you agree to participate in the research, we will interview your medical details. After 24h, 48h, 72h, the researcher will examine your condition again. All visits will not cause you any harm. Participation in this study does not require changes to your surgical methods and postoperative treatment. Except for randomly entering a study group and receiving different administration methods of muscle relaxants, other anaesthesia management will not be affected in any way. Both medication regimens are safe. If you enter any research group, we will try your best to ensure that your surgery goes smoothly.

7. POSSIBLE BENEFITS of PARTICIPATING in the STUDY

The depth of anaesthesia will be under our strict monitoring during the operation. The results obtained from this study may perioperative anaesthesia management plans and improve PSD in patients undergoing spinal surgery.

8. POSSIBLE ADVERSE REACTIONS, RISKS and DISCOMFORT, INCONVENIENCES of PARTICIPATING in the STUDY

The adverse reactions of esketamine include bradycardia, hypotension, tachycardia, hypertension, arrhythmia, nystagmus, hypersalivation, euphoria, emergence agitation, hallucinations, dreaminess and nightmares. In this study, the dosage of esketamine is small and will not cause obvious adverse reactions. We have also formulated a detailed response plan if any adverse reactions occur after surgery; hypertension and tachycardia can be relieved by giving antihypertensive drugs.

If your health does suffer from research-related damage due to participation in this research, please notify the doctor immediately, who will be responsible for taking appropriate treatment

INFORMED CONSENT

version: 2.0, Date: 2024-1-2

measures for you. The sponsor, Beijing Tiatan Hospital, will bear the cost of treatment and provide you with corresponding financial compensation in accordance with relevant national regulations. Even if you have signed this informed consent form, you still retain all your legal rights.

9. OTHER TREATMENT CHOICE

If you do not participate in this study, you can choose your anesthesia treatment according to your anesthesiologist's suggestion.

10. YOU MAY VOLUNTARILY CHOOSE TO PARTICIPATE in the STUDY and WITHDRAW from the STUDY

Whether to participate in the study is entirely up to you. You may refuse to participate in the study or withdraw from the study at any time during the study, which will not affect your relationship with your doctor or affect your medical service or other benefits.

Before making decision, you can discuss with your family or friend, or you can talk with your doctor for any question, until you fully understand this study.

11. RELATED EXPENSES

Anesthetic drugs and surgical procedures are not free of charge. If you combine the treatment and examination required for other diseases, and if the treatment fails, the cost of changing to other treatment is not free of charge. If any medical expense happened due to adverse event, you will be exempted from the charge.

12. CONFIDENTIALITY of PERSONAL INFORMATION

Your medical records (study records /CRF, lab sheets, etc.) will be kept intact at the hospital. Your doctor will record the results of tests and other tests on your medical record. Researchers, ethics committees, and drug regulators will be allowed access to your medical records. Any public reports on the results of this study will not disclose your personal identity. We will make every effort to protect the privacy of your personal medical data within the law.

13. HOW TO GET MORE INFORMATION?

You can ask any questions about this study at any time and get answers. Your anesthesiologist will be ready to answer any of your questions before, during and after the study.

14. HOW THE STUDY MAY EFFECT YOUR LIFE?

You may feel the visit and examination uncomfortable and special arrangement is needed. You can consult your doctor in any steps of the study.

15. CONSULTING

If you have any related questions, please contact Dr. Jian Minyu (phone: 010-59976656 or cell phone: 13522550438).

If you have any concerns about your personal benefits, or you want to complain or express your concerns about the study, please contact the Ethics Committee of Beijing Tiantan Hospital, Capital Medical University (phone: 010-59975178, email: tyyirb@163.com)

SINGATURE PAGE OF AGREEMENT

Study title: Effect of esketamine on postoperative sleep disturbance in patients undergoing spinal surgery: a randomized, double-blinded, placebo-controlled clinical trial

Principal Investigator: Ruquan Han, Beijing Tiantan Hospital, CMU

DECLARATION of CONSENT

I have read the introduction about the study above and have the opportunity to discuss with doctors and ask the questions about the study. All my questions have been answered satisfactorily.

I am aware of the possible risk and benefits of participating in this study. I know that participating in the study is voluntary. I have taken it into full consideration, and known that:

- I can ask my doctor for more information at any time.
- I can withdraw from this study at any time without discrimination or retaliation, and my medical treatment and rights will not be affected.

I am also aware that if I withdraw from the study, especially if I withdraw due to medication, it will be of great benefit to the whole study if I tell my doctor about my condition and complete the corresponding physical examination and physical and chemical inspection.

If I need to take any other medication due to a change in my condition, I will consult my doctor beforehand or tell him afterwards truthfully.

I agree that the ethics committee of the drug regulatory authority or the representative of the sponsor may have access to my research information.

I will be provided with a signed and dated copy of the informed consent.

In the end, I agreed to participate in the study and promised to follow my doctors' advice as much as possible.

Signature of patient/legal relative: _____

Relation: _____

Date: _____ (yyyy/mm/dd)

I confirm that I have explained the details of the trial to the patients, including its rights and possible benefits and risks, and have given them a signed copy of the informed consent.

Signature of doctor: _____

Date: _____ (yyyy/mm/dd)