# Informed Consent Form

| | |
|---|---|
| **Medical research title:** | **a Prospective Randomized Controlled Study of the Effects of Different Therapy Regimens on Menopausal Sleep Disorders** |
| **Main Research Institute:** | **Peking Union Medical College Hospital** |
| **Version:** | **3.0** |
| **Version Date:** | **2023-09-06** |
| **Subject Name** | |
| **Subject ID** | |

Dear participants,

We would like to invite you to participate in a clinical study titled "Prospective randomized controlled study on the intervention effects of different drug regimens on menopausal sleep disorders".

Before deciding whether to participate or not, please carefully read this informed consent form and ask researchers about your concerns. You can also ask your family, friends, or other individuals. You need to sign this form if you decide to join in.

**1. Background**

Sleep disorders are one of the most common menopausal symptoms. Long-term chronic sleep disorders can cause a series of health problems, seriously affecting physical and mental health and lowering quality of life of perimenopausal women. Menopausal hormone therapy (MHT) is an effective treatment for menopausal related symptoms, which may have a indirectly therapeutic effect on menopausal sleep disorders by improving other menopausal symptoms such as vasomotor symptoms. Traditional Chinese medicine also has therapeutic effects on perimenopausal sleep disorders. At present, there is no domestic prospective randomized controlled study on medical treatment of menopausal sleep disorders. Our team plans to carry out a multicenter, prospective, randomized controlled study to compare the effectiveness of menopausal hormone treatment (Tibolone), traditional Chinese patent medicine (Xiangshao Granule) and the combination of both treatment for moderate to severe menopausal sleep disorders. This study has been approved by the Ethics Committee of Peking Union Medical College Hospital.

**2. What is the objective of this study?**

The objective of this study is to evaluate the intervention effects of different drug regimens on moderate to severe menopausal sleep disorders.

**3. Method**

This is an intervention study, participating with approximately 180 patients. The subjects will be divided into three groups: Group A (Tibolone), Group B (Xiangshao Granules), and Group C (Tibolone+Xiangshao Granules). The proportion of participants is 1:1:1 in the three groups. The grouping method is random (like drawing lots), so neither you nor the researcher can choose specific group beforehand.

**4. research process**

(1) Before participating in this study, you need to sign this informed consent form.

(2) During the screening period, researchers will inquire and collect your personal information, past diagnosis and treatment history, and concomitant medication. Arrange you to undergo complete blood count, urinalysis, liver function, kidney function, blood lipids and blood glucose, thyroid function, sex hormones, ultrasound examination (pelvic, abdominal, breast), and other examinations. Physical examination will be conducted, including gynecological

examination and TCT cervical screening. If you have undergone complete blood count, urinalysis, abdominal ultrasound, and TCT cervical screening within the past year with normal results, there is no need to repeat corresponding items this time. You need to record your sleep diary every day since screening period.

(3) If you meet inclusion criteria, you will need to take the medication orally every day. Group A protocol: 1.25mg orally once a day. Group B protocol: Xiangshao granules 4 g orally 3 times a day. Group C protocol: Tibolone 1.25mg orally once a day+Xiangshao granules 4 g orally 3 times a day.

(4) During research period, you are not allowed to take other sex hormone drugs or traditional Chinese medicine/botanical drugs that affect menopausal symptoms. Anti anxiety and depression drugs, or sedative and hypnotic drugs are also not allowed. If you take drugs above, you will automatically withdraw from this study. Then conventional therapies will be given in the future.

(5) You need to follow the plan requirements and come to the hospital for follow-up every 4 weeks from the first day of medication. Researcher will inquire about your current medication status, improvement of sleep symptoms, and whether there are any drug related adverse reactions at each follow-up. At the last follow-up in week 8, we will arrange you to repeat examination of liver function, kidney function, blood lipids, blood glucose, and sex hormones.

(6) During the screening period and the week 8 follow-up, you need to go to the hospital for polysomnography (PSG) monitoring. PSG is a non-invasive examination that collects data on your brain waves, respiratory function, and other parameters through external lead before bedtime. It usually requires your cooperation until the next day after waking up. The PSG test results are only for medical research purposes and will not be disclosed to you personally.

(7) During the screening period and follow-up at weeks 4 and 8, you need to fill out a menopausal symptom questionnaire, which mainly includes improved Kupperman score, MENQOL Scale, PSQI questionnaire, Self-Rating Anxiety Scale (SAS), and Center for Epidemiological Survey, Depression Scale (CES-D) .

(8) Research process is arranged as follows:

V0 screening period: Preliminary screening shows that your situation meets all the inclusion criteria for in this study, and does not meet any of the exclusion criteria. Collect approximately 15ml of venous blood and 10ml of urine sample. Conduct pelvic, breast, and abdominal ultrasound. Conduct physical examination and cervical TCT screening. Complete symptom related questionnaire. Receive and start filling out a sleep diary. Conduct PSG monitoring.

V1 follow-up period (day 1): within 7 days from the V0 screening period. Receive sleep diary.

After confirming that all criteria are met, patient are randomly assigned to different group and receive medication to begin treatment.

V2 follow-up period (week 4): Repeat symptom questionnaire, return/receive sleep diary, and receive medication.

V3 follow-up period (week 8): Repeat symptom questionnaire, return/receive sleep diary and conduct physical examination. Collect approximately 10ml of venous blood, conduct PSG monitoring. Withdraw remaining drugs.

**5. How will this study end?**

(1) If you have completed all follow-up of this study, which will last for 8 weeks, the study medication will no longer be provided to you, and you will receive subsequent treatment according to conventional clinical practice.

(2) You can choose to withdraw from the study at any time, and the research doctor may ask you to quit this study considering your health and benefits. Before exiting, the research doctor may arrange relevant examinations to ensure your safe exit.

(3) During the research process, the research doctor, research sponsor, regulatory authorities, and ethics committee have authority to terminate the study.

**6. Research Benefits**

(1) Your health condition may be improved by participating in this study, but the improvement cannot be guaranteed.

(2) Your participation in this study may help doctors learn more about the effectiveness of different regimens in treating menopausal sleep disorders. Other patients with the same or similar diseases may benefit from this information in the future.

**7. Risks and inconveniences**

(1) Any research carries known or unknown risks. Some are mild and temporary, while others are severe and permanent. Whether risks arise, which ones occur, and their severity vary from person to person. Your research doctor will take all preventive measures and monitor your condition closely. If any discomfort occurs, please inform your research doctor immediately so necessary measures can be taken in a timely manner.

(2) Adverse reactions found in previous studies and clinical applications of the research drug include: 1. breast swelling and pain, 2. gastrointestinal discomfort, 3. drug allergy, 4. abnormal uterine bleeding.

(3) Possible risks of studying related procedures include hematoma and infection at the puncture site of venous blood collection.

(4) Possible inconvenience caused by the study: To participate in this study, You will need to

come to the hospital 4 times and may receive telephone follow-up. During the follow-up, you may need to fill out relevant questionnaires, which will take about 15 minutes. You need to undergo PolySomnoGraphy twice, and each time requires one night stay in the hospital. During the research process, you are required to fill out sleep diary every day. Please fully consider these inconveniences when deciding whether to participate in this study.

**8. Alternative solutions**

If you do not participate in this study, you can choose cognitive behavioral therapy for insomnia without drugs, or accept currently approved sedative and hypnotic drugs, sex hormone therapy, or other medical treatments without sex hormones. Your research doctor will explain the potential benefits and risks of relevant treatments to you.

**9. New information during the research process**

During the research process, if researchers receive the latest important information related to the study, we will inform you timely and it's up to you whether to continue participating in this study.

**10. Research related expenses**

(1) You do not need to bear any research related costs. The medicine (Tibolone or Xiangshao granules) and examination related will be borne by researchers.

(2) You will not receive reward for participating in this clinical study.

**11. Research related damages**

If you experience any discomfort during the research process, please contact the research doctor in time, who will guide you in subsequent diagnosis and treatment. Researchers have purchased insurance for this study. If your health is damaged due to participating in this study, the insurance company will be responsible for providing treatment and compensation.

**12. How to handle my samples**

- This study will collect 25ml of your blood and 10ml of your urine.
- Samples collected in this study and their usage are shown in the table below:

| visit | sample type | sample amount | testing items | laboratory |
|---|---|---|---|---|
| V0 | blood | 15ml | complete blood count, thyroid function, liver function, kidney function, blood lipids, blood glucose, sex hormones | PUMCH |
| V0 | urine | 10ml | urinalysis | PUMCH |
| V3 | blood | 10ml | liver function, kidney function, blood lipids, blood glucose, sex | PUMCH |

| | | | | |
|---|---|---|---|---|
| | | | hormones | |

- The blood samples collected in the study will be tested and analyzed in our hospital, and the remaining will be destroyed according to medical conventions.
- Your biological sample will only be used for the purposes described in this study protocol and this informed consent form.
- If you withdraw from the study in advance, we will no longer collect new samples, but samples or data that have already been collected or analyzed will be retained.

**13. Confidentiality System**

(1) In this study, personal and medical information may be collected or processed, including but not limited to: your name, gender, birthday, address, phone number, diagnosis and treatment, medical examination, medical imaging, etc.

(2) Your personal information will only be used for the purposes described in this study protocol and this informed consent form.

(3) The medical information obtained from your participation in this research will be kept confidential. The research results will not disclose any identifiable information when published in academic journals.

(4) Researchers are responsible for storing and using all your personal data in this study. Peking Union Medical College Hospital, Ethics Committee, or Clinical Research Supervision Department may have access to your personal data.

**14. Possible conflicts of interest in funding sources**

This study was funded by the Clinical Research Special Project of the Central High level Hospital of Peking Union Medical College Hospital. There is no conflict of interest between the researcher and this study.

**15. voluntary participation**

Your participation is completely voluntary. You may reject to participate or withdraw your consent from this study at any time during the research process, which will not affect your relationship with medical staff, and your conventional medical care will not be affected in any way.

**16. Patients note**

(1) Please truthfully inform the research doctor of your health status and medication use;
(2) Please take your medication and attend the follow-up at the hospital on time;
(3) If you experience any discomfort, please inform your research doctor in time;
(4) During the research, drugs that cannot be taken include: other sex hormone drugs, traditional Chinese medicine/botanical drugs that affect menopausal symptoms, anti anxiety and depression drugs, sedative and hypnotic drugs. If you take any drug above, you will

withdraw from this study automatically. Then you will receive conventional treatment in the future.

17. **Contact**

If you experience any discomfort or have any questions about this study, you can contact the researcher:

| | | |
|---|---|---|
| Title: Research Assistant | Name：Lingjin Yang | Phone number：15650795133 |

If you have any questions about your rights as a subject, you can contact the Ethics Committee:

| | | |
|---|---|---|
| Title: Ethics Secretary | Name：Jiayue Li | Phone number：010-69156874 |

Thank you for reading and considering whether to participate in this study.

**18. Signature Page**

**Subject:**

I confirm the following information:

(1) I have read and understood the information above and have sufficient time to consider whether to participate in the study.

(2) All my questions have been answered satisfactorily.

(3) I voluntarily participate in this study and willing to follow the research procedures.

(4) I know that I can withdraw from this study at any time without giving any reason, and my treatment and rights will not be affected.

(5) I have received an informed notice and signed consent form for my own retention.

(6) I agree to collect and use my samples as described in this informed consent form.

(7) I allow the collection and use of my personal information in this study.

(8) I know there might be contact in the future to obtain permission for this study or any related sub studies.

By signing this document, I agree to participate in this study as stated in the informed consent form.

Subject Name (in regular script): _____

Subject Signature: _____ Date: _____

**The following is only applicable to subjects without behavioral ability, and the guardian's signature is required.**

[Subject Name (in regular script):_____, The relationship between the guardian and the subject is_____.]

Guardian's Name (in regular script):_____ Phone Number: _____

Guardian Signature:_____ Date:_____

**The following is only applicable to subjects without reading and writing abilities, and requires the signature of an impartial witness.**

Witness Name (in regular script):_____ Phone Number:_____

Witness signature:_____ Date:_____

Researcher/Authorized personnel name (in regular script): _____

Researcher/Authorized personnel signature:_____Date: _____

---