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Informed Consent Form

Effect of Transcranial Magnetic Stimulation vs Sham Stimulation Combined With Pinaverium Bromide vs Bifidobacteria in Diarrhea-Predominant Irritable Bowel Syndrome: A 2×2 Factorial Randomized Clinical Trial

Dear Madam/Sir,

You are invited to participate in a clinical research study. The following sections describe the background, objectives, methods, potential benefits and risks, inconveniences, and your rights related to this study. Please read this document carefully before deciding to participate. This informed consent form provides information to help you make an informed decision. If you have any questions, please ask the study physician to ensure you fully understand the content. Participation in this study is voluntary. If you agree to participate, please sign the signature page of this informed consent form.

1. Study Background

Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder characterized by abdominal pain, bloating, or discomfort, often relieved by defecation. It is frequently associated with changes in bowel habits, such as abnormal stool frequency or consistency, but lacks clear morphological, imaging, or endoscopic abnormalities. Epidemiological studies indicate that the prevalence of IBS in China ranges from 5% to 11%. In the gastroenterology specialty clinic of our hospital, IBS patients account for over one-third of all patients. Although IBS is not life-threatening, its high prevalence, chronic course, and limited response to pharmacological treatments can significantly impair quality of life and impose a substantial socioeconomic burden. Due to the absence of obvious intestinal inflammation or pathological/biochemical abnormalities, as well as the scarcity of ideal animal models, research progress in IBS has been slow. The unclear etiology also contributes to the lack of effective clinical treatments. Our preliminary research has shown that repetitive transcranial magnetic stimulation (rTMS) can significantly improve visceral hypersensitivity in IBS patients by modulating cortical excitability and neural plasticity. Therefore, we aim to further validate the synergistic therapeutic effects of rTMS combined with intestinal

medications (pinaverium bromide/bifidobacterium) to provide a novel neuro-gut axis modulation strategy for IBS treatment.

2. Study Title and Objectives

The title of this study is: Effect of Transcranial Magnetic Stimulation vs Sham Stimulation Combined With Pinaverium Bromide vs Bifidobacteria in Diarrhea-Predominant Irritable Bowel Syndrome: A 2×2 Factorial Randomized Clinical Trial

This is a randomized, controlled study. You will be randomly assigned to one of the following four treatment groups:1.rTMS stimulation + pinaverium bromide;2.rTMS stimulation + bifidobacterium;3.Sham rTMS + pinaverium bromide;4.Sham rTMS + bifidobacterium.

To ensure the validity of the study, the treatment assignment will be blinded to you.

The primary objective of this study is to evaluate the feasibility of repetitive transcranial magnetic stimulation (rTMS) in alleviating chronic visceral pain in patients with diarrhea-predominant irritable bowel syndrome.

3. Study Methods and Procedures

This study utilizes transcranial magnetic stimulation (TMS) as an intervention.

Transcranial Magnetic Stimulation (TMS)

(1) Introduction

TMS is a non-invasive, painless, and non-destructive neuromodulation technique. It uses an electromagnetic coil placed on the head to deliver repetitive magnetic stimuli. When energy is transmitted to brain tissue, it generates electric currents. TMS is a simple, non-invasive treatment method applicable for various conditions, including pain, movement disorders, consciousness disorders, tinnitus, depression, and anxiety disorders.

(2) Treatment Procedure

Treatment duration: Patients will receive TMS treatment once daily for 7 days per week, over a period of 2 weeks.

rTMS parameters: 1 Hz, 80% motor threshold (MT), 20 minutes per day.

4. Study Process and Timeline

The study consists of a screening period, intervention period, and follow-up period. The treatment phase will last approximately 2 weeks and does not require hospitalization. Follow-up will be conducted over 3 months. Assessments may include functional magnetic resonance imaging (fMRI), anorectal manometry, analysis of fecal microbiota and metabolites, and relevant scale evaluations. Additional tests may be added based on your condition.

5. Study Costs and Compensation

Participants will receive the following free diagnostic and treatment items: repetitive transcranial magnetic stimulation (rTMS). Additionally, participants in the control group will receive compensation for transportation or lost wages. After one treatment course, transportation subsidies will be provided at 300 RMB per person. If transportation subsidies are provided, no additional compensation for lost wages will be given. If transportation subsidies are not needed, lost wage compensation will also be 300 RMB per person.

6.Potential Benefits of Participation

You may or may not directly benefit from this study. Potential benefits include possible improvement in your condition. Analysis of your samples and/or medical data may contribute to advancements in IBS treatment technologies. We sincerely thank you for your participation and contribution to scientific research and medical progress.

7.Potential Risks and Discomforts

Risks associated with TMS

(1) Syncope or seizures during treatment.

(2) Post-treatment discomfort (including headache, neck pain, insomnia, etc.).

8.Treatment and Compensation for Study-Related Injuries

The study physician will make every effort to prevent and treat any injuries resulting from this study. If an adverse event occurs during the trial, a medical expert committee will determine whether it is related to the study treatment. The sponsor has provided liability insurance for this study. If an adverse reaction caused by the study drug or diagnostic procedures required by the study protocol results in injury, the sponsor will cover the related treatment costs and provide

appropriate compensation in accordance with China's "Good Clinical Practice" guidelines, unless the injury is due to medical malpractice.

Treatments and examinations for other concurrent diseases are not covered. Costs associated with voluntary or involuntary withdrawal from the study or post-study treatments (excluding related adverse events) are not covered by the sponsor.

Signing this document does not waive your legal rights to seek compensation for bodily injury sustained in this study.

9. Conventional Treatment Options Outside This Study

Conventional treatment options outside this study include: all enrolled patients will receive standardized IBS health management (low FODMAP diet guidance + stress management training). Basic symptomatic medications are permitted (loperamide ≤4mg/day for acute diarrhea control, antispasmodics as needed ≤10 times/month). Neuromodulatory drugs that may affect study results (tricyclic antidepressants, SSRIs) are prohibited. Patients may continue existing treatments for chronic conditions (e.g., antihypertensives, hypoglycemics), but detailed medication information must be recorded. Outpatient follow-ups every 3 months will monitor complete blood count, liver and kidney function. Alarm symptoms (weight loss >10%, bloody stools) will trigger immediate colonoscopy. Initiation of new IBS-related treatments (e.g., cognitive behavioral therapy) during the study period is considered a protocol deviation and must be reported to the ethics committee. All conventional treatment data will be automatically captured via the electronic medical record system and included as covariates in the final analysis model.

10. Subject Rights

Participation in this study is voluntary. You may choose not to participate or withdraw at any time without discrimination or retaliation. Your medical care and rights will not be affected. If you experience any study-related injury, you are entitled to free treatment or appropriate compensation.

11. Subject Responsibilities

As a study participant, you are responsible for: providing accurate information about your medical history and current health status; informing the study physician of any discomfort experienced

during the study; and disclosing whether you have recently participated or are currently participating in other research studies.

12. Confidentiality of Clinical Research Data

If you decide to participate, your personal data will be kept confidential. Your biological samples will be identified by a study code number rather than your name. Identifiable information will not be disclosed to anyone outside the research team without your permission. All research personnel are required to maintain confidentiality. Your records will be stored in locked cabinets accessible only to authorized researchers. Government regulatory authorities or ethics committee members may review your records to ensure compliance with regulations. Any published results will not disclose your personal information.

13. Collection and Management of Human Biological Samples

Not applicable.

14. Contact Information

If you have questions about this study, experience any discomfort or injury during the study, or have concerns about your rights as a participant, you may contact:

Ruixia Weng

Tel: 15206214921

If you have questions or complaints regarding your rights or well-being as a participant, you may contact the institutional ethics committee:

Zhoulin Lu

Tel: 0512-67972861

15. Declaration and Signatures

Subject Declaration:

I have carefully read this informed consent form and have had the opportunity to ask questions, which have been answered to my satisfaction. I understand that participation is voluntary, and I may choose not to participate or withdraw at any time without discrimination or retaliation. My medical care and rights will not be affected.

The study physician may discontinue my participation if I require other treatments, fail to comply with the study plan, or for any other valid reason.

I voluntarily agree to participate in this clinical study and will receive a signed copy of this informed consent form.

Subject Name (Printed): _____

Subject Signature: _____

Date: _____ (Month/Day/Year)

Phone: _____

Legal Representative (if applicable):

Legal Representative Name (Printed): _____

Legal Representative Signature: _____

Date:_____ (Month/Day/Year)

Phone: _____

Relationship to Subject: _____

Reason subject cannot sign: _____

Investigator Declaration:

I have accurately explained the contents of this informed consent form to the subject and answered all questions. The subject voluntarily agrees to participate in this clinical study.

Investigator Name (Printed): _____

Investigator Signature: _____

Date:_____ (Month/Day/Year)

Phone: _____