Official Title:
Exploring the Efficacy of Respiratory Training Intervention in Patients with Emotion Regulation–Related Sleep Disorders

ClinicalTrials.gov Identifier: Pending

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Informed Consent Form

Official Title: Exploring the Efficacy of Respiratory Training Intervention in Patients with Emotion Regulation Sleep Disorders	
Research Institution: Qilu Hospital of Shandong University	
Department/Division: Geriatric Medicine	Phone: 18560082210
Principal Investigator: Jiang Wenjing	Title: Chief Physician
Co-Principal Investigator/Participant:	Title:
Emergency Contact: Li Haiyun	Emergency Contact Number: 18560088921
Volunteer Participant Name:	ID Number:
Gender:	Age:
Mailing Address:	Phone:
Medical Record Number:	

(I) Study Purpose:

We cordially invite you to participate in a medical research program involving 188 patients in China. This program builds upon prior research to further investigate the efficacy of respiratory training interventionin patients with emotion-regulated sleep disorders. The study will help elucidate the underlying mechanisms related to heart-brain axis activity, potentially offering new intervention approaches and efficacy assessment methods for the diagnosis and treatment of sleep disorders.

Your participation will enable us to further explore the pathogenesis of sleep disorders.

(II) Trial Methods: (Including subject inclusion criteria and numbers; trial design and procedures; trial duration and schedule; follow-up or rehabilitation plan; evaluation and statistical methods)

(1)Subject Inclusion and Exclusion Criteria and Numbers

3.2.1 Inclusion Criteria:

Diagnostic Criteria for Insomnia:

Based on Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria, patients were screened by two neurologists with 15 years of experience using a semi-standardized mental and sleep-related interview. Selected subjects met the following criteria:

① Self-reported difficulty falling asleep, difficulty maintaining sleep, or early awakening;

② Symptoms occurring at least three times per week for a minimum of three months;

③ At least one associated daytime impairment (e.g., fatigue, mood disturbance, or impaired cognitive function);

④ No other sleep disorders (e.g., obstructive sleep apnea or sleep-related movement disorders), severe organic diseases, or psychiatric conditions such as depression or generalized anxiety disorder;

⑤ All selected patients abstained from any psychoactive medications for at least 2 weeks prior to and during the study to eliminate drug effects;

Insomnia with Mood Disorders

Inclusion Criteria:

① Meets the above diagnostic criteria for insomnia;

② Aged 18 to 80 years;

③ PSQI > 5, ISI > 7, HAMA > 7, and/or HAMD ≥ 7;

④ No communication barriers;

⑤ Signed informed consent form.

Exclusion Criteria

① Secondary insomnia caused by other physical illnesses;

② Other types of sleep disorders and mood disorders;

③ Long-term sleep disruption due to environmental or other human factors.

Determination of Sample Size

Using PASS software, sleep improvement was assessed based on PSG sleep data, PSQI scores, and ISI scores. According to literature reports, the improvement rate in the control group was 74%, while the estimated improvement rate in the study group was 92%. With $\alpha=0.05$ and $1-\beta = 0.90$. Each group's sample size was calculated, accounting for 5% loss to follow-up or dropout. The final sample size per group was determined to be 89 cases, totaling 188 cases.

（2） Trial Design and Primary Procedures

Trial Design

(1)Study Type: Single-center randomized controlled trial

Use the "Random Number Generator" in the "Transform" toolbar of SPSS software to generate a specified number of random numbers between 0 and 1. Then, under "Transform" → "Compute Variable," define it as "Random Number" and set the numeric expression to "RV.UNIFORM(0,1)". We used the "Visual Binning" feature in "Transform" to group the random numbers (and their corresponding subjects). The binning variable was set as "Group." To divide into two groups, we set the number of bins so that the "Group" variable appeared. Patients assigned to Group 1 were included in the study group, while those assigned to Group 2 were included in the control group.

(2) Sample Size Calculation: Using PASS software, we assessed sleep improvement based on PSG sleep data, PSQI scores, and ISI scores. According to literature reports, the improvement rate in the control group was 74%, while the estimated improvement rate in the study group was 92%. Setting $\alpha=0.05$ and and $1-\beta = 0.90$. Considering a 5% attrition rate, the calculated sample size per group is 89 cases, totaling 188 cases.

Research Variables (Factors) and Measurement

(1) Pre-experimental measurements

Includes general clinical data, scale assessments, Holter monitoring, blood pressure, and basal metabolic rate. Scale assessments comprise: - Pittsburgh Sleep Quality Index (PSQI) (Scoring: 0-5 Excellent, 6-10 Fair, 11-15 Moderate, 16-21 Poor) - Insomnia Severity Index (ISI) (Scoring: Total range: 0-28; 0-7 indicates no clinically significant insomnia, 8-14 subthreshold insomnia, 15-21 moderate clinical insomnia, 22-28 severe clinical insomnia), Montreal Cognitive Assessment (MoCA) (Note: ≥26 indicates normal), Mini-Mental State Examination (MMSE) (Note: ≥27 indicates normal, 21-26 points: mild, 12-20 points: moderate, <12 points: severe), Hamilton Anxiety Scale (HAMA) (Note: ≥21 points: possible severe anxiety, ≥21 points: definite significant anxiety, ≥14 points: definite anxiety, >7 points: possible anxiety, ≤7 points: normal), Hamilton Depression Rating Scale (HAMD) (Note: <7 points indicates no depression, 7-12 points indicates mild depression, 18-24 points indicates moderate depression, >24 points indicates severe depression), Epworth Sleepiness Scale (ESS), SF-36 Health Survey, and other relevant scales. A simplified formula is used to estimate basal

metabolic rate (BMR), such as the Gale formula: BMR% = (pulse rate + pulse pressure) - 111.

(2) Variables measured during the experiment:

Measure the following data from 0 to 30 minutes after lights-out:

0 minutes before experiment start: Measure mood state (POMS scale), blood pressure, basal metabolic rate, and EEG.

ECG/EMG and EEG/EMG monitoring: Sympathetic nervous system activity. (Full 30-minute duration)

Treatment administered to subjects

The control group received routine clinical intervention, including health education for patients and their families. Before the examination, patients and families were instructed on necessary precautions and provided with full accompaniment and guidance throughout the examination. They were informed about medication precautions, given dietary guidance, and their emotional state was closely monitored.

The research team supplemented conventional clinical interventions with respiratory training, comprising three sequential protocols: ① Pursed-lip breathing: Instruct patients to keep their mouths closed, inhale through the nose, and exhale by pursing their lips as if whistling, gently releasing the air. Maintain a 2:1 ratio of exhalation to inhalation time, performing deep inhalations and slow, steady exhalations. For patients with non-standard technique, healthcare providers should demonstrate and guide repeatedly to ensure each patient achieves proper form. Train three times daily for 15 minutes per session. ② Balloon Inflation Training: Using balloons with a capacity of approximately 1000ml, instruct patients to inflate 5 balloons within 15 minutes. The number of balloons may be adjusted based on the patient's physical condition and respiratory function. Ensure balloons are inflated slowly and evenly to prevent bursting. Training duration is 45 minutes daily, divided into 15-minute sessions. ③ Respiratory Trainer Exercise: The patient sits upright with the upper body straight. Gently exhale through the mouthpiece, then inhale forcefully and rapidly to raise the ball inside the trainer. Hold the ball in the raised position for approximately 5 seconds before releasing the

mouthpiece. Repeat this sequence 5–10 times. Perform this exercise three times daily, with each session lasting 15 minutes. The three training methods are rotated: one method per day, two rotations per week, for a total of two weeks. All training is conducted in the outpatient setting.

Subject Grouping Method

This study is a single-center randomized controlled trial. Study groups: The research comprises two groups:

Study Group: (Respiratory Training Intervention) Control Group: (Standard Clinical Intervention)

（3） Biological Sample and Medical Information Handling Protocol

Includes clinical data, scale assessments, blood pressure, Holter monitoring, electroencephalogram (EEG), basal metabolic rate, and sympathetic nervous system activity. Strict confidentiality measures are implemented for all information.

(4) Trial Duration and Schedule

This trial will be conducted from August 2024 to August 2027, with an estimated enrollment of 188 patients.

(5) Follow-up Plan

Measure the following data from 0 to 30 minutes after lights-out

0 minutes before trial initiation: Measure mood state (POMS scale), blood pressure, basal metabolic rate, and EEG.

ECG/EMG and EEG/EMG monitoring: Sympathetic nervous system activity. (30 minutes total)

(6) Evaluation and Statistical Methods

Comparative assessments of subjects' scale scores, Holter ECG, EEG, blood pressure, basal metabolic rate, and sympathetic nervous system activity levels were conducted before and after respiratory training intervention. By evaluating changes and differences in various assessment indicators post-intervention and integrating clinical efficacy data, potential factors influencing the therapeutic effect of respiratory training intervention were further analyzed.

Statistical and Analytical Plan

Data were analyzed using SPSS. Continuous variables were described using mean ± standard deviation, while categorical variables were described using frequency and percentage (%). For comparisons between groups, continuous variables were analyzed using t-tests or rank-sum tests, and categorical variables were analyzed using chi-square tests. Univariate correlation analyses were performed using Pearson or Spearman correlation analyses. All parameters will be considered statistically significant at $p < 0.05$.

(III) Trial Cost Participation Statement:

□ Free □ Partially Free □ Not Free □ Not Applicable

Please provide detailed information regarding costs:

(IV) Potential Benefits of Trial Participation:

□ Yes

Compensation Amount:

Compensation Payment Method: □ Paid in installments at follow-up observation points, □ Paid in a lump sum based on completed follow-up observation workload, □ Paid after completing all follow-up observations

□ None

(V) Potential Side Effects and Risks (Detailed Description):

Adverse events are defined as adverse medical incidents occurring after patients receive respiratory training intervention, though not necessarily causally related to the intervention. For subjects, anticipated adverse events include abdominal distension, vomiting, and throat discomfort.

Severe adverse events, such as aspiration or choking, warrant immediate trial termination.

(VI) Current Alternative Treatments or Diagnostic Methods (Detailed Description):

If adverse reactions such as abdominal distension, vomiting, or throat discomfort occur during the clinical trial, or if the patient's condition deteriorates, these adverse events will be deemed related to the respiratory training intervention. Adverse events will be accurately documented during the trial, with regular follow-up visits to record and manage any related adverse events. Severe reactions such as aspiration or suffocation constitute serious adverse events and will result in trial termination.

(VII) Your Rights and Responsibilities:

Your personal rights and interests in this clinical trial are protected under the following conditions:

If harm occurs due to the implementation of the trial protocol, the sponsor shall bear liability for damages in accordance with the law.

1. The institution conducting this clinical trial (the investigational drug has been approved for use in China) will safeguard your rights throughout the trial process.

2. Protection of Your Privacy

(1) The study physicians and staff will keep your medical records confidential. All collected data, test results, and physician diagnoses will be kept confidential and coded to protect your anonymity. We will safeguard your privacy except when required by law for investigations by relevant authorities.

(2) Data obtained from the trial may be published for academic purposes, but your privacy (such as name, medical record number, etc.) will not be disclosed and will be kept strictly confidential.

3. Should you experience any harm during the trial or have questions regarding your rights, please contact Li Haiyun . Her contact information is: 18560088921

(VIII) You have the right to refuse participation in the trial without providing any reason and may withdraw your consent to exit the study at any time. This decision will not cause any unpleasantness or affect your future medical care by physicians.

Principal Investigator Signature: Date:

(IX) I have thoroughly reviewed the above information. The principal investigator has provided detailed explanations regarding any questions about this clinical trial protocol. Having understood the entire trial process and given it careful consideration, I agree to participate as a voluntary subject in this clinical trial.

Volunteer Participant Agreement and Signature:

Legal Representative: Relationship to Subject:

ID Number: Phone:

See Certificate Person: Relationship to subject:

ID Number: Phone:

Date: