Clinical Study of Transcranial Magnetoelectric Therapy for Depression

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Abstract

[Objective] To evaluate the efficacy and safety of the transcranial magnetic-electric depression (insomnia) therapeutic device (trade name: Aobo Baiyoudu) in the treatment of depression. [Methods] A randomized, placebo-controlled, multicenter 4-week clinical trial was conducted in 80 patients with mild to moderate depression, with 40 cases in each of the treatment group and the control group. The treatment group received treatment with the transcranial magnetic-electric depression (insomnia) therapeutic device, while the control group received simulated treatment (audio placebo) with the same device. [Results] The clinical trial results demonstrated that after 4 weeks of treatment, the total markedly effective rate and total effective rate in the control group were 5.00% (2/40) and 35.00% (14/40), respectively, with 95% confidence intervals of (0.00–11.75) and (20.22–49.78). The total markedly effective rate and total effective rate in the treatment group were 65.00% (26/40) and 80.00% (32/40), respectively, with 95% confidence intervals of (50.22–79.78) and (67.60–92.40). There were differences among centers (P=0.0009). The superiority test for total effective rate and total markedly effective rate between the two groups showed P<0.0001, with the treatment group being higher than the control group, indicating that the treatment group was superior to the control group. No adverse reactions occurred in either group. [Conclusion] The transcranial magnetic-electric depression (insomnia) therapeutic device (trade name: Aobo Baiyoudu) is safe to use and has definite therapeutic efficacy in treating depression, particularly showing significant improvement in major symptoms such as "depression, guilt, sleep disturbance, work and interest, retardation, agitation, and anxiety."

Full Text

Clinical Study of Transcranial Magnetoelectric Depression Treatment Instrument for Depression

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Abstract

[**Objective**] To evaluate the efficacy and safety of the transcranial magnetoelectric depression (insomnia) treatment instrument (trade name: AOBO BAIYOUDU) for depression treatment. [**Methods**] A randomized, placebo-controlled, multicenter 4-week clinical trial was conducted on 80 patients with mild to moderate depression, with 40 cases each in the treatment group and control group. The treatment group received therapy with the transcranial magnetoelectric depression (insomnia) treatment instrument, while the control group received simulated treatment (audio placebo) using the same device. The treatment course lasted 4 weeks. The Hamilton Depression Scale (24-item HAMD) was used to evaluate efficacy, and safety assessments were performed. [**Results**] After 4 weeks of treatment, the total markedly effective rate and total effective rate in the control group were 5.00% (2/40) and 35.00% (14/40), respectively, while those in the treatment group were 65.00% (26/40) and 80.00% (32/40), respectively. Superiority testing for both total effective rate and total markedly effective rate showed $P<0.0001$, with the treatment group significantly higher than the control group, demonstrating the superiority of the treatment group. No adverse reactions occurred in either group. [**Conclusion**] The transcranial magnetoelectric depression (insomnia) treatment instrument (trade name: AOBO BAIYOUDU) is safe and effective for depression treatment, producing significant improvements particularly in core symptoms including depression, guilt, sleep disturbances, work and interest, psychomotor retardation, irritability, and anxiety.

Keywords: Transcranial magnetoelectric; Depression treatment instrument; Depression

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Depression is an affective mental disorder characterized by a self-experienced

depressive mood as the central symptom cluster. Clinical manifestations include persistent low mood, slowed thinking and speech, physical discomfort, and sleep disturbances, with severe cases involving suicidal ideation and behavior, and some patients experiencing hallucinations and delusions. Statistics indicate that the lifetime prevalence of depression currently ranges from 6.1% to 9.5%, with approximately 340 million people worldwide experiencing depressive symptoms. Addressing depression is not merely a biomedical issue but also an increasingly recognized social concern.

The transcranial magnetoelectric depression treatment instrument [1], which can be understood as endogenous neurotransmitter modulation technology, is a patented product developed by Harbin Aobo Medical Apparatus Co., Ltd. based on the "Brain Cell Activation Theory" [2,3] (Invention Patent No.: ZL200910071876.4). Building upon the core technology of transcranial computer function rehabilitation therapy instruments [4,5], this non-invasive physical therapy device applies pulsating current, biomagnetic fields, and audio signals to the patient' s head and auditory system for depression rehabilitation. We report the clinical research results on the efficacy and safety of this instrument, which served as partial clinical basis for national medical device regulatory approval in 2011 (Medical Device Registration No.: Heilongjiang Food and Drug Administration (Approval) No. 2011226002).

1. Methods

1.1 General Patient Information

Eighty patients were enrolled from the First and Second Affiliated Hospitals of Heilongjiang University of Chinese Medicine. Following multicenter, randomized, double-blind, placebo-controlled principles, patients were randomly assigned to the treatment group (n=40; 10 males, 30 females; age 21-65 years, 44.88±12.38 years) or control group (n=40; 12 males, 28 females; age 20-65 years, 42.90±14.24 years). At baseline, no statistically significant differences existed between groups in demographic indicators (age, gender) or vital signs (height, weight, blood pressure, respiratory rate, heart rate), nor in disease status or previous treatment/allergy history ($P>0.05$). Comparison of individual HAMD scale items at enrollment showed no significant differences except for somatic anxiety and diurnal variation (evening) ($P>0.05$), indicating balanced baseline comparability.

Diagnostic criteria for depression followed the *Chinese Classification and Diagnostic Criteria of Mental Disorders* Third Edition (CCMD-3): predominant low mood disproportionate to circumstances, ranging from unhappiness to despair, potentially progressing to stupor.

Symptom Criteria: Predominant low mood with at least four of the following: (1) loss of interest or pleasure; (2) decreased energy or fatigue; (3) psychomotor retardation or agitation; (4) low self-esteem, self-blame, or guilt; (5) difficulty concentrating or decreased thinking ability; (6) recurrent thoughts of death or

suicidal/self-injurious behavior; (7) sleep disturbances (insomnia, early awakening, or hypersomnia); (8) appetite loss or significant weight reduction; (9) decreased libido.

Severity Criteria: Social functional impairment causing personal distress or adverse consequences.

Duration Criteria: (1) Symptoms meeting criteria must persist for at least 2 weeks; (2) Certain schizoid symptoms may exist without meeting schizophrenia diagnosis. If schizophrenia criteria are simultaneously met, depressive episode criteria must be satisfied for at least 2 weeks after schizoid symptom remission.

Inclusion Criteria: (1) Meeting depression diagnostic criteria; (2) Age 18-65 years (inclusive); (3) Mild to moderate depression (HAMD score 20-35); (4) No other antidepressant medication within 2 weeks; (5) Voluntary participation with signed informed consent.

1.4 Exclusion Criteria

(1) Age <18 or >65 years, pregnant or lactating women; (2) Organic mental disorders or depression caused by psychoactive substances or non-addictive substances; (3) Severe comorbid physical diseases (cardiac, cerebral, renal, hematological); (4) Alcohol or drug dependence; (5) Non-adherence or loss to follow-up preventing efficacy determination, incomplete data affecting evaluation, or non-compliance with protocol.

2. Research Methods

Study Centers: First and Second Affiliated Hospitals of Heilongjiang University of Chinese Medicine. **Statistical Analysis Unit:** School of Public Health, Harbin Medical University.

2.2 Trial Methods

The transcranial magnetoelectric depression treatment instrument was provided by Harbin Aobo Medical Apparatus Co., Ltd.

Treatment Group: Received transcranial magnetoelectric depression (insomnia) treatment instrument therapy incorporating magnetic, electrical, and audio components. Treatment was administered once daily for 30 minutes per session, with 7 days constituting one course, for a total of 4 consecutive courses.

Control Group: Received simulated treatment with the same instrument without magnetic or electrical components, receiving only audio therapy. Treatment frequency and duration matched the treatment group.

2.3 Medication Regulations

Use of other antidepressant medications was prohibited during the trial. If concomitant medication or therapy was required for other conditions, drug name (or therapy), dosage, indication, frequency, and duration were recorded in case report forms for analysis. Pre-existing comorbidities were documented in detail; any new conditions emerging during the study were recorded as adverse events.

2.4 Observation Indicators and Efficacy Evaluation

(1) Observation Indicator: Hamilton Depression Scale (24-item HAMD).

(2) Efficacy Criteria: Based on HAMD score reduction rate calculated as: (pretreatment total score - posttreatment total score)/pretreatment total score × 100%. **Recovery:** Complete symptom disappearance with unaffected work/life function, HAMD reduction 75%; **Markedly Effective:** Basic symptom disappearance with work capability but not at premorbid level, HAMD reduction 50%; **Effective:** Symptom alleviation or partial disappearance with poor work/life function, HAMD reduction 25%; **Ineffective:** No or minimal improvement, HAMD reduction <25%. Total effective rate = (recovery + markedly effective + effective cases)/total cases.

(3) Safety Evaluation: Performed at baseline (0 weeks) and treatment completion (4 weeks) including: Vital signs (blood pressure, respiratory rate, heart rate); Laboratory tests (blood routine, urine routine, liver function [ALT, AST], renal function [BUN, Cr]); Electrophysiological examination (ECG); Real-time monitoring of any adverse reactions.

2.5 Statistical Analysis

SAS 9.1.3 statistical software was used. Primary efficacy evaluation was calculated for both Full Analysis Set (FAS) and Per Protocol Set (PPS), while safety evaluation used the Safety Set (SAS).

3. Results

3.1 Primary Endpoint Efficacy Analysis

After 4 weeks of treatment, the control group' s total markedly effective rate and total effective rate were 5.00% (2/40) and 35.00% (14/40), respectively, with 95% confidence intervals of (0.00-11.75) and (20.22-49.78). The treatment group's corresponding rates were 65.00% (26/40) and 80.00% (32/40), with 95% confidence intervals of (50.22-79.78) and (67.60-92.40). Center effects differed significantly (P=0.0009). Superiority testing for both total effective rate and total markedly effective rate showed P<0.0001, with the treatment group significantly higher than the control group, demonstrating treatment superiority .

After 2 weeks of treatment, the control group' s total markedly effective rate and total effective rate were 0% (0/40) and 12.50% (5/40), respectively, with 95% confidence intervals of (0) and (2.25-22.75). The treatment group' s rates were 0% (0/40) and 52.50% (21/40), with 95% confidence intervals of (0) and (37.02-67.98). Center effects differed (P=0.0009). Superiority testing for total effective rate showed P=0.0001, favoring the treatment group; however, both groups had 0% markedly effective rate (P=1), indicating no significant difference. These results demonstrate that at 2 weeks, neither group showed marked efficacy, though the treatment group had more effective cases than the control group .

3.2 Analysis of Individual HAMD Items

HAMD scale item analysis at 2 and 4 weeks (PPS and FAS) revealed: At 2 weeks, no significant differences existed between groups in any items except "insight" (P>0.05). At 4 weeks, no significant differences were observed in "suicide, gastrointestinal symptoms, general somatic symptoms, sexual symptoms, diurnal variation (morning/evening), depersonalization/derealization, obsession, decreased capacity, hopelessness, or self-depreciation" between groups, while all other items showed significant differences (P<0.05) .

3.3 Safety Evaluation

Among 40 treatment group and 40 control group patients, each group had one case of mild adverse event requiring no intervention or trial discontinuation. These events were unrelated to the study instrument and not considered device-related adverse reactions. During treatment, all patients maintained stable vital signs, with no significant changes in blood/urine routine or blood biochemistry tests (P>0.05).

4. Discussion

Depression, an affective disorder, exhibits bipolar characteristics. Bipolar affective disorder shares pathological mechanisms with schizophrenia, though the latter shows more pronounced brain structural and neurophysiological abnormalities. Affective disorders, also known as manic-depressive illness, present with two symptom types: positive symptoms (mania) and negative symptoms (depression). Biochemical pathological hypotheses for bipolar disorder include catecholamine neurotransmitter hypothesis, serotonin hypothesis, combined catecholamine-serotonin hypothesis, and -aminobutyric acid (GABA) hypothesis [6]. Increased catecholamine neurotransmitters cause mania ("positive" neurotransmitters), while GABA has inhibitory effects on nerves ("negative" neurotransmitters).

The total content of these two neurotransmitters in the brain synaptic cleft remains relatively balanced in normal physiological states. All endogenous neurotransmitters are released from presynaptic terminal vesicles through calcium-dependent rapid regulated vesicular exocytosis. Three possible states exist for

negative and positive neurotransmitters in the synaptic cleft: balanced (normal), positive-predominant (mania), and negative-predominant (depression). Depression pathogenesis involves neurotransmitters and ion channels.

The transcranial magnetoelectric depression treatment instrument applied to patients' heads produces phosphenes when eyes are closed, consistent with Müller' s "law of specific nerve energies." The device' s configured constant magnetic therapy unit exerts Lorentz force on moving charged substances, affecting cell membrane ion permeability and transmembrane potential, thereby altering ion channel configuration and interfering with abnormal brain electrical and magnetic activity generation and propagation, achieving sedative, calming, antidepressant, and anxiolytic effects. Research confirms that moderate-intensity constant magnetic fields affect ion channels possibly through charge movement associated with membrane ion channels [7].

The audio signals applied to the auditory system via the transcranial magnetoelectric depression treatment instrument constitute a special "audio prescription" that blocks external interference. Sound vibration mechanical energy may be converted to neural signals through the cochlea. This mechanical-electrical conversion occurs at hair cell stereocilia via mechanogated channels that allow potassium influx, causing depolarization and opening voltage-gated calcium channels on hair cell bodies. Auditory nerves can receive bidirectional excitatory and inhibitory stimulation from hair cells. All sensory organs transduce internal and external environmental changes, and all receptors can be excited by electrical currents to activate neurotransmitter neurons, establishing new neurotransmitter balance in brain synaptic clefts.

These trial results confirm that at 2 weeks, neither group showed marked efficacy, though the treatment group had more effective cases than the control group. After 4 weeks, the treatment group' s total markedly effective rate and total effective rate were significantly higher than the control group's, demonstrating significant efficacy and treatment superiority. The device is safe, with no device-related adverse events. After 4 weeks of treatment, most patients showed symptom alleviation, particularly in core symptoms including depression, guilt, sleep disturbances, work and interest, psychomotor retardation, irritability, and anxiety.

Depression, this "unhappiness," has been termed "mental cold" or "blue melancholy," with high-risk groups including high-position, high-salary, highly educated successful individuals and adolescents. While depression was previously treated primarily with medication, the emergence of transcranial magnetoelectric depression treatment instruments provides a new therapeutic approach for human "unhappiness." This treatment modality demonstrates definite efficacy, safety, convenient operation, and suitability for both clinical and home use.

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Author Contributions

Zou Wei, Tang Qiang: Proposed research concepts and primary clinical trial design;
Sun Zuodong: Research concept proposer, clinical trial design participant, inventor of transcranial magnetoelectric brain disease treatment instrument, primary author of "Introduction" and "Discussion" sections, responsible for manuscript drafting and final revision;
Sun Wuyi, Wang Wenhua: Co-inventors of transcranial magnetoelectric brain disease treatment instrument, co-authors of "Introduction" and "Discussion" sections;
Yu Xueping, Xing Yanli: Primary participants in clinical trial design and implementation leaders;
Teng Xiuying, Zhang Li: Clinical trial implementers;
Li Kang: Primary participant in clinical trial design and responsible for statistical analysis;
Hou Yan: Clinical trial data analyst.

Note: Figure translations are in progress. See original paper for figures.