Alpha Psychiatry

ORIGINAL ARTICLE
Alpha Psychiatry 2024;25(6):700-704
DOI: 10.5152/alphapsychiatry.2024.231473

Efficacy of Modified Electroconvulsive Therapy in Treatment-Resistant Schizophrenia

ABSTRACT

Objective: The aim of the study was to investigate the therapeutic effects of modified electroconvulsive therapy (MECT) in combination with risperidone tablets and psychotherapy in the treatment of patients with treatment-resistant schizophrenia (TRS).

Methods: Patients with TRS admitted to the psychiatric department of our hospital between January 2018 and December 2019 were selected as study participants. They were randomly divided into a control group and a study group, with the control group receiving risperidone tablets and psychotherapy, and the study group undergoing MECT as well as the control group treatment. The mood scores, efficacy, and side effects of the 2 groups were compared.

Results: After treatment, the Hamilton Anxiety Rating Scale ($t = 2.316$, $P = .021$) and Hamilton Depression Rating Scale ($t = 2.919$, $P = .013$) scores of the study group were significantly lower than those of the control group. The overall remission rate in the study group was 96.3%, which was higher than that of the control group ($\chi^2 = 9.319$, $P = .007$). The Positive and Negative Syndrome Scale ($t = 8.126$, $P = .003$), Traumatic Exposure Severity Scale ($t = 13.210$, $P = .002$), and Brief Psychiatric Rating Scale ($t = 6.412$, $P = .001$) scores were significantly lower in the study group than in the control group. The Wechsler Memory Scale score was higher in the study group than in the control group ($t = 3.971$, $P = .002$).

Conclusion: The use of MECT in combination with risperidone tablets and psychotherapy can effectively improve patient mood, increase efficacy, reduce adverse effects, promote memory recovery, and shorten recovery time in patients with TRS.

Keywords: Modified electroconvulsive therapy, schizophrenia, risperidone tablets, psychotherapy

Hong-Yuan Chen[1#]
Xiao-Jun Wang[1#]
Ping Guo[1#]
Hai-Ying Chen[1]
Wen-Jie Wei[1]
Yu Chen[1]
Yun-Jiao Hu[1]
Juan Qiao[1]
Hua-Xin Lu[1]
Ming-Chao Li[2]
Qiu-Ming Ji[1]

[1]*Department of Psychiatry, Wuhan Wudong Hospital, Wuhan, China*
[2]*Department of Psychiatry, Wuhan Mental Health Center, Wuhan, China*

[#]*These authors were contributed to this study equally.*

Corresponding author:
Qiu-Ming Ji or Hai-Ying Chen or Wen-Jie Wei
✉ jiqiuming79@163.com or chenhy2021_6@21cn.com or weiwenjie28@21cn.com

Received: December 8, 2023
Revision Requested: December 25, 2023
Last Revision Received: April 9, 2024
Accepted: April 10, 2024
Publication Date: December 15, 2024

Cite this article as: Chen H, Wang X, Guo P, et al. Efficacy of modified electroconvulsive therapy in treatment-resistant schizophrenia. *Alpha Psychiatry.* 2024;25(6):700-704.

Introduction

Schizophrenia (SP) is a chronic mental disorder, typically affecting young adults. The disease presents with physical, sensory, and emotional disturbances, impaired logical thinking, and behavioral irregularities, among other manifestations.[1] As the disease progresses over time, it can have significant adverse effects on the patient's physical health, family life, and society.[2] The mainstay of clinical SP treatment is pharmacological therapy supplemented by psychological and social support, but a lack of scientifically-based treatment may lead to the development of treatment-resistant schizophrenia (TRS).[3] Patients with TRS can be defined as follows: (1) patients who, within the last 5 years, received the appropriate dosage and duration of treatment with 2 antipsychotic drugs but experienced poor outcomes; (2) patients who cannot tolerate the adverse reactions associated with antipsychotic medication; and (3) patients who continue to deteriorate or relapse even after receiving preventive or maintenance treatment.[4,5] TRS tends to have a protracted course and is challenging to cure. Patients may exhibit varying degrees of depression, along with negative emotions, thoughts, and behaviors, and the disease carries a high disability and mortality rate, profoundly impacting the patient's overall quality of life and well-being. Therefore, immediate and proactive treatment is imperative upon disease onset.[6]

At present, clinical practice primarily employs drug therapy and psychological therapy to manage this condition. Commonly prescribed medications include clozapine and risperidone, which can effectively alleviate positive symptoms in patients.[7] In recent years, behavioral therapy has emerged as a reliable psychological intervention method applied in clinical practice in combination with medication. Yu et al[8] investigated the use of risperidone in conjunction with psychotherapy for treating patients with TRS and demonstrated its potential to enhance their mental state, psychological well-being, and sleep quality. However, each patient's condition is unique. Prolonged medication use unavoidably impacts the patient's immune function and may entail certain side effects, drug resistance, and even resistance to psychotherapy. Non-convulsive electroconvulsive therapy, also known as modified electroconvulsive therapy (MECT), administers a brief, moderate electrical current to the brain, inducing temporary unconsciousness and improving mental state.[9] While some reports exist on the combined use of MECT and antipsychotic drugs in treating patients with TRS, research on the combined use of MECT with risperidone and psychotherapy in TRS is limited. Therefore, this article aims to explore the efficacy of combining MECT with risperidone and psychotherapy in improving the emotions and symptoms of patients with TRS. To this end, the present study recruited 108 patients who were diagnosed with TRS and admitted to the hospital's psychiatric department. The relevant findings are reported below.

Material and Methods

General Information

This study involved patients with TRS who were admitted to the psychiatric department of our hospital between January 2018 and December 2019. Using a random number table, the patients were divided into a control group and a study group, each comprising 54 patients. The control group was administered risperidone tablets and psychotherapy, while the study group received MECT in addition to the control group treatment.

The inclusion criteria were as follows: patients (1) aged >18 years old; (2) with complete medical records; (3) with Positive and Negative Syndrome Scale (PANSS) scores for both positive and negative symptoms >60 points;[10] (4) with a clinical diagnosis of TRS;[11] (5) who had had TRS for >5 years; (6) who had had previous treatment with 2 or more antipsychotic drugs of different chemical structures, each at a sufficient dosage, with no significant improvement after continuous treatment for more than 2 months; and (7) those who did not show drug intolerance or maladaptation during the course of this study. The exclusion criteria were as follows: patients (1) with autoimmune diseases, malignant tumors, or other severe chronic illnesses; (2) who had used antipsychotic drugs within the 3 months prior to their participation in the study; (3) with severe underlying organ diseases such as heart, lung, liver, or kidney disorders; (4) who withdrew from the study without providing a valid reason; and (5) those who were pregnant or lactating. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of our hospital (approval number: WDYY-LL-2017-12, date: December 30, 2017).

Research Methods

Control Group: The control group was treated with risperidone combined with psychotherapy. Patients were orally administered risperidone tablets (Xi'an Janssen Pharmaceutical Ltd., Xi'an, China; Chinese Pharmacopoeia Registration Number H20010309). Medication was initiated at a daily dose of 1 mg for 7 consecutive days. Subsequently, the dosage was gradually increased to 4-6 mg per day. Depending on the patient's individual condition, medication dosage was adjusted as needed to ensure a maximum daily dose of less than 6 mg.

The psychotherapy took the following form. (1) The therapists sought to establish effective communication with patients by engaging with them upon admission, earning their trust through sincerity, assisting them with various examinations and systematic interventions, informing patients of the benefits of timely psychotherapy for enhanced treatment efficacy and overall treatment outcomes, and encouraging active participation and cooperation of both patients and their families. (2) Information about the disease was shared with patients and their families during hospitalization, using books, manuals, videos, and images. (3) Given that patients with TRS can exhibit severe speech and behavioral abnormalities during the onset of the disease, the therapists endeavored to listen patiently to their patients' concerns, gain an understanding of their true thoughts, evaluate their mental state, and actively provide positive psychological treatment and guidance. This approach was carried out over a total of 2 months.

Study Group: The study group underwent MECT in addition to the treatment given to the control group. The MECT procedure was as follows: The Thymatron® System IV (Xingmaitong Therapeutic Apparatus, US Somex Co., Ltd., National Machinery Injection 20163092400, model: Thymatron System IV) instrument was used for MECT. Patients were advised to refrain from consuming food, water, and alcohol for at least 8 hours before the treatment and to reduce their usual medication dosage by half. The patient was positioned in a supine posture, and 1 mg of Atropine (Wuhu Kangqi Pharmaceutical Co., Ltd., Wuhu, China; Chinese Pharmacopoeia Registration Number H34021900) was administered via the intravenous route, followed by an intravenous injection of 1.5 mg/kg propofol (Guangdong Jiabo Pharmaceutical Co., Ltd., Guangdong, China; Chinese Pharmacopoeia Registration Number H20051843). Once the eyelash reflex disappeared, 1-1.5 mg/kg of succinylcholine chloride (Shanghai Xudong Haipu Pharmaceutical Co., Ltd., Shanghai, China; Chinese Pharmacopoeia Registration Number H31020599) was administered intravenously. The muscle status of the patient was monitored, and, after the disappearance of any generalized muscle tremor, a mouth protector was put in place, and the patient was connected to the Thymatron®

MAIN POINTS

- *Treatment-resistant schizophrenia causes prolonged and intractable illness, and patients suffer from emotional, mental, and behavioral symptoms, with a high rate of disability and death.*
- *The combination of modified electroconvulsive therapy (MECT) with antipsychotic drugs has been reported in the treatment of patients with SP. However, there are few studies on the combination of MECT with risperidone and psychotherapy for the treatment of treatment-resistant schizophrenia (TRS).*
- *Using MECT in combination with risperidone tablets and psychotherapy can improve the mood of patients with TRS, reduce the occurrence of adverse effects, and promote the recovery of patients' memory.*

System IV machine. The temporal side of the dominant hemisphere of the patient was connected to an electrode, with the amount of electricity set according to the patient's age and resistance <1000 Ω. The electrode was then energized for 5 seconds. During the treatment period, the patient's vital signs were monitored closely, and their orbicularis oculi, mouth corners, fingers, and toes twitched slightly. After the electrical stimulation ceased, oxygen therapy was administered to the patient's limbs and face. The MECT therapy was carried out 3 times a week, and the frequency was gradually reduced based on the individual patient's condition. A treatment course consisted of approximately 8~12 sessions spanning roughly 2 months.

Outcome Measures

After 2 months of treatment, the treatment outcomes of the control group and the study group were evaluated using the following methods.

1. Each patient's emotional state was assessed using the Hamilton Anxiety Rating Scale (HAMA) and the Hamilton Depression Rating Scale (HAMD), and the scores of the 2 groups were compared. A HAMA score of >29 was defined as severe anxiety, 21-28 as moderate anxiety, 14-20 as mild anxiety, 7-13 as possible anxiety, and <7 points as no anxiety. A HAMD score of <8 was classified as normal, 8-20 as possible depression, 20-35 as moderate depression, and >35 as severe depression.[12]
2. The 2 groups' PANSS scores, which evaluated the severity of positive and negative symptoms before and after treatment, were compared to assess treatment efficacy. The total PANSS score ranges from 30 to 120, with a higher score indicating more severe symptoms.[13] The assessment categories were as follows: i) significant improvement was a significant decrease in the PANSS score by 75% or more compared with the pre-treatment level; ii) remission was a mild reduction in the PANSS score by 25% to 74% compared with the baseline; iii) no response signified a modest decline in the PANSS score by <25% after treatment.[14]

   The main points of distinction between the depressive symptoms and negative symptoms of the participants are as follows: Symptom characteristics: The negative symptoms of SP are mainly apathy, poor thinking, decreased speech, and withdrawn behavior. The symptoms of depression are mainly characterized by depression, fatigue, decreased interest, depressed mood, and cognitive impairment. The duration of the disease: the personality of negative patients with SP changes due to the influence of their illness, and the duration of the disease is continuous at this time. However, patients with depression mainly change their mental state, which is mainly manifested as an intermittent duration of the disease.[15]
3. The Traumatic Exposure Severity Scale (TESS) scores of the 2 groups were compared, with a higher score indicating more severe adverse reactions.[16]
4. The Brief Psychiatric Rating Scale (BPRS) scores of the 2 groups were compared. The BPRS scale comprises a total score (18-126), individual scores (0-7 points), and factor scores (0-7 points). The total score reflects the overall disease severity, with a higher score representing a more severe condition.[17] A contour map was plotted using the BPRS scores.
5. The Wechsler Memory Scale (WMS) scores of the 2 groups were compared. The scale has a total score of 100 points, and a higher score indicates better memory recovery.[18]

Statistical Methods

The data were analyzed using Statistical Product and Service Solutions 22.0 statistical software (SPSS Inc., Chicago, IL, USA). Count data (gender and treatment efficacy) were expressed in frequency and percentage (%); measured data (age, duration of disease, HAMA, HAMD, PANSS, TESS, BPRS, and WMS scores) were expressed as mean Standard Deviation (SD). Count data between the 2 groups were compared by Chi-square test. The differences in measured data were compared by 2-sample *t*-test.

Results

Clinical Information

This study involved 108 patients (74 men and 34 women), who were randomly divided into a study group and a control group. The study group consisted of 54 patients, including 38 men and 16 women, with an average age of [35.25 (SD = 11.65)] years and an average disease course of [8.23 (SD = 3.61)] years. The control group included 54 patients, comprising 36 men and 18 women, with an average age of [39.15 (SD = 10.35)] years and an average disease course of (7.21 (SD = 3.51)) years. A comparison of the 2 groups in terms of gender, age, disease duration, HAMA, HAMD, PANSS, TESS, BPRS, and WMS scores showed no statistically significant differences ($P > .05$), indicating that the 2 groups were comparable (Table 1).

Treatment Efficacy

Among the 54 patients in the control group, 25 (46.30%) showed significant improvement, 19 (35.19%) exhibited remission, and 10 (18.52%) had no response to the treatment, yielding a total remission rate of 81.48%. Among the 54 patients in the study group, 34 (62.96%) achieved significant improvement, 18 (33.33%) displayed partial remission, and 2 (3.70%) showed no response, resulting in an overall remission rate of 96.30%. The therapeutic effect in the control group was inferior to that in the study group, and the difference between the 2 groups was statistically significant ($P < .05$) (Table 2).

Comparison of Parameters After Treatment

After 2 months of treatment, the HAMA [7.89 (SD = 2.73) vs. 9.12 (SD = 3.02)] and HAMD scores [13.92 (SD = 4.24) vs. 11.38 (SD = 3.97)] of the study group were lower than those of the control group ($P < .05$). The PANSS score of the study group was also lower than that of the control group (51.51 (SD = 2.92) vs. 57.92 (SD = 2.45)), and the

Table 1. General Information

Items	Control Group (54)	Study Group (54)	$t/^2$	*P*
Age (years)	39.15 (SD = 10.35)	35.25 (SD = 11.65)	1.637	.117
Gender (male)	36 (66.67%)	38 (70.37%)	1.241	.072
Disease duration (years)	7.21 (SD = 3.51)	8.23 (SD = 3.61)	1.046	.085
HAMA	10.78 (SD = 4.02)	10.49 (SD = 3.97)	2.781	.084
HAMD	14.73 (SD = 4.38)	14.91 (SD = 4.74)	1.281	.143
PANSS	99.10 (SD = 10.18)	98.87 (SD = 9.92)	0.912	.891
TESS	2.72 (SD = 0.81)	2.69 (SD = 0.73)	0.812	.813
BPRS	80.73 (SD = 7.08)	80.14 (SD = 6.89)	0.712	.910
WMS	70.66 (SD = 9.12)	70.51 (SD = 8.98)	1.813	.831

BPRS, Brief Psychiatric Rating Scale; HAMA, Hamilton Anxiety Scale; HAMD, Hamilton Depression Scale; PANSS, Positive and Negative Syndrome Scale; TESS, Treatment Emergent Symptom Scale; WMS, Wechsler Memory Scale; SD, Standard Deviation.

Table 2. Comparison of Treatment Efficacy Between the 2 Groups [n (%)]

Group	n	Significant Improvement	Remission	No Response	Overall Remission Rate
Control Group	54	25 (46.30)	19 (35.19)	10 (18.52)	44 (81.48)
Study Group	54	34 (62.96)	18 (33.33)	2 (3.70)	52 (96.30)
χ^2					9.319
P					.007

difference between the 2 groups was statistically significant ($P < .05$). Furthermore, the TESS score of the study group was significantly lower compared with the control group's score [1.04 (SD = 0.41) vs. 1.92 (SD = 0.57))] ($P < .05$), and the BPRS score was significantly lower in the study group compared with the control group [29.69 (SD = 7.34) vs. 37.42 (SD = 7.11)] ($P < .05$). Conversely, the WMS score was significantly higher in the study group than in the control group [83.62 (SD = 12.82) vs. 72.47 (SD = 11.28)] ($P < .05$) (Table 3).

Discussion

Characterized by varying degrees of disorder in thinking, emotions, cognition, and behavior, TRS leads to low social adaptability and has a high recurrence rate.[19] At present, approximately 30% of all SP cases are classified as treatment-resistant.[20] The most commonly used antipsychotic drug is risperidone.[21] However, long-term medication may lead to side effects and drug tolerance, potentially affecting the therapeutic outcome. In recent years, alongside medical advancements, certain physical therapies have gained clinical importance, the most common being MECT,[22] which involves the administration of appropriate anesthetics and muscle relaxants prior to electroconvulsive therapy. The treatment involves the use of a controlled electric current to stimulate the patient's brain, inducing unconsciousness to achieve the therapeutic goal without convulsions.[23]

Although Electroconvulsive therapy (ECT) is considered an effective intervention in low- and middle-income countries, the use of unmodified ECT remains controversial.[21] Chiu et al[22] concluded that risperidone combined with MECT treatment is an effective method for controlling the symptoms of SP, and risperidone combined with MECT treatment significantly reduced the total PANSS score at the end of the 8th week of treatment compared with the risperidone group alone, with the difference between the 2 groups statistically significant. Some studies have also shown that MECT combined with risperidone oral solution and risperidone oral solution alone are effective in the acute phase of SP with euphoria and agitation, and that the treatment is fast-acting and safe, with mild adverse effects.[23] This view was confirmed by the study of Sun Ning,[24] which showed that olanzapine improved positive symptoms and general psychopathological scale scores significantly more than it improved negative symptoms. In contrast, MECT has been shown to be effective in controlling negative symptoms in patients with SP, and Grover S. et al[25] also used ECT as a potentiator complementary to pharmacological treatment modalities. Therefore, the combination of MECT and antipsychotics appears to have a greater impact on symptom control in patients with SP than medicine alone.

Table 3. Comparison of Parameters Between the 2 Groups After Treatment

Items	Control Group (54)	Study Group (54)	*t*	*P*
HAMA	9.12 (SD = 3.02)	7.89 (SD = 2.73)	2.316	.021
HAMD	13.92 (SD = 4.24)	11.38 (SD = 3.97)	2.919	.013
PANSS	57.92 (SD = 2.45)	51.51 (SD = 2.92)	8.126	.003
TESS	1.92 (SD = 0.57)	1.04 (SD = 0.41)	13.210	.002
BPRS	37.42 (SD = 7.11)	29.69 (SD = 7.34)	6.412	.001
WMS	72.47 (SD = 11.28)	83.62 (SD = 12.82)	3.971	.002

BPRS, Brief Psychiatric Rating Scale; HAMA, Hamilton Anxiety Scale; HAMD, Hamilton Depression Scale; PANSS, Positive and Negative Syndrome Scale; TESS, Treatment Emergent Symptom Scale; WMS, Wechsler Memory Scale.

In this study, risperidone tablets, MECT, and psychotherapy were employed simultaneously to improve treatment outcomes for patients with TRS. The results indicated that the HAMA and HAMD scores in the study group were significantly better than those in the control group. The control group had a response rate of 81.48%, which was significantly lower than the 96.30% observed in the study group. After the treatment, the PANSS, TESS, and BPRS scores in the study group were significantly lower than those in the control group, while the WMS score in the study group was significantly higher than that in the control group, which aligns with the findings of Ji et al.[26] These results demonstrate that the combination treatment using risperidone tablets, psychotherapy, and MECT can significantly improve the emotional well-being and symptoms of patients with TRS. Fu et al[27] reported that the combination of psychotherapy and neuroleptics in the treatment of SP-related negative symptoms led to improved scores across various factors of psychological resilience. Psychotherapy can help patients feel cared for, enhance trust in medical staff, and aid patients in breaking free from negative emotions, thus maintaining a positive state. The MECT treatment approach, which is known for its high safety and tolerance, can effectively increase brain-derived neurotrophic factor protein within the brain, leading to favorable outcomes for patients.[28] Arumugham S. et al[29] predicted the change in the cerebral nerves caused by MECT based on resting-state functional magnetic resonance imaging of brain connectivity, and Jiang Y. et al[30] showed that MECT induced insular changes that may contribute to the mechanism of MECT.

There are some limitations to this study. First, the sample size was relatively small due to time and financial constraints, and only patients with TRS attending 1 hospital were included as study participants. In addition, critically ill patients who may have been suicidal or experiencing other psychiatric emergencies, where electroconvulsive therapy is known to be beneficial, were excluded. Thus, the results may be biased. Lastly, the study design did not include a sham MECT group, and, as a result, the combination treatment will need to be validated by further double-blind randomized controlled trials. The authors plan to expand the sample size and investigate the therapeutic effects of MECT plus hyperbaric oxygen intervention in the future.

Conclusion

In conclusion, the combined treatment of risperidone tablets with MECT and psychotherapy can significantly improve the symptoms and emotions of patients with refractory SP, help patients recover

cognitive function as soon as possible, reduce the occurrence of side effects, and promote patient recovery. Despite the therapeutic effect being obvious in the patients involved in this study, further validation is required.

Data Availability Statement: *All data generated or analyzed during this study are included in this published article.*

Ethics Committee Approval: *This study was approved by the Ethics Committee of Wuhan Wudong Hospital (approval number: No.WDYY-LL-2017-12; date: December 30, 2017).*

Informed Consent: *Verbal/written informed consent was obtained from the patients/patient who agreed to take part in the study.*

Peer-review: *Externally peer-reviewed.*

Author Contributions: *Concept – Hong Y.C.; Design – Hong Y.C., X.-J.W., P.G., Y.-J.H., Q.-M.J.; Supervision – X.-J.W., P.G., W.-J.W., Y.C.; Materials – Hong Y.C., X.-J.W., P.G., Hua Y.C., W.-J.W., Y.C., H.-X.L., Y.-J.H., M.-C.L., J.Q., Q.-M.J.; Data Collection and/or Processing – X.-J.W., P.G., H.-Y.C., H.-X.L., Y.-J.H., M.-C.L., J.Q.; Analysis and/or Interpretation – X.-J.W., Hai Y.C., W.-J.W., Y.C., H.-X.L., Y.-J.H., M.-C.L., Q.-M.J.; Literature Search – Hong Y.C., Hai Y.C., Y.C., M.-C.L., J.Q.; Writing – Hong Y.C., X.-J.W., P.G., Hai Y.C., W.-J.W., Y.C., H.-X.L., Y.-J.H., Q.-M.J.; Critical Review – Hong Y.C., X.-J.W., Hai Y.C., W.-J.W., H.-X.L., M.-C.L., J.Q., Q.-M.J.*

Acknowledgement: *We would like to express our gratitude to all those who helped us during the writing of this manuscript.*

Declaration of Interests: *The authors have no conflicts of interest to declare.*

Funding: *The authors declare that this study received no financial support.*

References

1. Jauhar S, Johnstone M, McKenna PJ. Schizophrenia. *Lancet*. 2022;399(10323):473-486. [CrossRef]
2. McCutcheon RA, Reis Marques T, Howes OD. Schizophrenia-an overview. *JAMA Psychiatry*. 2020;77(2):201-210. [CrossRef]
3. Yang L, Shen J, Zhu YQ. Clinical efficacy of ziprasidone combined with clozapine in the treatment of refractory schizophrenia. *Chin J Clin Ration Drug Use*. 2023;16(29):70-73.
4. Pacitti F, Bersani G, Aloe L, et al. Nerve growth factor serum levels in treatment-resistant schizophrenic patients following electroconvulsive therapy. *Clin Ter*. 2021;171(1):e67-e74. [CrossRef]
5. Wagner E, Kane JM, Correll CU, et al. Clozapine combination and augmentation strategies in patients with schizophrenia -Recommendations from an international expert survey among the treatment response and resistance in psychosis (TRRIP) working group. *Schizophr Bull*. 2020;46(6):1459-1470. [CrossRef]
6. Qin WG, Han CL, Xiao PP, et al. A study on the efficacy and safety of clozapine combined therapy for refractory schizophrenia. *J Clin Psychiatry*. 2022;32(3):231-235.
7. Yang YF, Zhong YH, Chen ZQ, Li HB. Comparison of clinical efficacy between olanzapine and risperidone in the treatment of schizophrenia. *Chin J Clin Ration Drug Use*. 2023;16(28):54-57.
8. Yu QG, Liu N, Sun LL. Effect analysis of risperidone combined with psychotherapy and behavioral therapy in the treatment of schizophrenia with insomnia. *Psychol Mon*. 2023;18(11):131-133, 136.
9. Ding H, Fang H, Li Y. The effect of medication combined with MECT in patients with refractory schizophrenia. *Psychol Mon*. 2022;17(9):17-19.
10. Si TM, Yang JZ, Shu L, et al. The reliability,validity of PANSS and its implication. *Chin Ment Health J*. 2004;18(1):45-47.
11. Wu DL. Experience in the diagnosis and treatment of refractory schizophrenia. *Chinese Medical Guidelines*. 2013;20:596-597.
12. Zhuoga QM, Zhuoma YX, Qi Mei DZ. Clinical efficacy of psychological counseling combined with risperidone in the treatment of refractory schizophrenia patients. *Psychol Mon*. 2022;17(9):29-31.
13. Zhu M, Xie LW, Ge WT. Clinical study of MECT combined with antipsychotic drugs in the treatment of refractory schizophrenia. *Psychol Mon*. 2021;16(17):30-31.
14. Li L. Study on the efficacy of MECT combined with antipsychotic drugs in the treatment of refractory schizophrenia. *China Pract Med*. 2022;17(12):137-139.
15. Zhang M, Yuan G, Yao J. Comparison of negative symptoms of schizophrenia and symptoms of depression. *Sichuan Ment Health*. 2002;15(4):209-210.
16. Sun WW. *A Study on the Correlation between Blood Concentration and Dose, Clinical Efficacy, and Side Effects of Paliperidone in the Treatment of Schizophrenia[D]*. Kunming Medical University; 2015.
17. Lu JY, Rong CL, Cheng GQ, Qiu G, Yang J, Li Y. The effect of psychological counseling intervention assisted drug therapy on refractory schizophrenia. *Chin Foreign Med Res*. 2020;18(24):88-91.
18. Xu L. Clinical study of risperidone combined with clozapine in the treatment of refractory schizophrenia. *Chin J Mod Drug Appl*. 2021;15(6):206-208.
19. Correll CU, Howes OD. Treatment-resistant schizophrenia: definition, predictors, and therapy options. *J Clin Psychiatry*. 2021;82(5):MY20096AH1C. [CrossRef]
20. Millgate E, Hide O, Lawrie SM, Murray RM, MacCabe JH, Kravariti E. Neuropsychological differences between treatment-resistant and treatment-responsive schizophrenia: a meta-analysis. *Psychol Med*. 2022;52(1):1-13. [CrossRef]
21. Daskalakis AA, Paric A, Ravindran N, Ravindran A. Evaluating the use of electroconvulsive therapy in low-middle income countries: a narrative review. *Asian J Psychiatr*. 2024;91:103856. [CrossRef]
22. Chiu YH, Hsu CY, Lu ML, Chen CH. Augmentation strategies for clozapine-resistant patients with schizophrenia. *Curr Pharm Des*. 2020;26(2):218-227. [CrossRef]
23. Peng C, Wang G, Zhang X, Tu M, Cai D, Liu B. Observation of the therapeutic effect of non convulsive electroconvulsive combined with risperidone oral solution on acute excitement and agitation in schizophrenia. *J Psychiatry*. 2014;27(6):427-429.
24. Sun N. *A Study on the Efficacy and Influencing Factors of Olanzapine in the Treatment of Early-Onset Schizophrenia [D]*. Kunming Medical University; 2019.
25. Grover S, Shouan A, Chakrabarti S, Sahoo S, Mehra A. Comparative study of effectiveness of augmentation with ECT in clozapine resistant schizophrenia (CRS) and non-clozapine resistant schizophrenia (non-CRS). *Nord J Psychiatry*. 2021;75(6):397-405. [CrossRef]
26. Ji J, Zhang QQ, Li TT, Ye J. The effect of MECT in patients with refractory schizophrenia. *Psychol Mon*. 2023;18(9):90-92.
27. Fu YJ, Chen LL. Observation on the effect of psychological intervention combined with antipsychotic drugs in the treatment of negative symptoms of schizophrenia. *J Shandong Med Coll*. 2021;43(6):429-431.
28. Xu YM, Xie WW, Zhang C, Wang YB, Li XX, Zhou DS. The effect of continuous oxygen inhalation after MECT on memory and cognitive function in patients with schizophrenia. *Mod Pract Med*. 2022;34(12):1587-1589.
29. Arumugham SS, Praharaj SK, Shreekantiah U, et al. Clinical efficacy and neurobiological correlates of electroconvulsive therapy in patients with clozapine-resistant/intolerant schizophrenia: study protocol of multisite parallel arm double-blind randomized sham-controlled study. *Wellcome Open Res*. 2022;7:212. [CrossRef]
30. Jiang Y, Xia M, Li X, et al. Insular changes induced by electroconvulsive therapy response to symptom improvements in schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry*. 2019;89:254-262. [CrossRef]