Efficacy and safety of modified electroconvulsive therapy for the refractory depression in older patients

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Abstract

Background: To explore the clinical efficacy and safety of modified electroconvulsive therapy (MECT) in the treatment of elderly patients with refractory depression.

Methods: A total of 43 older patients (18 male and 25 female) with refractory depression were enrolled in our study from March 2014 to February 2015, with the average age of 65±4.8 years old. Modified electroconvulsive therapy (MECT) was performed in these patients after physical examinations and anesthesia procedures. Hamilton Depression Scale (HAMD) and Hamilton Anxiety Scale (HAMA) were used to assess the efficacy of MECT, and Wechsler Memory Scale (WMS) and mini mental state examination (MMSE) were used to evaluate the memory ability and cognitive function. The preoperative, intraoperative and postoperative care were conducted in patients accompanied by physical diseases.

Results: The rate of efficacy was calculated as 67.44% after 4 weeks of MECT treatment. Our results showed HAMA and HAMD scores after 2 weeks of MECT treatment were significantly lower than that before treatment (P<0.05), and the differences were more significant after 4 weeks of MECT treatment (P<0.01). Compared with before treatment, the scores of memory quotient and immediate memory of WMS decreased significantly after 1 week of treatment (P<0.05). However, these events were not be presented with the progress of treatment, except for after 2 weeks of treatment. Our results demonstrated that compared with before treatment, the scores of MMSE significantly increased significantly after 4 weeks of treatment (P<0.05). There were no serious adverse events in all patients, including cardiovascular and cerebrovascular events. Among them, 7 patients had
transient blood pressure rise and slight headache, which were relieved spontaneously after resting.

Conclusion: MECT is an effective, well tolerated and safe method for the treatment of older patients with refractory depression, which is temporary and reversible for cognitive impairment. MECT can be recommended for the treatment of these patients after conducting effective risk control of comorbid somatic diseases.

Background

Geriatric depression generally refers to the depression in older patients (≥60 years old), including primary depression and various secondary depression in geriatric period [1]. Compared with the patients with typical depression, the symptoms of older patients with geriatric depression are clinically atypical, including somatic discomfort as the main complaint, hypochondriasis, anxiety, agitation, which are commonly accompanied by cognitive dysfunction and somatic diseases. Nowadays, antidepressants are mainly used in the treatment of geriatric depression. However, 30%-50% of older patients with depression have a limited response to antidepressant treatment or their efficacy is not stable due to various reasons, which makes typical depression evolve into refractory depression, resulting in the decline of their qualities of life, the increase of family treatment costs, and the increase of suicide mortality risk [2]. It has become a difficult psychiatric problem at present, and there is no feasible way to cure it. Studies have shown that the effective rate of modified electroconvulsive therapy (MECT) can achieve 80-90% in the acute stage of the elderly patients with geriatric depression, and the rate of its safety is also relatively high[3]. MECT is a method to treat psychosis by giving a certain amount of electric current to stimulate the brain after intravenous injection
of anesthetics and muscle relaxants, so as to induce epileptic discharge in the cerebral cortex to cause patients’ loss of consciousness without muscle convulsion. Compared with the traditional electroshock, this method has higher safety, wider application and less adverse reactions. A large number of studies have shown that MECT may reshape the balance of the brain function loop of depression patients by affecting the default network and the functional connection of the attention network, so as to coordinate the brain structure involved in the control of emotion and cognitive function, which was considered to be effective in patients with depression[4–6]. However, there are few reports on the treatment of refractory depression olderly patients using MECT. Our study aimed to explore the efficacy and safety of MECT in the treatment of older patients with refractory depression.

Methods

Inclusion and exclusion criteria

Prospective study was conducted among patients hospitalized in the Department of Geriatrics, Wuhan mental health center from March 2014 to February 2015.

Inclusion criteria: (1) meet the diagnostic criteria of depression(international classification of Diseases 10th Edition); (2) age ≥ 60 years old; (3) meet the criteria for refractory depression: according to their history of diseases, the treatments over 3 months with two or more antidepressants with different chemical structures in sufficient quantity are ineffective; furthermore, for patients with primary (first-attack) depression, the treatments over 6 months with two antidepressants with different chemical structures in sufficient quantity are ineffective; (3) no MECT contraindications (including anesthesia allergy, intracranial space occupying lesions, active pulmonary inflammation, recent myocardial infarction, recent
cerebral hemorrhage, retinal detachment, untreated glaucoma, etc.); (4) primary school education or above; (5) patients and guardians fully understood the process and voluntarily signed informed consents.

Exclusion criteria: (1) schizophrenia, schizophrenic affective disorder, bipolar affective disorder or other psychiatric disorders; (2) comorbidity of severe cardiovascular and cerebrovascular diseases, pulmonary infection and other physical diseases; (3) received electroconvulsive treatment one month before admission. This procedure has been approved by the ethics committee of Wuhan Mental Health Center, and the informed consents were obtained from all patients.

Clinical data

A total of 46 patients were enrolled in our study, 3 patients failed to complete the treatment due to discharge, and 43 patients (18 male and 25 female) completed the tests and their results were analyzed subsequently. Among them, the age ranged 60–75 years old, the average age was 65 ± 4.8 years old and average course of disease was 7.5 ± 5.1 years. In addition, the initial average score of HAMD was 35.89 ± 6.84, and it was calculated as 22.16 ± 6.56 in terms of HAMA.

MECT

Physical examinations were carried out before operation, including routine blood examination, urine routine, liver and kidney function, blood glucose, myocardial enzyme spectrum, electrocardiogram, chest film and head CT. For patients accompanied by hypertension, coronary disease and diabetes, the following related indexes should be controlled before operation: (1) blood pressure was controlled to less than 140/less than 90 mmHg; (2) myocardial enzyme spectrum and cardiac troponin were in the normal range; (3) the value of fasting blood glucose was
controlled to less than 8.0 mmol/l, and urine glucose was detected to be negative. Before MECT, etomidate (0.15 mg/kg) and propofol (1 mg/kg) were administered by intravenous bolus after an intravenous bolus of atropine (0.5 mg). After the disappearance of ciliary reflex and fixation of eyeball, 0.2% succinylcholine chloride (1 mg/kg) was administered by intravenous bolus injection, then MECT could be carried out. Electrodes were placed on the bilateral temporal side of the patients, and multi-functional electrospasmodic therapeutic apparatus (type IV)(Somatics, US) was used for MECT in this study. Based on the age and weight, the pulse electric stimulation therapy was carried out according to the energy percentage. The heart rate, blood pressure, respiration, blood oxygen saturation (SpO₂) and electrocardiogram (ECG) were monitored dynamically during the treatment. After the operation, ECG monitoring was carried out for 2 hours, as well as vital signs and SpO₂ were monitored continuously.

MECT treatment was taken once every other day, three times a week, and 8–12 times in total for each patient. If patients received an administration of benzodiazepines, they should be stopped once before each MECT, and the dosages of antidepressants used before and after operation remained constant despite application of MECT.

Detection parameters

The scales were assessed before treatment and after 1 week, 2 weeks, 3 weeks and 4 weeks of treatment. Hamilton Depression Scale (HAMD-17) [7] and Hamilton Anxiety Scale (HAMA) [7] were used to assess the efficacy, and Wechsler Memory Scale (WMS) [8] and mini mental state examination (MMSE) [9] were used to assess the memory ability and cognitive function. There are 5 factors in HAMD-17 scale,
including anxiety somatization (including item 10, 11, 12, 15, 17), body mass (item 16), cognitive disorder (including item 2, 3, 9), block behavior (including item 1, 7, 8, 14) and sleep disorder (including item 4-6) [7]. Wechsler Memory Scale (WMS) included the following tests: (1) long-term memory: ① personal experience; ② directional time and space; ③ numerical sequence (1→100 and 100→1); (2) short-term memory: ① visual recognition; ② picture recall; ③ visual regeneration; ④ associative learning; ⑤ touch test; ⑥ understanding and memory; (3) immediate memory: forward and backward numbers.

In addition, the heart rate, blood pressure and electrocardiogram of patients were assessed before treatment and after 1 week, 2 weeks, 3 weeks and 4 weeks of treatment, so as to evaluate the changes of the above indicators and safety of MECT.

All the clinicians who participated in the scale evaluation received the training before the treatment. The correlation coefficient ICC value in the group was 0.81-0.84, indicating good consistency.

Evaluation of efficacy

The clinical efficacy was determined by reduction rate of HAMD score. The reduction rate of HAMD score was classified into following four grades: 75%, 50%-74%, 25%-49% and < 25% (considered to be invalid).

The rate of clinical efficacy= [cases(75%) + cases(50%-74%)] / total cases × 100%.

Evaluation of safety

The adverse events during and after treatment were recorded to evaluate the safety of treatment, such as sustained epilepsy, delirium, prolonged respiratory recovery, sustained hypertension, arrhythmia, headache, nausea and vomiting, myalgia, etc.
At the same time, using the scores of WMS and MMSE, the safety of treatment was evaluated in terms of memory and cognitive function.

Statistical analysis

SPSS19.0 was used for data statistical analysis. All measurement data were expressed as mean ± SD, and counting data were expressed as n(%). Before and after treatment, T test was used for comparison of measurement data, while counting data were examined by $\chi^2$ test. P < 0.05 was considered as statistical significant difference.

Results

Evaluation of overall efficacy

A total of 43 patients completed the study and their results were showed in the analysis, including 9 cases (20.9%) for reduction rate grade 75%, 20 cases (46.5%) for reduction rate grade 50%-74%, 7 cases (16.2%) for reduction rate grade 25%-49%, 6 cases (0.13%) for reduction rate grade < 25%, and the rate of clinical efficacy was calculated as 67.44%.

HAMD scores of patients after MECT treatment were statistically lower than that before treatment

There was a significant difference in HAMD scores of the patients between before treatment and after 2 weeks of MECT treatment (P < 0.05). With the progress of treatment, the difference was more significant after 4 weeks of MECT treatment (P < 0.01). The score of each factor showed that anxiety somatization and sleep disorder were significantly improved after 2 weeks of MECT (P < 0.05), the scores of block behavior and cognitive disorder decreased significantly after 3 weeks of
treatment (P < 0.01), while these events were present in body mass after 4 weeks of MECT (P < 0.05) (Table 1).

| MECT                     | Total scores | Anxiety somatization | Body mass | Cognitive disorder | Block behavior | Sleep disorder |
|--------------------------|--------------|----------------------|-----------|--------------------|----------------|----------------|
| Before treatment         | 35.89 ± 6.84 | 8.95 ± 1.78          | 1.19 ± 0.58 | 10.84 ± 2.86      | 9.34 ± 2.18    | 3.52 ± 1.75    |
| After 1 week of treatment| 33.86 ± 5.98 | 8.58 ± 1.02          | 1.18 ± 0.49 | 10.64 ± 2.07      | 9.20 ± 2.17    | 3.29 ± 1.56    |
| After 2 weeks of treatment| 32.98 ± 5.27* | 8.19 ± 1.2*          | 1.05 ± 0.58 | 9.98 ± 2.19       | 8.44 ± 1.98    | 2.18 ± 1.16**  |
| After 3 weeks of treatment| 20.81 ± 3.82** | 5.85 ± 1.7**         | 0.96 ± 0.64 | 6.64 ± 1.98**     | 5.76 ± 1.02**  | 1.68 ± 0.23**  |
| After 4 weeks of treatment| 14.07 ± 2.86** | 3.12 ± 1.84**        | 0.89 ± 0.71* | 4.10 ± 2.75**     | 4.96 ± 1.56**  | 1.25 ± 0.57**  |

Note: *P<0.05, **P<0.01, compared with before treatment.

HAMA scores of patients after MECT treatment were statistically lower than that before treatment.

The HAMA scores after 2 weeks of MECT treatment were significantly lower than that before treatment (P < 0.05), and the difference was more significant after 4 weeks of MECT treatment (P < 0.01). With the progress of treatment, the difference was more significant after 4 weeks of MECT treatment (P < 0.01). The score of each factor showed that compared with before treatment, mental anxiety improved after 2 weeks of MECT (P < 0.05), and its scores were more significantly lower after 2 weeks of treatment (P < 0.01), while there was a significant difference in physical anxiety between before treatment and after 4 weeks of MECT treatment (P < 0.05) (Table 2).

| MECT                     | Total scores | Anxiety somatization | Body mass | Cognitive disorder | Block behavior | Sleep disorder |
|--------------------------|--------------|----------------------|-----------|--------------------|----------------|----------------|
| Before treatment         | 22.16 ± 6.56 | 9.08 ± 3.09          | 14.28 ± 3.87 |                     |                |                |
| After 1 week of treatment| 21.48 ± 5.45 | 8.76 ± 2.21          | 13.02 ± 3.04 |                     |                |                |
| After 2 weeks of treatment| 19.85 ± 3.14* | 8.25 ± 3.04          | 12.53 ± 3.14* |                     |                |                |
| After 3 weeks of treatment| 16.87 ± 4.03** | 7.85 ± 2.83          | 9.76 ± 2.97** |                     |                |                |
| After 4 weeks of treatment| 10.42 ± 4.24** | 7.54 ± 2.98*         | 3.87 ± 2.46** |                     |                |                |

Note: *P<0.05, **P<0.01, compared with before treatment.
There were differences in WMS and MMSE scores between before and after MECT treatment

After 1 week of treatment, the scores of memory quotient and immediate memory of WMS were lower than that before treatment with a statistically significant difference (P < 0.05). After 2 weeks of treatment, except for the significant decrease of immediate memory scores (P < 0.05), there were no significant differences in scores of memory quotient, long-term memory and short-term memory between before and after treatment (P > 0.05). Besides, there were no statistical differences in each parameter of WMS between before treatment and after 3 and 4 weeks of treatment (P > 0.05). Our results found that compared with before treatment, the scores of MMSE significantly increased significantly after 4 weeks of treatment (P < 0.05) (Table 3).

| MECT                        | Memory quotient | Long-term memory | Short-term memory | Immediate memory | MMSE        |
|-----------------------------|-----------------|------------------|-------------------|------------------|-------------|
| Before treatment            | 83.54 ± 11.24   | 32.34 ± 4.01     | 41.28 ± 7.08      | 11.05 ± 2.21     | 24.08 ± 5.68|
| After 1 week of treatment   | 78.51 ± 11.57*  | 30.98 ± 3.76     | 39.78 ± 6.64      | 9.87 ± 2.45*     | 22.98 ± 5.12|
| After 2 weeks of treatment  | 80.22 ± 11.05   | 31.36 ± 3.02     | 39.56 ± 6.49      | 9.96 ± 2.71*     | 22.49 ± 4.95|
| After 3 weeks of treatment  | 82.46 ± 10.97   | 32.07 ± 2.78     | 40.27 ± 6.43      | 10.86 ± 2.67     | 24.67 ± 5.02|
| After 4 weeks of treatment  | 81.52 ± 12.01   | 31.46 ± 3.49     | 40.16 ± 7.15      | 11.01 ± 2.13     | 26.54 ± 5.16*|

Note: *P<0.05, compared with before treatment.

Adverse events associated with MECT treatment

During the treatment, there was no significant change in heart rate, blood pressure, respiration, SpO$_2$ and ECG. There were no serious adverse events in all patients, including cardiovascular and cerebrovascular events. Among them, 3 patients had transient hypertension, 4 patients had slight headache and no special treatment was conducted. These symptoms relieved spontaneously after resting.
Discussion

According to the statistics of the World Health Organization, the older patients with depression account for 7-10% of the total older population. Because the older patients with depression are commonly accompanied by various chronic diseases, the interaction between physical diseases and mental diseases is easy to form a vicious circle, leading to a heavier degree of depression [10]. Additionally, older patients are prone to recurrent depression due to sudden negative life events such as separation of relatives, loss of family members, and decrease of economic income. Meanwhile, older patients with depression have poor tolerance to antidepressant drugs with comorbidity of somatic diseases. Many antidepressant drugs have effects on cardiovascular, blood glucose, weight and gastrointestinal tract, while different kinds of drugs are prone to interact with each other, resulting in increased adverse reactions in older patients[1]. These reasons lead to the older patients with depression more prone to accidents and adverse events, leading to drug treatment difficult to achieve satisfactory effect [11]. Studies have shown that MECT has a certain effect on geriatric depression [10–13], but whether MECT is effective for the treatment of refractory depression, especially in the older patients with comorbidity of somatic diseases, remains unknown. Besides, there are few studies on the safety of treatment, adverse reactions and its effect on cognitive function.

In this study, after MECT treatment, the rate of clinical efficacy was calculated as 67.4%. HAMD scores gradually decreased with the progress of treatment. There was statistical difference between before treatment and after 2 weeks of MECT treatment, and the difference was more significant after 4 weeks of treatment, suggesting that the treatment was more effective for the improvement of HAMD
scores with the course of treatment. Our results showed the scores of anxiety somatization and sleep disorder decreased significantly after 2 weeks of MECT treatment. It has been suggested that there is a certain correlation between sleep disorder and depression, and sleep disorder can be considered as a predictive factor for the risk of onset and recurrence of depression[14]. The more serious the depression is, the more likely the patients are to have symptoms of sleep disorder. Furthermore, effective improvement of sleep disorder can improve the prognosis of depression or prevent the onset of depression. In this study, the sleep disorder of the patients improved significantly after MECT treatment, which was consistent with the improvement of refractory depression in the older patients. Besides, block behavior and cognitive disorder were improved significantly after 3 weeks of treatment. It has been reported that the total score of repeated neuropsychological tests (RBANS) was positively correlated with the cognitive disorder, sleep disorder and behavior block of HAMD, and negatively correlated with age in patients with depression accompanied by sleep disorder, suggesting that other factors gradually improved with the improvement of sleep disorder, leading to the gradual improvement of symptoms of depression[15].

The results of HAMA showed its total score after 2 weeks of MECT treatment was significantly lower than that before treatment, and more significant difference was demonstrated after 4 weeks of MECT. Because of atypical symptoms of older patients with geriatric depression, including anxiety and physical discomfort, the improvement of geriatric depression, especially the refractory depression, is limited. Our study found HAMA and HAMD scores were improved after 2 weeks of MECT treatment, suggesting that MECT had a certain effect on the treatment for the older patients with refractory depression after 2 weeks of treatment, thereby
reducing the risk of suicide and improving the confidence of patients in the treatment. In terms of factors of HAMA, the physical anxiety was improved later than mental anxiety. The reason may be that the physical anxiety symptoms of older patients with refractory depression were too serious to improve.

The results of safety showed that the limitation of MECT was due to the comorbidity of various diseases in the older patients. There were no serious adverse events in our study, and 7 patients had transient blood pressure rise and slight headache, which were relieved by themselves after resting. These results suggested that as long as the risk assessment before treatment, effective intervention of possible adverse events and postoperative care were carried out for the older patients with refractory depression with comorbidity of somatic diseases, the risks related to MECT treatment of somatic diseases can be reduced, which was consistent with the previous reports [16].

The effect of MECT on cognitive function of older patients with refractory depression also needs attention. Studies have shown that memory fades of patients were found at the end of MECT treatment, but their ability of memory recovered one month after treatment, and MMSE scores increased significantly compared with that before treatment. It was also reported that except for the speed of information processing, the high-level cognitive function of patients was not damaged by MECT [17, 18]. In our study, after 1 week of treatment, the scores of memory quotient and immediate memory decreased significantly compared with that before treatment, and these events were not be presented with the progress of treatment, except for after 2 weeks of treatment. These results are consistent with the above reports. In addition, there was no significant difference in MMSE scores between before treatment and after 1 week, 2 weeks, and 3 weeks of treatment. However, the score
after 4 weeks of treatment was higher than that before treatment, which may be related to the influence of depression on cognitive disorder of patients. With the improvement of symptoms of depression, the cognitive function of patients has also been improved, but the results of tests cannot exclude the learning effect of multiple measurements.

Conclusion
In conclusion, MECT is an effective, well tolerated and safe method for the treatment of older patients with refractory depression. It is temporary and reversible for the damage of cognitive function, and this method can be recommended for the treatment of these patients. In addition, the application of MECT is limited due to the somatic comorbidities. Therefore, it is necessary to carry out assessment of risk before treatment, control relevant risk factors, and strengthen monitoring during and after treatment to ensure the safety of treatment. In this study, the short term and small sample size can be considered as the limitations of our investigation. Our study only provides a reference for the treatment of the older patients with refractory depression, and the maintenance treatment of these patients with refractory depression after the symptoms are relieved and how to prevent the recurrence of depression need further study.

Abbreviations
modified electroconvulsive therapy MECT
Hamilton Depression Scale HAMD
Hamilton Anxiety Scale HAMA
Wechsler Memory Scale WMS
mini mental state examination MMSE

electrocardiogram ECG

Declarations

Ethics approval and consent to participate The study protocol was approved by the Ethics Committee of Wuhan Mental Health Center. Informed consent was obtained from all the study subjects before enrollment.

Consent for publication: Not applicable.

Availability of data and material The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions Xue Jiang and Qin Xie contributed to the conception and design of the study; Lian-Zhong Liu and Lian-Zhong Liu performed the experiments, collected and analyzed data; Xue Jiang and Qin Xie wrote the manuscript; All authors reviewed and approved the final version of the manuscript.

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