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Original Article

Effects of modified electroconvulsive therapy on the cognitive function and blood parameters in female patients with schizophrenia

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Abstract: Background: This study aimed to investigate the effects of modified electroconvulsive therapy (MECT) on cognitive function and blood parameters in female patients with schizophrenia. Materials and methods: Female patients with schizophrenia (n = 23) received MECT while maintaining antipsychotic therapy. 1) White blood cell (WBC), alanine aminotransferase (ALT), creatine kinase (CK) and creatine kinase MB (CKMB) were measured at 10 min before and after MECT. 2) The severity of symptoms was evaluated before and after MECT by using the Positive and Negative Symptoms Scale (PANSS) and then the therapeutic effects of MECT were assessed. 3) Single nerve psychology test was used to assess the cognitive function. Results: 1) There were no significant differences in WBC, ALT, CK and CKMB before and after MECT ($P > 0.05$). 2) WBC, ALT and CKMB remained stable at different time points after MECT treatment ($P > 0.05$). But CK had statistical differences at different times before or after MECT treatment ($P < 0.05$). CK decreased since the first MECT and thereafter increased after the 7th treatment ($P < 0.05$). 3) The total score of PANSS decreased significantly after MECT ($P < 0.05$). 4) Digit span test showed no statistically significant differences in different time points ($P > 0.05$); Digital sign test and verbal fluency test showed significant differences in different times ($P < 0.05$). Conclusion: The CK figure decreased from the first to sixth MECT treatment and increased in the 7th MECT treatment, and the CKMB also increased in the 7th treatment. MECT treatment had significant effects on female patients with schizophrenia and could obviously improve patient's cognitive function.

Keywords: Schizophrenia, modified electroconvulsive therapy, creatine kinase, cognitive function

Introduction

Schizophrenia is a group of mental disorders of unknown causes and characterized by the disorder of perception, thinking, emotion, behavior and mental activities. It is often found in young adults aged 15-35 years whose social function is significantly impaired and labor ability is lost. Schizophrenia has become a public health problem worldwide because it needs repeated treatments. According to the World Health Organization Statistics in 2001, schizophrenia accounted for 2.8% of the global disease burden [1]. Thus, to optimize the strategies for the treatment of schizophrenia has been a focus in studies on psychiatric diseases.

Recently, great progress has been achieved in the pharmacotherapy of schizophrenia. However, some schizophrenia patients still present treatment-resistance. Electroconvulsive therapy (ECT) is still the choice of treatment for schizophrenia and has been found to be effective and safe for schizophrenia. In recent years, Modified Electroconvulsive therapy (MECT) is developed for the therapy of schizophrenia in which anesthetics and muscle relaxant are administered, and the blood pressure and electrocardiogram are closely monitored. Under this condition, patients have no strong muscle twitching and EEG is near normal. MECT is widely used in clinic and has become an indispensable psychiatric treatment. MECT has its advantages for treatment-resistant schizophrenia and recurrent refractory mania [2]. It has also been revealed that continuous ECT is safe, effective and low-cost [3].

A majority of schizophrenia patients have cognitive impairment which is a major symptom of

Table 1. WBC count, ALT, CK and CKMB before and after MECT

		Number	$\bar{x} \pm s$	*t*	P
WBC	Before	176	7.96 ± 2.38	0.562	0.575
	After	176	7.72 ± 2.65		
ALT	Before	176	29.63 ± 24.34	0.281	0.779
	After	176	28.89 ± 24.56		
CK	Before	176	143.01 ± 291.18	0.060	0.952
	After	176	141.17 ± 280.32		
CKMB	Before	176	18.27 ± 13.36	0.550	0.583
	After	176	19.03 ± 12.58		

schizophrenia. In the present study WAIS-R test was performed before and after MECT in schizophrenia patients, and our study minimized the impact of drugs on the cognitive function, and then the effects of MECT on the cognitive function and blood parameters were evaluated.

In addition, our previous study showed the serum CK level of schizophrenia outpatients appeared increased to different increasing degree in the clinics. Gao et al. [4] studied investigated the CK activity in 195 schizophrenia patients receiving concomitant pharmacotherapy before and at 4th and 8th weeks after drug therapy. Their results showed the CK activity in schizophrenia patients were significantly higher than that in control group and CK activity was positively associated with positive symptoms of schizophrenia. Northoff et al. [5] found that the serum CK activity in patients with schizophrenia of tension-type was significantly higher than that in control group and non-nervous schizophrenia patients without movement disorders. The serum CK activity was comparable in tension and non-nervous schizophrenia patients with movement disorders, which suggests that the serum CK activity is positively related to Parkinson's disease. However, the CK activity had no relevance with involuntary movement disorder in three groups, which indicates that the increased serum CK activity is caused by movement disorders. As we know, MECT is effective for acute stage and excited agitation of schizophrenia. However, whether the CK activity changes during MECT is still unclear. The correlation of WBC count with MECT is still required to be elucidated. In this study, blood biochemical parameters and cognitive function were determined in schizophrenia patients before and after MECT to evaluate the therapeutic efficacy and safety of MECT.

Materials and methods

Materials

Female schizophrenia patients (n = 23; 30.57 ± 8.03 years) were recruited from Henan Mental Hospital from March 2011 to July 2011. Schizophrenia was diagnosed according to the diagnostic criteria for schizophrenia in CCMD-3. Patients had no history of vaccination and infection. Patients with major or unstable cardiovascular, respiratory, nervous system or cerebrovascular disease (including epilepsy), kidney disease, liver disease, endocrine disease and immune system disease were excluded from this study.

This study was approved by the Ethics Committee of The Second Affiliated Hospital of Xinxiang Medical University, and signed informed consent for MECT was obtained from each patient before this study.

Pharmacotherapy

All the patients maintained the prior antipsychotic therapy before and after MECT.

Sample collection and processing

MECT treatment was done 6-8 times every other day. Venous blood was collected before and after MECT therapy and anti-coagulated with EDTA. Immediately, blood biochemical test was performed in the Department of Clinical Laboratory of Henan Mental Hospital. The white blood cell (WBC) count, ALT, CK and CKMB were determined at 10 min before and after MECT (normal ranges: 3.96-9.16 10^9/L for WBC, 5-40 U/L for ALT, 25-195 U/L for CK, 0-25 U/L for CKMB).

MECT

All the patients received food and water deprivation for 6 h, and venous access was established. MECT was performed with the Thymatron (Somatic U.S.A.). DGX mode was set for the monitoring of EEG and ECG. The static resistance was 100-3000 Ω according to the instructions for electroconvulsive therapy. In addition, 0.5-1.0 mg of atropine, propofol at 1.5-2 mg/kg and SiKeLin at 0.6-1.0 mg/kg were also intravenously administered. The body condition, EEG and ECG were closely monitored in the whole process of MECT.

Table 2. WBC count, ALT, CK and CKMB before and after MECT at each therapy

		Number of MECT									
		1	2	3	4	5	6	7	8	*F*	P
WBC	Before	8.22 ± 1.92	7.41 ± 1.73	7.77 ± 2.30	8.29 ± 2.68	7.80 ± 1.82	7.73 ± 1.93	7.80 ± 2.06	8.70 ± 4.10	1.289	0.260
	After	7.93 ± 2.00	7.38 ± 1.86	7.12 ± 2.75	7.66 ± 3.12	7.51 ± 2.07	7.83 ± 1.99	7.77 ± 2.29	8.76 ± 4.46	1.401	0.209
ALT	Before	36.48 ± 45.87	30.35 ± 28.90	31.17 ± 23.29	29.13 ± 19.96	26.87 ± 15.21	24.24 ± 11.92	27.60 ± 11.88	30.55 ± 17.19	0.833	0.562
	After	35.70 ± 47.41	28.43 ± 29.87	29.57 ± 22.48	28.74 ± 19.34	26.96 ± 14.53	24.43 ± 12.14	26.95 ± 11.76	29.85 ± 16.55	0.674	0.694
CK	Before	268.39 ± 633.52	214.17 ± 316.95	173.19 ± 278.32	129.43 ± 203.05	84.35 ± 58.86	73.05 ± 44.42	94.65 ± 85.13	86.95 ± 85.14	2.082	0.049
	After	263.35 ± 606.30	212.17 ± 310.39	167.87 ± 262.65	129.91 ± 201.00	84.74 ± 58.62	73.76 ± 44.59	91.30 ± 81.90	86.80 ± 85.58	2.156	0.041
CKMB	Before	20.70 ± 16.91	18.52 ± 10.90	18.00 ± 10.47	19.91 ± 12.68	15.87 ± 7.62	14.81 ± 8.09	21.20 ± 25.00	17.10 ± 7.67	0.770	0.614
	After	22.61 ± 16.81	18.55 ± 9.69	20.17 ± 9.88	17.96 ± 9.27	19.13 ± 6.44	17.52 ± 8.57	19.90 ± 24.78	16.00 ± 5.90	0.539	0.804

Table 3. PANSS score before and after MECT

	Number	$\bar{x} \pm s$	*t*	P
Before treatment	23	88.48 ± 23.81	9.481	0.000
After treatment	23	51.74 ± 12.79		

Evaluation of cognitive function

Positive and Negative Symptoms Scale (PANSS) was used to evaluate before and after MECT. Neuropsychological tests were employed to assess the cognitive function (including digit span test, digit symbol test and verbal fluency test) before and at 24 h after the first, fourth and eighth MECT.

Statistical analysis

SPSS version 17.0 was employed for statistical analysis. Data were expressed as mean ± standard deviation. t test and analysis of variance (ANOVA) were used to compare the WBC count, ALT, CK and CKMB, PANSS score and cognitive function before and after MECT. Two-factor ANOVA was used to compare the WBC count, ALT, CK and CKMB at different time points after MECT. A value of $P < 0.05$ was considered statistically significant.

Results

General data

A total of 23 female schizophrenia patients were enrolled in this study with an average age of 30.57 ± 8.03 years old (range: 19-49 years). Among them, 20 patients completed eight times of MECT, while the other three achieved six times of MECT. Sample collection: WBC count, ALT and CK were tested 176 times before and after treatments separately, CKMB was measured 176 times before treatments and 175 times after treatments in total.

WBC count, ALT, CK and CKMB before and after MECT

Values of WBC count, ALT, CK and CKMB before and after every treatment were analyzed with *t* test. As shown in **Table 1**, WBC count, ALT and CK decreased, and CKMB increased after each MECT, but there was no significant difference ($P > 0.05$). Therefore, our findings are in line with the idea that electroconvulsive procedures were safe in schizophrenia. The levels of WBC and ALT may be uncorrelated with contraindications and adverse events of ECT.

WBC count, ALT, CK and CKMB before and after MECT at each therapy

Results of two-factor ANOVA showed that there were no significant differences in WBC count, ALT and CKMB before and after MECT at each therapy separately ($P > 0.05$), but significant difference was observed in CK before and after each therapy separately (before treatment: $F = 2.082$, $P < 0.05$; after treatment: $F = 2.156$, $P < 0.05$). Result also indicated that CK gradually decreased with the increase in times of MECT, but increased since the seventh MECT ($P > 0.05$). CKMB didn't reduce with the decrease in CK. The changes in CKMB were irregular with the increase in times of MECT, but CKMB increased slightly after the seventh MECT ($P > 0.05$) (**Table 2**).

PANSS score

Results of comparison between PANSS scores before MECT and after 6-8 times of treatments indicated that significant difference was observed in PANSS score before and after MECT ($P < 0.05$) (**Table 3**). CK significantly decreased with the increase in times of MECT, which is consistent with the changes of PANSS scores.

Scores of neuropsychological tests before and after MECT treatment

ANOVA was adopted to analyze results of digit span test, digit symbol test and verbal fluency test. Results showed that the scores of digit span test remained stable at different time points ($P > 0.05$), which decreased after the first MECT and then increased. The scores of digit symbol test and verbal fluency test increased significantly with the increase in MECT ($P < 0.05$). It is suggested that the ability to learn a new contact, visual-motion coordination, fine motor, enduring ability, operation speed and fluency, word semantic memory storage function, classification and organization skills have been improved, while the short-term memory has not been influenced after MECT. There was cognition impairment in schizophrenia patients. Thus, symptoms improved as well as attention, thoughts, judgment and ability of words integration after MECT (**Table 4**).

Discussion

CK is a cytosolic enzyme and widely distributed in the human heart, liver, bone, muscle, lung

Table 4. Scores of neuropsychological tests before and after MECT

	Before 1st MECT	After 1st MECT	After 4th MECT	After 8th MECT	*F*	P
Digit span test	12.74 ± 2.14	12.52 ± 2.19	13.39 ± 1.62	13.65 ± 1.53	1.826	0.148
Digit symbol test	34.74 ± 5.09	35.70 ± 6.29	39.09 ± 6.09	39.87 ± 6.06	4.163	0.008
Verbal fluency test	16.26 ± 3.85	16.61 ± 3.14	18.61 ± 3.63	19.30 ± 3.43	4.115	0.009

and other tissues. When the organs and tissues are damaged, the integrity of cell membrane is destroyed and CK is released into the blood. There are three types of CK isozyme: CK-BB, CK-MB and CK-MM. Many diseases (such as muscular trauma, myocardial damage and brain disorders) may increase the activity of serum CK. Schizophrenia is a functional disease of the brain and CK is often used as a diagnostic indicator of neuroleptic malignant syndrome (NMS). In recent years, studies show that the serum CK activity changes significantly in non-malignant syndrome patients with schizophrenia.

In clinical practice, clinicians have found that serum CK increases in many patients with schizophrenia which is not controlled by pharmacotherapy and often requires ECT. Studies have shown that ECT combined with antipsychotic drugs have advantages in improving the time and the quality of curative effect [6-10]. Gao et al. [4] detected CK activity in 195 schizophrenia patients before and at 4 and 8 weeks after pharmacotherapy, and the disease severity was evaluated with BPRS, SANS and SAPS. In their study, 69 health subjects were also recruited as controls. Their results showed that CK activity of schizophrenia patients was significantly higher than that in control group and it was positively correlated with positive schizophrenia symptoms. Li and Wu [11] found that serum CK activity was significantly associated with clinical subtypes of schizophrenia. In their study, serum CK activity was detected in 80 schizophrenia patients and 30 healthy controls. Results showed that serum CK activity increased significantly in excited schizophrenia patients. Lin et al. [12] also found that CK activity varied in patients with different subtypes of schizophrenia, and serum CK activity in patients with schizophrenia paranoid type, hebephrenic, tension-type was significantly higher than that in healthy controls, CK activity in simple group was lower than that in healthy controls, but CK activity in undifferentiated group was similar to that in control group. Thus, we speculate that serum CK activity is important for the evaluation of illness change and diagnosis of schizophrenia.

Northoff et al. [5] found that the serum CK activity in patients with schizophrenia of tension-type was significantly higher than that in healthy controls and those with non-nervous without movement schizophrenia. However, serum CK activity was comparable between patients with movement schizophrenia of tension and non-tension subtypes. Thus, serum CK activity may significantly correlate with Parkinson's disease. However, CK activity has no relevance with involuntary movement disorder in all the three groups, which indicates that the increased serum CK activity is ascribed to the movement disorders. Most investigators speculate that schizophrenia patients due to the excited state, the activity increased, agitation or in a state of emergency, the sympathetic nervous function increased, the level of serum catecholamine concentration rose, which causes vasoconstriction, focal ischemia and hypoxia, cell energy metabolism dysfunction, and increased permeability of muscle cells and brain cells, resulting in the release of intracellular CK into blood and subsequent increase in serum CK activity [4, 7]

In the present study, serum CK was detected in patients before and after MECT and the symptoms were evaluated with PANSS. Results showed CK decreased significantly and PANSS scale reduced markedly with the increase in MECT, which confirms the findings of Gao et al. who found CK activity was positively related to the symptoms of schizophrenia [4]. Our findings also confirm that MECT is helpful to improve the symptoms of schizophrenia.

In this study, our results also revealed that CK gradually declined since 1st MECT, suggesting that the symptoms (especially the excited symptom) are quickly improved. However, CK and CKMB increased since the 7th MECT, which suggests that to increase MECT fails to further improve these symptoms. This was consistent with what we observed in clinical practice. Our findings provided a basis to define the reasonable number of MECT for schizophrenia.

In addition, WBC count, ALT, CK and CKMB remained stable before and after MECT at each therapy, which suggests that MECT is safe. In the acute stage of schizophrenia, MECT and antipsychotic drugs at reduced doses may be used to avoid ALT elevations as in therapy with antipsychotic drugs at high doses.

Many studies have confirmed that schizophrenia patients have cognitive impairment which is one of major symptoms of schizophrenia [13, 14]. Medalia et al. [15] found that the incidence of cognitive impairment was at least 40%-60% in schizophrenia patients, and Piskulic et al. [16] speculated that about 85% of schizophrenia patients had cognitive impairment. Xue et al. [17] found schizophrenia patients had no impaired memory after MECT evaluated by WMS. Pisvejc et al. [18] found that the memory of schizophrenia patients was improved after MECT. Sun et al. [19] found that cognitive function of schizophrenia patients would be further improved with MECT as assessed with WCST and WAIS-R. However, some investigators found that patients developed cognitive impairment after ECT and MECT evaluated by psychological tests and imaging examinations [20-25].

In the present, results showed the scores of digit span, digit symbol and semantic fluency test increased after MECT, which suggest that the cognitive function does not decline. On the contrary, some patients had significantly improved cognitive function after MECT, which suggests that schizophrenia patients have cognitive dysfunction. Thus, MECT may improve the symptoms of schizophrenia patients and improve their attention, thinking, judgment and speech capabilities to different extents. The MECT therapy may improve cognitive function of schizophrenia patients.

The score of digit span test remained stable during the MECT, which reflects that the instantaneous memory ability is not influenced by MECT. The score of digit span test declined after the first MECT, but increased after following therapies, which indicates that the influence of MECT on the memory is temporary and reversible. Ros et al. found 25%-29% of schizophrenia patients complained of persistent memory loss after ECT [26]. Thus, we speculated that the subjective memory loss of schizophrenia patients because of impaired long-term memory.

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Disclosure of conflict of interest

None.

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