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Original Article

Effects of carbamazepine and sodium valproate on efficacy, cognitive function and uric acid in epileptic patients with first generalized seizure

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Abstract: Objective: To investigate the effects of carbamazepine and sodium valproate on efficacy, cognitive function and uric acid in epileptic patients with first generalized seizure. Methods: 120 epilepsy patients with first generalized seizure who admitted to our hospital from March 2017 to March 2019, were selected and randomly divided into carbamazepine-group and sodium valproate-group, with 60 objects in each group. Both groups of patients received medication for one year. Subsequently, the changes in clinical efficacy, cognitive function, and blood uric acid of the two groups of patients 1 year after treatment were compared, and the correlation between blood uric acid and cognitive function was analyzed between the two groups. Results: The two groups had statistically insignificant difference in the total effective rate (*P>0.05*). The cognitive function scores of the two groups after 6 months and 1 year of treatment were critically higher than those before treatment (*P<0.05*), and the comparison of cognitive function and blood uric acid degree between groups before treatment, 6 months after treatment and 1 year after treatment had statistically insignificant difference (*P>0.05*). There was a significant positive correlation between Mini-mental State Examination (MMSE) score of cognitive function and level of blood uric acid in patients with epilepsy (r=0.279, P=0.012). Conclusion: Both carbamazepine and valproate can effectively improve the cognitive function of patients with first generalized seizure, and the two medications have similar clinical efficacy. Patient's blood uric acid level increases after treatment, and there is a affirmative relationship between blood uric acid level and cognitive function of patients.

Keywords: Carbamazepine, sodium valproate, epilepsy, cognitive function, uric acid

Introduction

Epilepsy is a chronic brain disease, and is a transient loss of central nervous system function caused by the abnormal discharge of brain neurons. The disease has repeated attacks, difficult treatment, and complicated clinical symptoms, which seriously affect the physical and mental health of patients [1]. At present, the pathogenesis of epilepsy has not been fully elucidated, but some studies suggest that oxidative stress may be the cause and result of epileptic seizures [2]. Uric acid is the final product of purine metabolism in nucleic acid, and is also the important antioxidant in human body. Most of the uric acid are excreted from the body through kidneys [3]. Uric acid does not harm the human body at normal levels, but when uric acid in human body is elevated, mitochondrial dysfunction, oxidative stress and apoptosis of cells may occur [4, 5]. At present, the treatment of epilepsy is mainly anti epileptic drugs, whether carbamazepine and sodium valproate, as commonly used antiepileptic drugs in clinic, can influence the treatment of patients by affecting their uric acid degree has not been reported. In this study, we analyzed the effects of carbamazepine and sodium valproate on efficacy, cognitive function and uric acid in epileptic patients with first generalized seizure.

Materials and methods

Research objects

We selected 120 epilepsy patients with first generalized seizure who admitted to our hospital from March 2017 to March 2019, and divided them into carbamazepine-group and sodium valproate-group by method of random number table. Each group contained 60 objects. The study was carried out after acquiring approval of the hospital ethics committee.

Inclusive and exclusive criteria

Inclusive criteria: (1) The patient met the diagnostic criteria of generalized seizure epilepsy in *Chinese Classification and Diagnostic Criteria for Mental Disorders* (3rd Edition) [6]. (2) Patients iagnostic Criteria Patients did not experience with anti-epileptic treatment; and (4) Patients who signed the informed consent voluntarily.

Exclusive criteria: (1) Patients had inherited metabolic diseases, and liver function or renal function damage; (2) Patients with anxiety, depression, diabetes, coronary heart disease or cerebral infarction; or (3) Patients with neurosyphilis, hyperthyroidism or AIDS.

Methods

The carbamazepine-group was treated with oral Carbamazepine Tablets (Shanghai Huanghai Pharmaceutical Co., Ltd., H31021493), 300 mg/d for 1 year; The sodium valproate-group received oral treatment of Sodium Valproate Sustained-release Tablets (Sanofi (Hangzhou) Pharmaceutical Co., Ltd., Chinese medicine approval H20010595). Patients were given an initial dose of 750 mg/d, and gradually increased to 2,000 mg/d, for 1 consecutive year.

Evaluation criteria of clinical efficacy

Referred to the literature standard [7], the clinical efficacy was compared by the number of times and frequency of epileptic seizures before and after treatment according to the formula f=t2/t1×100%. t1 referred to the average seizure frequency per 28 days before treatment, and t2 represented the reduced seizure frequency per 28 days after treatment. If f=100%, it referred that the disease was completely controlled. When f was 75%-99%, the curative effect was remarkable. When f was 50%-74%, it referred to the effective treatment, and if f was below 50%, the treatment was ineffective. The total effective rate of treatment = complete control rate + remarkable efficient rate + effective rate.

Observation of indexes

(1) The cognitive function of the two groups was evaluated by Mini-mental State Examination (MMSE) before treatment, 6 months and 1 year after treatment. The examination included orientation (10 points), memory (3 points), attention and numeracy (5 points), recall (3 points) and verbal ability (9 points), with a total of 30 points. Patients with scores of 27-30 points were considered normal, and those with scores <27 were classified as cognitive dysfunction.

(2) The blood uric acid levels of the two groups of patients were measured before treatment, 6 months and 1 year of treatment. 5 ml of fasting venous blood was collected from the patients in the morning. After centrifugation, the serum was separated and detected by automatic biochemical analyzer (Beckman Company, USA). The measurement was performed in strict accordance with the kit instructions.

Statistical analysis

The data included in this study was carried out by statistical software SPSS 22.0. The measurement data was compared by t-test, and the enumeration data was compared by X^2 test. The statistically significant difference was set by $P<0.05$. The graphic software was by Excel and Graphpad prism9.

Results

Clinical data

The two groups of patients had statistically insignificant difference in terms of gender, age, BMI or EEG, as shown in **Table 1**.

Comparison of clinical efficacy

The total effective rate of carbamazepine-group was 78.33%, and that of valproate-group was 82.67%. The two groups had statistical insig-

Table 1. Comparison of clinical data between the two groups

Group	Number of cases	Gender		Age (yd, $\overline{X}$±s)	BMI (kg/m^2, $\overline{X}$±s)	EEG			
		Male	Female			Normal	Mildly abnormal	Moderately abnormal	Highly abnormal
Carbamazepine-group	60	35	25	44.95±7.39	23.47±2.10	3	28	22	7
Sodium valproate-group	60	38	22	45.20±8.34	23.63±2.52	2	25	23	10
t/X^2	-	0.315		0.174	0.378	0.901			
P	-	0.575		0.862	0.706	0.368			

Table 2. Comparison of clinical efficacy between two groups of patients [n (%)]

Group	Number of cases	Completely control	Remarkable effective	Effective	Invalid	Total effective rate (%)
Carbamazepine-group	60	17 (28.33)	14 (23.33)	16 (26.67)	13 (21.67)	78.33
Sodium valproate-group	60	21 (35.00)	15 (25.00)	13 (21.67)	11 (18.33)	82.67
X^2	-	-	-	-	-	0.208
P	-	-	-	-	-	0.648

Table 3. Cognitive function scores before and after treatment in the two groups (points, $\overline{x}$±s)

Group	Number of cases	Before treatment	6 months of treatment	1 year of treatment
Carbamazepine-group	60	24.37±1.38	26.39±2.02*	27.52±1.79*
Sodium valproate-group	60	24.19±1.55	26.57±2.17*	27.64±1.83*
t	-	0.672	0.470	0.363
P	-	0.503	0.639	0.717

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

nificant difference of total effective rate ($P>0.05$) (**Table 2**).

Comparison of changes in cognitive function before and after treatment

The cognitive function scores of the two groups after 6 months and 1 year of treatment were critically higher than those before treatment [(26.39±2.02) vs. (24.37±1.38); (27.52±1.79) vs. (24.37±1.38); (26.57±2.17) vs. (24.19±1.55); (27.64±1.83) vs. (24.19±1.55)] ($P<0.05$), and the comparison of cognitive function of the two groups before treatment, 6 months after treatment and 1 year after treatment had statistically insignificant difference [(24.37±1.38) vs. (24.19±1.55); (26.39±2.02) vs. (26.57±2.17); (27.52±1.79) vs. (27.64±1.83)] ($P>0.05$) (**Table 3**).

Comparison of changes in blood uric acid levels before and after treatment

The blood uric acid degree of the two groups of patients after 6 months and 1 year of treatment were obviously higher than those before treatment [(369.17±49.82) vs. (326.28±46.21); (398.79±50.93) vs. (326.28±46.21); (370.92±51.03) vs. (319.85±57.47); (410.21±64.29) vs. (319.85±57.47)] ($P<0.05$), and the comparison between groups before treatment, 6 months and 1 year after treatment had statistically insignificant difference [(326.28±46.21) vs. (319.85±57.47); (369.17±49.82) vs. (370.92±51.03); (398.79±50.93) vs. (410.21±64.29)] ($P>0.05$) (**Table 4**).

Correlation between cognitive function and blood uric acid level in patients with epilepsy

We analyzed the correlation between the cognitive function MMSE score and the blood uric acid level of epilepsy patients, and the results showed that the cognitive function MMSE score of epilepsy patients was notably positively correlated with the blood uric acid level (r=0.279, P=0.012) (**Figure 1**).

Discussion

Epilepsy is a common chronic disease of nervous system, which is characterized by recur-

Table 4. Comparison of blood uric acid levels before and after treatment between the two groups ($\bar{x}$±s)

Group	Number of cases	Before treatment	6 months of treatment	1 year of treatment
Carbamazepine-group	60	326.28±46.21	369.17±49.82*	398.79±50.93*
Sodium valproate-group	60	319.85±57.47	370.92±51.03*	410.21±64.29*
t	-	0.675	0.190	1.079
P	-	0.501	0.850	0.283

Note: compared with prior-treatment, **P<0.05*.

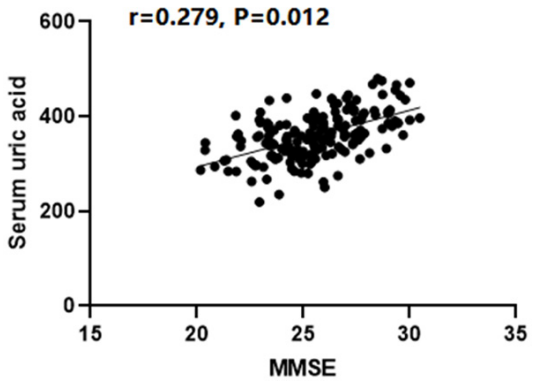

Figure 1. Correlation analysis of cognitive function and blood uric acid level in patients with epilepsy.

rent seizures. The disease can occur in people of any age, with sudden and unexplained seizures [8]. Epilepsy is caused by the abnormal discharge of brain neurons. The disease is repetitive and transient, and the course is long and clinical treatment is difficult [9]. Carbamazepine and sodium valproate are common used drugs for the clinical treatment of epilepsy. Carbamazepine can inhibit the release of glutamate in patients and block voltage dependent sodium channels, relieve hyperactive nerve cells, and achieve antiepileptic effect by reducing synaptic signal transmission [10, 11]. Sodium valproate can regulate the content of γ-aminobutyric acid in human body, reduce the excitability of neurons, and achieve the anticonvulsant effect by inhibiting N-methyl-D-aspartate receptor [12, 13]. Sodium valproate can be applied for different types of epilepsy given its function of regulating and balancing nerve excitability [14, 15].

This study investigated the effects of carbamazepine and sodium valproate on efficacy, cognitive function and uric acid in epileptic patients with first generalized seizure. The results showed that for patients with generalized seizures without a history of anti-epileptic drugs, both carbamazepine and sodium valproate can exert effective anti-epileptic effects. The total effective rate of carbamazepine-group-patient was 78.33%, and that of valproate-group was 82.67%; The two groups had statistical insignificant difference in total effective rate. Besides, the cognitive function scores of the two groups after 6 months and 1 year of treatment were critically higher than those before treatment, and the comparison between groups before treatment, 6 months after treatment and 1 year after treatment had statistically insignificant difference. This result is consistent with those reported previously [16, 17]. For patients with generalized seizures, both carbamazepine and valproate can be used as routine drugs in clinical treatment and the clinical efficacy of two medicines is similar. Scholars have reported [18] that uric acid in cerebrospinal fluid and serum of patients with epilepsy has significantly increased. Uric acid is an organic complex that composed of oxygen, nitrogen and hydrogen, and is the final metabolite of purine metabolism in specific species such as human, dogs and primates. The main sources of uric acid can be classified as endogenous and exogenous. Endogenous uric acid accounts for around 80% of total uric acid, and is derived from the synthesis of amino acids, ribose phosphate and other small molecules and catabolism of nucleic acids in body. Exogenous uric acid is primary decomposition of nucleotides in food [19, 20]. More than 99% of uric acid is present in form of ionization under the condition of normal physiological concentration and blood pH value; and two-thirds of uric acid is excreted with urine, and the rest is excreted through feces [21, 22]. The physiological role and mechanism of uric acid in the body is not fully understood at present. Studies have found that the blood uric acid level in patients with Alzheimer disease and Parkinson disease

is decreased, and uric acid can improve the learning ability and memory of Alzheimer-rats [23, 24]. There are scholars who believe that uric acid is a significant physiological natural antioxidant, free radical scavenger and iron chelator. It can inhibit a series of secondary injury and apoptosis of nerve cells through a variety of mechanisms, and has the effect of anti-oxidative stress and neuron protective function [25, 26]. On the contrary, there are also reports which stated that high uric acid can increase the oxidative damage and lead to atherosclerosis and damage of nerve cells [27].

The results of this study indicate that the blood uric acid degree of the two groups of patients after 6 months and 1 year of treatment were obviously higher than those before treatment, and the comparison of blood uric acid degree between groups before treatment, 6 months and 1 year after treatment had statistically insignificant difference; In addition, MMSE score of cognitive function was positively correlated with serum uric acid level in patients with epilepsy. This is consistent with the results as previously reported [28], there might be a certain correlation between the level of blood uric acid and cognitive function, and the blood uric acid may play a positive role in patients' rehabilitation of cognitive function. However, the patient's blood uric acid level increased after treatment, which is considered to be related to the progression of the disease and the damage to the kidney function caused by medication. Therefore, further expand of sample size and the extension of the observation time is necessary to determine the long-term effects of carbamazepine and sodium valproate on patients with epilepsy.

In conclusion, both carbamazepine and valproate can effectively improve the cognitive function of patients with first generalized seizure, and the two medications have similar clinical efficacy. Patient's blood uric acid level increases after treatment, and there is a certain relationship between blood uric acid level and cognitive function of patients.

Disclosure of conflict of interest

None.

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