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Comparison of impact on seizure frequency and epileptiform discharges of children with epilepsy from topiramate and phenobarbital

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Abstract. – OBJECTIVE: To study the impact on seizure frequency and epileptiform discharges of children with epilepsy from topiramate (TPM) and phenobarbital (PB).

PATIENTS AND METHODS: Two hundred cases children with epilepsy from August 2010 to August 2013 in our hospital were sampled and randomly divided into two groups. The observation group was treated with TPM while the control group with PB, and then comparing seizure frequency, efficiency, and adverse reactions of two groups.

RESULTS: The reduced number of partial seizures, generalized seizures, and total seizures in the observation group were significantly higher than those in the control group, and the rate of cure, markedly effective and total efficiency in observation group were significantly higher than those in the control group. However, the adverse reactions in observation group were significantly lower than those in the control group. Thus, differences were statistically significant ($p<0.05$).

CONCLUSIONS: Compared with PB, TPM showed a better effect on epilepsy treatment with less adverse reactions which were worthy of clinical recommendation.

Key Words:
Topiramate, Phenobarbital, Epilepsy, Seizure frequency, Epileptiform discharges.

Introduction

Epilepsy is commonly known as "Yang'er Feng", it is one of the most common chronic diseases of the nervous system in children, the prevalence rate is from 3‰ to 6‰[1,2]. Epilepsy is brought about by the abnormal synchronous discharge of brain cells because of a variety of causes, and it can lead to the sudden onset of brain dysfunction. Its clinical manifestation is diversified; it may lead to many patients performances such as consciousness change or loss, body twitch, sensory abnormalities, and special behavior, etc.[3,4]. In the past, people had less knowledge and studies on epilepsy which led to that many patients were not scientifically treated and their seizure control was running below expectations. Since the 1980s, a large number of new drugs have come out and have greatly improved the treatment efficiency of epilepsy and it is not "incurable disease" anymore[5]. Since August 2010, topiramate (TPM) has showed its significant effect on epilepsy treatment in our hospital and the efficiency report is as follows.

Patients and Methods

Patients

Two hundred cases children with epilepsy from August 2010 to August 2013 in our hospital were observed and randomly divided into two groups. The criteria used for the diagnosis: 1. Repeated attack, which can be self-relieved. 2. With acute onset. Restored after the treatment. 3. No sign of symptoms shown before the onset but existing inducement. 4. Abnormal EEG. The observation group included 55 male and 45 female patients (aged from 4.1 ± 2.5), among them, 67 patients had generalized seizures and 33 patients had partial seizures. The control group included 56 male and 44 female patients (aged from 4.3 ± 1.9), among them, 67 patients had generalized seizures and 33 patients had partial seizures. The difference in gender, age and condition of patients between the two groups was not statistically significant ($p>0.05$); thus, it is comparable.

Treatment Methods

To give a medicine based on the weight of children. The observation group was given TPM treatment, and its initial oral intake was 0.5 to 1 mg/(kg·d) and 2 times/day, then added 0.5 to 1

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mg/(kg·d) every week until intake turned to 4 to 8 mg/ (kg·d) after 4 to 8 weeks and maintained it. The control group was given phenobarbital (PB) treatment, and its initial oral intake was 2 to 3 mg/(kg·d) and 1-2 times/day, then added up to 3 to 5 mg/(kg·d) by the second week. There was more than 3 months follow-up to patients in two groups after reaching maintained medicine intake.

Observation Index

Observation index is the observation and comparison of seizure frequency, treatment efficiency, and adverse reactions of patients in two groups before and after three months treatment.

Treatment Efficiency Evaluation

According to patients condition after treatment, it could be cure-EEG showed that epileptiform discharges disappeared, be markedly-EEG showed that epileptiform discharge was significantly reduced, be effective-EEG showed that epileptiform discharge reduced, and be invalid-EEG showed that epileptiform discharge had no change or increased[6]. Among them, the rate of markedly effective was equal to the sum rate of cure and markedly, while total efficiency was equal to the sum rate of cure, markedly and effective.

Statistical Analysis

With statistical software SPSS 13.0 (IBM, New York, US), analysis of data comparison was worked out by χ^2test while measurement data with *t*-test, and if $p< 0.05$, the difference was statistically significant.

Results

The Comparison of the Seizure Numbers of the Two Groups

The reduced number of partial seizures was (6.3±1.3) times, generalized seizures was (7.1±2.5) times, and total seizures were (6.7±2.2) times in observation group which were significantly higher than those (reduced number of partial seizures was (4.1±1.5) times, generalized seizures were (6.1±1.8) times, and total seizures were (5.9±1.7)) in control group. Thus, differences were statistically significant ($p<0.05$), which meant that treatment efficiency in observation group is better than that in the control group. See below Table I.

The Comparison of the Treatment Efficiency with the Different Treatment Methods

The rate of cure, markedly effective, and total efficiency in observation group were 42% (42/100), 80.00% (80/100), and 88.00% (88/100), which were significantly higher than those [28.00% (28/100), 55.00% (55/100), 77.00% (77/100)] in control group. Thus, the difference was statistically significant ($p<0.05$), which meant that the treatment efficiency in the observation group is better than that in the control group. See below Table II.

Adverse Reactions

There were no seizure numbers increased, illness deteriorated, routine blood, liver and kidney became abnormal, and electrocardiography (ECG) and electroencephalogram (EEG) changed in any children patients during the treatment period. All 200 patients in this research were treated for three months. Among those in the observation group, there were somnolence in 15 patients, anorexia in 2 patients, fatigue in 2 patients, cool response in 1 patient, and weight loss in 2 patients, and all of those adverse reactions were alleviated through adding dose slowly and taking medicine after meals during additional medicine dose period. Meanwhile, there were mild aminotransferase rise in 4 patients, somnolence in 34 patients, headache in 3 patients, nervous hyperactivity in 2 patients. Differences be-

Table I. The comparison of seizure frequency with different treatment methods.

Group	Reduce number of partial seizures (n = 33)	Reduce number of generalized seizures (n = 67)	Reduce number of total seizures (n = 100)
Observation group	6.3 ± 1.3*	7.1 ± 2.5*	6.7 ± 2.2*
Control group	4.1 ± 1.5	6.1 ± 1.8	5.9 ± 1.7
t	6.367	2.657	2.877
p	0.000	0.009	0.004

Note: Compared with the control group, *$p<0.05$.

Table II. Comparison of the clinical efficiency between two groups with different treatment methods.

Group	n	Cure	Markedly	Effective	Invalid	Markedly effective rate	Total efficiency
Observation group group	100	42 (42.00)*	38 (38.00)	8 (8.00)*	12 (12.00)*	80 (80.00)*	88 (88.00)*
Control group	100	28 (28.00)	27 (27.00)	22 (22.00)	23 (23.00)	55 (55.00)	77 (77.00)
x2		4.308	2.758	7.686	4.190	14.245	4.190
p		0.038	0.097	0.006	0.041	0.000	0.041

Note: Compared with the control group, *$p<0.05$.

tween the two groups were statistically significant ($p<0.05$), which meant that the adverse reactions in the observation group was significantly less than those in the control group.

Discussion

In 1980, TPM was synthesized initially. In 1986, it was used for epilepsy treatment for the first time. In 1995, it joined in the market in the UK firstly. In 1999, it joined in China market. Compared with the traditional antiepileptic drug (AED), TPM has many advantages such as multiple action mechanisms that play a stronger and broad-spectrum role in epilepsy treatment[7,8]. There were three unique action mechanisms of TPM: 1) TPM blocked Na^+ channels to inhibit repeated and sustained discharge. 2) GABA-A receptor increased the activity of GABA so as to enhance neural inhibition of GABA mediacy. 3) TPM intercepted AMPA subtype of glutamate receptors to block nerve excitability of mediacy[9].

The results of this study showed that the reduced number of partial seizures, generalized seizures and total seizures in the observation group were significantly higher than those in control group, which accorded with the report of Siniscalchi et al[10] and others. The reason of this may be that the structure of TPM is different from other types of AED, and TPM is monosaccharide derivatives with sulfanilamide group and has multiple anti-epilepsy mechanisms. TPM can block Na+ channels to inhibit repeated and sustained discharge, enhance neural inhibition of GABA mediacy by increasing the activity of GABA, and block nerve excitability of AMPA subtype of glutamate mediacy[11]. TPM is an efficient, broad-spectrum and safe AED, it is not only suitable for the partial seizures but the generalized seizures, and it also can be absorbed completely and quickly through oral intake.

Tran et al[12] reported that antiepileptic characteristic of TPM was different from propyl benzene two nitrogen, and it may take effect through regulating less sensitive GABA subtype receptor of propyl benzene two nitrogen. TPM could block the start of subtype Kainate/AMPA with kainic acid while had no effect on subtype NMDA receptor. Moreover, TPM could also inhibit the effect of part of carbonic anhydrase isozyme[13,14]. Meanwhile, PB belonged to the barbiturate AED and it could enhance inhibitory GABA effect on epileptiform discharge and diffusion which had advantages such as fast and good effect, thus it had priority of using as epilepsy treatment medicine for a long time. However, Marion et al[15] thought that PB could affect children IQ and cognitive function of children and had sedation; thus, they suggested that PB should be used less as far as possible.

The results of this study showed that the treatment efficiency in the observation group was significantly higher than that in the control group, which accorded with the report of Dewis et al[16] and others[17-20]. Adverse reactions of TPM mainly related to central nervous system (CNS) and it were mostly in the light of moderate tolerance range[21-25]. Most adverse reactions of TPM in this study were somnolence, anorexia, fatigue, and weight loss, and most somnolence and anorexia disappeared after taking medicine in 10 to 15 days, which suggested that adverse reactions happened easily during additional medicine dose period and most of them were tolerant and transient[26-29]. The reason of weight loss was still not clear and it may be related to anorexia. Besides, the result showed that TPM did not lead to

common adverse reactions such as blood and pancreatic injury and allergic reactions as other AED. Moreover, it led to better tolerance of children patients.

Conclusions

Compared with PB, TPM shows the better effect on epilepsy treatment with less adverse reactions which is worthy of clinical recommendation.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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