Biomedical Research 2017; 28 (19): 8501-8504 *ISSN 0970-938X*
www.biomedres.info

Influence of carbamazepine-phenobarbital combined treatment on IL-1β, IL-6, Bcl-2 and Bax expression in children with epilepsy.

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Abstract

Objective: To observe and analyze the influence of carbamazepine-phenobarbital combined treatment on IL-1β, IL-6, Bcl-2, and Bax expression levels in children with epilepsy.

Method: A total of 94 children with epilepsy in our hospital from January 2015 to September 2016 were selected and equally divided into an observation group (n=47) and a control group (n=47) through random number table. Children in the control group were given only carbamazepine tablets, whereas those in the observation group were additionally administered with phenobarbital, and the therapeutic effects in the two groups were compared.

Results: The total treatment effective rate of patients in the observation group was significantly higher than that in the control group (P<0.05); moreover, the frequency of epileptic seizures, epilepsy integrals, and HAD scores of patients in the observation group after treatment were significantly lower than those in the control group (P<0.05), but the MoCA score was significantly higher than that in the control group (P<0.05). Positive expression quantities of IL-1β and Bax proteins in children in the observation group after treatment were significantly lower than those in the control group (P<0.05), whereas positive expression quantities of IL-6 and Bcl-2 were significantly higher than those in the control group (P<0.05).

Conclusion: Carbamazepine-phenobarbital combined treatment can reduce IL-1β and Bax expression levels but increase IL-6 and Bcl-2 expression levels in children with epilepsy; moreover, it can protect neurons, relieve neuronal damage, improve anxiety and depression degrees and cognitive function, and reduce the frequency of epileptic seizures. Moreover, the combined treatment offers significant clinical effects, as well as promotion and application values.

Keywords: Epilepsy, Carbamazepine, Phenobarbital, IL-1β, IL-6, Bcl-2, Bax.

Accepted September 27, 2017

Introduction

As a nervous system disease, epilepsy is a syndrome of transient brain dysfunction characterized by chronic and recurrent seizures caused by the paradoxical discharge of cerebral neurons [1]. Epilepsy has a high prevalence rate and severely influences neurobiology, cognitive function, and psychological function in pediatric patients and may give rise to cardiac failure and sudden cardiac arrest [2], seriously endangering their life. Interleukin-1β (IL-1β) participates in the pathogenesis of epilepsy, whereas interleukin-6 (IL-6) influences the occurrence of epilepsy; furthermore, Bax is a neuronal apoptosis factor and Bcl-2 inhibits neuronal apoptosis; both play significant roles in epilepsy [3]. In this study, the influences of carbamazepine-phenobarbital combined treatment on IL-1β, IL-6, Bcl-2, and Bax expressions in children with epilepsy were observed and analyzed to provide reference for clinical treatment.

General Data and Methodology

General data

A total of 94 children with epilepsy in our hospital from January 2015 to September 2016 were selected. All children passed the examination and met the diagnostic criteria in Clinical Practice Guideline: Fascicule for Epilepsy; however, children with cognitive disorders, mental diseases, serious liver and kidney dysfunction, drug allergies, and malignant tumors were excluded. This study obtained permission from the Medical Ethics Committee in our hospital, and children with epilepsy and their family members signed informed consent forms. The random number table method was used to equally divide children with epilepsy into the observation group (n=47) and the control group (n=47).

The observation group comprised 24 males and 23 females with ages 2 to 12 years old (mean: 6.82 ± 1.45 years old), and

the course of the disease lasted 6 months to 6 years (mean: 2.12 ± 1.56 years). The control group comprised 25 males and 22 females with ages 2 to 11 years old (mean: 6.69 ± 1.77 years old), and the course of the disease lasted 4 months to5 years (mean: 2.23 ± 1.37 years). Comparative differences between the two groups in general data, such as gender, age, and course of disease, were assessed for statistical significance, and the two groups were comparable (P>0.05).

Therapeutic method

Children with epilepsy were orally administered with carbamazepine tablets for treatment (Shijiazhuang Kanghewei Pharmaceutical Co., Ltd; No. H13020748; specification: 0.1 g × 100 tablets/bottle/box). The initial drug dosage was 2 tablets twice per day and was adjusted to 3 tablets twice per day 1 week after the treatment. The treatment was continuous and lasted for 8 weeks. Phenobarbital treatment was orally administered to children in the observation group (Zhangjiakou Yunfeng Pharmaceutical Factory; No. H13020689; specification: 30 mg/tablets), with the dosage of 1 tablet thrice a day. The treatment was continuous and lasted for 8 weeks.

Observational indexes

Clinical effects, anxiety and depression degree, cognitive function, frequency of epileptic seizure, epilepsy integrals, and the expression levels of IL-1β, IL-6, Bax, and Bcl-2 of pediatric patients in the two groups were observed. In reference to Standards for Epilepsy Diagnosis and Evaluation of Therapeutic Effects, the clinical effects were divided into basically controlled, excellent, effective, and ineffective, using the formula: total treatment effective rate=(basically controlled + excellent + effective)/total number of cases × 100%. The epilepsy integral evaluation contents included disturbance of consciousness from epilepsy and duration, whereby a higher score corresponds to a more serious form of epilepsy. HAD evaluation is used to assess the degree of anxiety and depression, whereby a higher score corresponds to a more serious illness. MoCA scale is used to evaluate cognitive function, whereby a higher score corresponds to better cognitive function.

Statistical analysis

SPSS 22.0 was used for statistical analysis, "$\bar{x} \pm S$" was used to express measurement data and t test was used between groups. "%" expressed enumeration data and χ^2 test was used between groups, whereby P<0.05 indicates statistical significance in the comparative differences of data.

Results

Comparison of clinical effects of pediatric patients in the two groups

Total treatment effective rate of pediatric patients in the observation group was significantly higher than that in the control group (P<0.05), as shown in Table 1.

Table 1. *Comparison of clinical effects between the two groups.*

Group	Basically controlled	Excellent	Effective	Ineffective	Total effective rate
Observation group (n=47)	20 (42.55%)	13 (27.66%)	9 (19.15%)	5 (10.64%)	44 (89.36%)
Control group (n=47)	17 (36.17%)	9 (19.15%)	10 (21.28%)	11 (23.40%)	36 (76.60%)
χ^2					5.764
P					0.016

Comparison of epilepsy integrals, seizure frequency, HAD scores, and MoCA scores between the two groups before and after treatment

The frequency of epileptic seizure, epilepsy integrals, and HAD scores of patients in the observation group after treatment were significantly lower than those in the control group (P<0.05), whereas MoCA scores of patients in the observation group were significantly higher than those in the control group (P<0.05), as shown in Table 2.

Table 2. *Comparison of epilepsy integrals, seizure frequency, HAD Scores, and MoCA scores between the two groups before and after treatment.*

Group	Time	Epilepsy integrals	Seizure frequency/ month	HAD score	MoCA score
Observation group (n=47)	Before treatment	9.77 ± 1.58	5.31 ± 0.48	16.38 ± 3.42	17.38 ± 3.46
	After treatment	4.25 ± 0.72*#	2.27 ± 0.22*#	2.32 ± 0.95*#	26.54 ± 2.21*#
Control group (n=47)	Before treatment	9.82 ± 1.54	5.27 ± 0.46	16.56 ± 3.48	17.45 ± 3.54
	After treatment	6.34 ± 0.83*	3.51 ± 0.25*	5.34 ± 1.04*	21.27 ± 2.15*

Note: *Comparison with before treatment, P<0.05; # comparison with the control group, P<0.05.

Comparison of IL-1β, IL-6, Bcl-2, and Bax between the two groups before and after the treatment

Positive expression quantities of IL-1β and Bax proteins in patients in the observation group were significantly lower than

those in the control group (P<0.05), whereas positive expression quantities of IL-6 and Bcl-2 proteins were significantly higher in the observation group than those in the control group (P<0.05), as shown in Table 3.

Table 3. *Comparison of IL-1β, IL-6, Bcl-2, and Bax expression levels between the two groups before and after Treatment.*

Group	Time	IL-1β	IL-6	Bcl-2	Bax
Observation group (n=47)	Before treatment	227.82 ± 36.45	136.24 ± 15.31	24.77 ± 2.72	38.61 ± 3.55
	After treatment	140.72 ± 16.18*#	217.54 ± 15.71*#	35.78 ± 3.64*#	21.52 ± 1.29*#
Control group (n=47)	Before treatment	225.65 ± 35.66	138.72 ± 16.82	24.85 ± 2.76	38.36 ± 3.14
	After treatment	169.67 ± 17.86*	176.651 ± 14.45*	29.97 ± 3.14*	26.49 ± 1.62*

Note: *means comparison with that before treatment, P<0.05; #means comparison with the control group, P<0.05.

Discussion

Epilepsy is difficult to prevent because of its complicated etiology and pathogenesis. Currently, about 70% children with epilepsy have an unknown etiology; thus, prevention could not be realized [4]. A considerable number of epileptic symptoms are difficult to prevent amidst clear causes, such as brain tumor and arteriovenous malformation. Moreover, epilepsy is the product of the comprehensive effects of multiple factors, including seizure frequency, nervous system disease, and other inducing factors, which aggravate the difficulty of prevention [5,6]. Long-term oral administration of sedative drugs results in malnutrition of children with epilepsy, and those under more serious conditions could suffer from disorders in electrolyte metabolism. The pathogenesis of epilepsy is currently still unclear; however, it is closely related to immune regulation [7]. As the key link in the immune regulation system, immune cell cytokines regulate neurogliocytes and neuronal functions in the human body and play a significant role during the pathogenesis of epilepsy.

As a proinflammatory cytokine, IL-1β induces immunocompetent cells to generate an inflammatory medium that participates in epileptic attacks; moreover, its overexpression is related to cerebral hippocampal damage and sclerosis [8]. IL-6, a new regulatory factor, facilitates the proliferation and differentiation of B cells, promotes astrocytes to generate nerve growth factors, inhibits the release of glutamic acids, and protects nerve cells. Cell apoptosis is the main feature of neuronal loss after epilepsy and causes epileptic seizures. Bax is a neuronal apoptosis factor that induces cell apoptosis, whereas Bcl-2 is factor that inhibits neuronal apoptosis; both are related to epileptic attacks [9]. Currently, clinical treatment still centers on the use of antiepileptic drugs. As an important drug for treating epilepsy, phenobarbital reduces the excitation of glutamic acids, strengthens the inhibitory effect of γ-aminobutyric acid (GABA), inhibits monosynaptic and polysynaptic transmissions of the central nervous system, and inhibits high-frequency discharge of the focus, thereby preventing it from ambient diffusion in order to reach the anti-epilepsy goal [10]. On the other hand, carbamazepine is one of the commonly used psychotomimetic drugs and reduces the release of glutamic acids, inhibits excessively excited nerve cells, and reduces synaptic signals to control epilepsy. In this study, the total treatment effective rate in the observation group was significantly higher than that in the control group (P<0.05). The frequency of epileptic seizure, epilepsy integrals, and HAD scores in the observation group were significantly lower than those in the control group (P<0.05), whereas MoCA scores were significantly higher in the observation group than in the control group (P<0.05). The positive expression quantities of IL-1β and Bax proteins in the observation group after treatment were significantly lower than those in the control group (P<0.05), whereas positive expression quantities of IL-6 and Bcl-2 were significantly higher than those in the control group (P<0.05). This study showed that carbamazepine-phenobarbital combined treatment can significantly reduce IL-1β and Bax expression levels but increase IL-6 and Bcl-2 expression levels, inhibit nerve cell apoptosis, and inhibit the release of glutamic acids; moreover, the combination protects nerve cells and nerves.

Conclusion

In conclusion, carbamazepine-phenobarbital combined treatment can protect the nerve cells of children with epilepsy, relieve the damage of nerve cells, reduce their anxiety and depression, improve their cognitive function, and reduce epileptic seizure frequency. These significant clinical effects offer promotion and application value.

References

1. Isler C, Kucukyuruk B, Ozkara C, Gunduz A, Is M, Tanriverdi T, Comunoglu N, Oz B, Uzan M. Comparison of clinical features and surgical outcome in focal cortical dysplasia type 1 and type 2. Epilepsy Res 2017; 136: 130-136.
2. Ghorab MM, Alsaid MS, Alqasoumi SI, Abdel-Kader MS. Semisynthesis of some novel urea, thiourea, carbamimidothioic acid and dihydrooxazole derivatives as a new class of anticancer agents. Lat Am J Pharm 2017; 36: 380-385.
3. Zaheri F, Ranaie F, Shahoei R, Hasheminasab L, Roshani D. Risk factors associated with neural tube defects in infants referred to western Iranian obstetrical centers; 2013-2014. Electron Physician 2017; 9: 4636-4642.
4. Suji RJ, Rajagopalan SP. Multi-ranked feature selection algorithm for effective breast cancer detection. Biomed Res-India 2016; 27: S99-S102.
5. Sajobi TT, Speechley KN, Liang Z, Goodwin SW, Ferro MA, Wiebe S. Response shift in parents' assessment of health-related quality of life of children with new-onsetepilepsy. Epilepsy Behav 2017; 75: 97-101.

6. Zheng M, Zhou N, Ma L, Jin W. Inhibitory effects of the active constituents of ginseng stems and leaves on lung cancer NCI-H1650 cells. Biomed Res-India 2015; 26: 646-650.
7. Sajobi TT, Wang M, Ferro MA, Brobbey A, Goodwin S, Speechley KN, Wiebe S. Multivariate trajectories across multiple domains of health-related quality of life in children with new-onset epilepsy. Epilepsy Behav 2017; 75: 72-78.
8. Belcastro V, Giordano L, Pruna D, Peruzzi C, Casellato S, Barca S, Carlone G, Striano P, Verrotti A. Follow-up study of idiopathic generalized epilepsy with associated absence seizure and myoclonic epilepsy of infancy. Epilepsy Res 2017; 136: 123-125.
9. Chavan MJ, Wakte PS, Shinde DB. Analgesic and Anti-inflammatory Activities of Saponified Fraction from Annona reticulata L. Bark. Lat Am J Pharm 2010; 29: 1246-1249.
10. Ibekwe R, Jeaven L, Wilmshurst JM. The role of melatonin to attain electroencephalograms in children in a sub-Saharan African setting. Seizure 2017; 51: 87-94.

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