CORRELATION BETWEEN SERUM NEURON SPECIFIC ENOLASE LEVEL AND NEURON INJURY INDEX AND NEURON APOPTOSIS INDEX IN PATIENTS WITH BRAIN INJURY

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ABSTRACT

Objective*: To analyze the correlation between the level of NSE and the indexes of neuron injury and apoptosis.*

Methods*: From May 2017 to June 2019, 66 patients with craniocerebral injury in the neurosurgery of our hospital were selected as the observation group and 66 healthy people as the control group. NSE level, neuron injury index [S100B, fatty acid binding protein (FABP), and insulin-like growth factor-1 (IGF-1)], and neuron apoptosis index [B lymphoma-2 (Bcl-2) and soluble wilt] were compared, as were the correlation of apoptosis-related factor ligand (sFasL) and soluble apoptosis-related factor (sFas).*

Results*: The NSE level of the observation group was significantly higher than that of the control group, and the difference was statistically significant ($P < 0.01$). The IGF-1 level of the observation group was significantly lower than that of the control group, and the FABP and S100B levels were significantly higher ($P < 0.01$). The sFasL and sFas levels of the observation group were significantly higher than those of the control group, and the Bcl-2 level was significantly lower ($P < 0.01$). NSE was positively correlated with S100B, FABP, sFasL, and sFas, and negatively correlated with IGF-1 and Bcl-2 ($P < 0.05$).*

Conclusion*: Serum NSE level in patients with craniocerebral injury can reflect the degree of neuron injury and apoptosis, which can predict the severity of the injury and has certain clinical value for patients.*

Keywords: *Brain Injury, Neuron Specific Enolase, Neuron Injury Index, Neuron Apoptosis.*

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Introduction

Brain injury is a type of traumatic disease characterized by high morbidity and mortality[1]. With the progress of social technology and the prolongation of human life, traumatic brain injury has become the second most common cause of systemic trauma and the leading factor in the death or disability of children and youth[2]. Although patients are no longer in danger of losing their lives, these conditions usually leave a variety of sequelae, which reduce the social adaptability and self-care ability of patients and seriously affect their quality of life. Some scholars have found that by judging the severity of the injury, treatment plans can be refined, improving the treatment effect and changing the prognosis[3].

At present, MRI is the most effective diagnostic tool for detecting the severity of craniocerebral injury; however, it has the disadvantages of slow imaging, long examination time, and moving patients, which may aggravate craniocerebral injury[4]. Generally, there is no clear quantitative index in the laboratory for the detection of nerve injury, with most detection relying on Glasgow Coma Score, CT scan, and MRI. As the understanding of brain injury advances, current research is primarily focused on

various cytokines of nerve injury, especially those neuron injuries that do not conform to the actual injury or even lack evidence (5). Therefore, additional information is required to study the correlation between serum NSE level, neuron injury index, and neuron apoptosis index.

Materials and methods

General information

From May 2017 to June 2019, 66 patients with craniocerebral injury were selected as the observation group. Inclusion criteria were as follows: definite trauma, with the time from trauma to admission being no more than 12 hours; no medical history for the heart, liver, kidney, brain, endocrine system, etc.; and intracranial CT and MRI definitively indicated brain injury[6]. Exclusion criteria were as follows: patients with history of cerebral infarction and cerebral hemorrhage; patients who died within 24 hours after admission; and patients with coagulation dysfunction. In the observation group, there were 34 males and 32 females, with an average age of (49.6 ± 14.6) years. At the same time, 66 healthy people were selected as the control group in our hospital. In the control group, 35 were male and 31 were female. The average age was (49.7 ± 15.2) years. There was no significant difference in gender and age between the two groups ($P > 0.05$).

Methods

In both observation groups, 5ml of peripheral venous blood was extracted; After being left at room temperature overnight, the blood was centrifuged at 2000r / min for 15min, and the supernatant was drawn and stored in a refrigerator at -70oC for standby.

Observation index

Neuron injury index was determined by enzyme-linked immunosorbent assay (ELISA). Neuron specific enolase (NSE), fatty acid binding protein (FABP), serum S100B, and insulin-like growth factor-1 (IGF-1) were detected. The specific steps were provided by the kangnaig company in Sweden according to the ELISA kit instruction manual. For the neuron apoptosis index, the serum soluble apoptotic related factors (sFas), soluble apoptosis-related factor ligand (sFasL), and B lymphacytoma-2 gene (Bcl-2) were detected by radioimmunoassay, and the detailed steps were carried out according to the manual.

Statistical method

SPSS 19.0 data analysis was used. A between-groups t test was used for comparison between groups, and the measurement data were expressed by ($\bar{x} \pm s$). A χ^2 test was used between groups, and the count data was expressed as (%). The Pearson correlation coefficient was used for correlation analysis, and statistically significance difference was indicated by $P < 0.05$.

Results

Comparison of NSE levels between two groups

The NSE level of the observation group was significantly higher than that of the control group ($P < 0.01$). See Table 1.

Group	Cases	NSE (μg/L)
Control group	66	14.47 ± 1.54
Observation group	66	30.87 ± 5.22
t		24.481
P		<0.01

Table 1: Comparison of NSE levels between two groups.

Comparison of injury indexes of neurons between two groups

Compared with the control group, the level of IGF-1 in the observation group was significantly lower, and the levels of FABP and S100B were significantly higher. The differences were statistically significant ($P < 0.01$). See Table 2.

Group	Cases	S100B (μg/L)	FABP (μg/mL)	IGF-1 (nmol/L)
Control group	66	0.99 ± 0.21	1.85 ± 0.33	73.52 ±8.37
Observation group	66	1.79 ± 0.31	5.23 ± 0.76	41.33 ± 4.35
t		17.358	33.141	27.723
P		<0.01	<0.01	<0.01

Table 2: Comparison of neuron injury indexes between the two groups.

Comparison of apoptosis indexes between two groups

Compared with the control group, the levels of sFasL and sFas in the observation group were significantly higher, and the level of Bcl-2 was significantly lower. The differences were statistically significant ($P < 0.01$). See Table 3.

Group	Cases	sFasL (pg/mL)	sFas (ng/mL)	Bcl-2 (U/mL)
Control group	66	1254.88 ± 155.59	2.19 ± 0.48	7.33 ± 1.04
Observation group	66	3751.66 ± 484.48	5.78 ± 0.59	3.65 ± 0.47
t		39.862	38.346	26.196
P		<0.01	<0.01	<0.01

Table 3: Comparison of neuron apoptosis indexes between the two groups.

Correlation analysis of NSE with neuron injury and apoptosis

NSE was positively correlated with S100B, FABP, sFasL, and sFas, and negatively correlated with IGF-1 and Bcl-2 ($P < 0.05$). See Table 4.

Index	NSE	
	r	*P*
S100B	0..465	<0.05
FABP	0.376	<0.05
IGF-1	-0.548	<0.05
sFasL	0.339	<0.05
sFas	0.348	<0.05
Bcl-2	-0.451	<0.05

Table 4: Correlation analysis of NSE with neuron injury and apoptosis.

Discussion

According to statistical data from different countries and periods, craniocerebral injury has the second highest incidence, following limb fracture; however, craniocerebral injury shows the highest death and disability rates[7]. With the increase of construction, traffic accidents, violent crimes, bungee jumping, alpine skiing, skydiving, and other dangerous and intense sports, the incidence of brain injury is increasing. The lack of sensitive and rapid diagnosis technology is one of the difficulties in the treatment of craniocerebral injury[8]. Especially in the process of emergency treatment before admission, some patients are not able to carry out imaging examination to confirm the condition in time, which delays the condition judgement and choice of treatment plan. When treatment level of craniocerebral injury was improved, mortality was reduced[9]).

However, many patients with craniocerebral injury, especially those with moderate or severe craniocerebral injury, are left with different degrees of physical dysfunction, consciousness disorder, and even vegetative state; this not only brings great pain to the patients' bodies and minds, but also causes a great burden on their families. Rehabilitation treatment helps patients with dysfunction to recover their psychological state, physical state, and social functioning[10].

It has been found that a common symptom after craniocerebral injury is the compression of intracranial hematoma, which leads to the injury of neurons; specifically, it damages the blood–brain barrier[11]. Under normal human conditions, NSE and S100B are expressed specifically in neurons. Once the blood–brain barrier and neurons are damaged, their content in serum increases significantly, because they can enter the systemic circulation directly through cerebral vessels[12]. Some studies have shown that the upregulation of FABP level can be used as a diagnostic index of brain injury. In addition, when neurons are damaged, free fatty acids will appear, causing a disordered state. FABP is a kind of intracellular protein that can maintain and regulate the homeostasis of free fatty acids. In addition, IGF-1, which can promote the proliferation and repair of neuronal injury, has been widely studied[13].

Our results demonstrate that the level of IGF-1 in the observation group was significantly lower than that in the control group, while the levels of FABP and S100B were significantly higher than those in the control group. The difference between the two groups was statistically significant ($P < 0.05$). In addition, serum NSE was negatively correlated with IGF-1 and positively correlated with S100B and FABP ($P < 0.05$). It is suggested that NSE is involved in the process of brain injury, and can reflect the degree of brain injury to a certain extent.

The abnormal expression of apoptosis gene is directly related to neuron apoptosis and injury, and its expression can directly estimate the clinical outcome and severity of brain injury[14]. Bcl-2 is one of the indexes of neuron apoptosis; it can protect nerve cells and has obvious anti-apoptosis activity. The sFas system is an important part of the signal pathway of apoptosis regulation, and sFasL and sFas have a regulatory effect on neuron apoptosis[15].

In this study, we compared the levels of sFasL, Bcl-2, and sFas in the observation group and the control group. The results demonstrated that the levels of sFasL and sFas in the observation group were significantly higher than those in the control group, and the levels of Bcl-2 were significantly lower ($P < 0.01$). In addition, NSE was positively correlated with sFas and sFasL, and negatively correlated with Bcl-2 ($P < 0.05$). It is suggested that NSE is related to the degree of neuron apoptosis in patients with craniocerebral injury.

In conclusion, the serum NSE level of patients with craniocerebral injury can reflect the degree of neuron injury and apoptosis, which can predict the degree of severity and has certain clinical value for patients.

References

1) Wang J, Yang YD, She QF, Chen GF. Effects of mild hypothermia on cerebral oxygen metabolism and brain injury in patients with severe craniocerebral injury. J Hainan Med Univ 2018; 1: 32.
2) Luan RL, Zhu MX, Sun HY. Effect of comprehensive nursing intervention in preventing postoperative pain, complications, and psychological pressure in the otolaryngology department. Medicine (Baltimore) 2019; 98: 15923.
3) Zhang C, Wang YL, Du ZH, Zhang S, Zhang WX. Outcomes of Early Different Types of Nutritional Support Applicated in Patients of ICU with Craniocerebral Injury. Med J Wuhan Univ 2017; 38: 283-288.
4) Han C, Yang Y, Ruan S, Guo L, Zhang X, et al. The predictive value of serum p-CREB level on secondary cognitive impairment in patients with mild-to-moderate craniocerebral trauma. Neurosurg Rev 2019; 42: 715-720.
5) Feng D, Wang B, Wang L, Abraham N, Tao K, et al. Pre-ischemia melatonin treatment alleviated acute neuronal injury after ischemic stroke by inhibiting ER stress-dependent autophagy via PERK and IRE1 signalings. J Pineal Res 2017; 62: 12395.
6) Talukdar AM, Bilen-Rosas G, Wilhelm M, Al-Subu A. The novel early use of dexmedetomidine in the management of tetanus. J Clin Anesth 2018; 50: 18-19.
7) Shai AN, Fedulova MV, Kvacheva YE, Shigeev SV, Kovalev AV. [The importance of marker proteins of the nervous tissue for morphological diagnostics of the craniocerebral injury]. Sud Med Ekspert 2017; 60: 40.
8) Miyata K, Ohnishi H, Maekawa K, Mikami T, Akiyama Y, et al. Therapeutic temperature modulation in severe or moderate traumatic brain injury: a propensity score analysis of data from the Nationwide Japan Neurotrauma Data Bank. J Neurosurg 2016; 124: 527-537.
9) Shai AN, Fedulova MV, Zavalishina LE, Kvacheva YE, Shigeev SV, et al. [The detection of the biomolecular markers of the axonal damage resulting from the craniocerebral injury by the immunohistological methods]. Sud Med Ekspert 2018; 61: 8-10.
10) Santos JGRPD, Zaninotto ALC, Zângaro RA, Carneiro AMC, Neville IS, et al. Effects of transcranial LED therapy on the cognitive rehabilitation for diffuse axonal injury due to severe acute traumatic brain injury: study protocol for a randomized controlled trial. Trials 2018; 19: 249.
11) Krohn M, Dreßler J, Bauer M, Schober K, Franke H, et al. Immunohistochemical investigation of S100 and NSE in cases of traumatic brain injury and its application for survival time determination. J Neurotrauma 2015; 32: 430-440.
12) Kok WF, Koerts J, Tucha O, Scheeren TW, Absalom AR. Neuronal damage biomarkers in the identification of patients at risk of long-term postoperative cognitive dysfunction after cardiac surgery. Anaesthesia 2017; 72: 359.
13) Wang YB, Wang LL, Zhong SL. Forensic Analysis of 25 Cases of Diffuse Brain Atrophy after Trauma. Fa Yi Xue Za Zhi 2019; 35: 48-51.
14) Bell M, Sopko NA, Matsui H, Hannan JL, Bivalacqua TJ. RhoA/ROCK activation in major pelvic ganglion mediates caspase-3 dependent nitrergic neuronal apoptosis following cavernous nerve injury. Neural Regen Res 2017; 12: 572.
15) Semevolos SA, Duesterdieck-Zellmer KF, Larson M, Kinsley MA. Expression of pro-apoptotic markers is increased along the osteochondral junction in naturally occurring osteochondrosis. Bone Rep 2018; 9: 19-26.

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