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Correlation of serum GFAP, S100B and NSE contents with post−traumatic oxidative stress response and insulin resistance in patients with traumatic brain injury

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ABSTRACT

Objective: To study the correlation of serum GFAP, S100B and NSE contents with post-traumatic oxidative stress response and insulin resistance in patients with traumatic brain injury. **Methods:** A total of 110 patients with traumatic brain injury who were treated in our hospital between January 2015 and December 2016 were collected as the observation group, and 60 healthy subjects who received physical examination in our hospital during the same period were collected as normal control group. Serum GFAP, S100B and NSE levels as well as oxidative stress index and insulin resistance index levels of two groups of subjects were detected, and Pearson test was used to further evaluate the correlation of serum GFAP, S100B and NSE contents with oxidative stress response and insulin resistance in patients with traumatic brain injury. **Results:** Serum GFAP, S100B and NSE contents of observation group were significantly higher than those of normal control group; serum oxidative stress indexes MDA, MPO and LPO contents were higher than those of normal control group while SOD and TAC contents were lower than those of normal control group; serum insulin resistance indexes GLU, INS and HOMA-IR levels were higher than those of control group. Pearson test showed that serum GFAP, S100B and NSE contents in patients with traumatic brain injury were directly correlated with post-traumatic oxidative stress and insulin resistance. **Conclusion:** The serum GFAP, S100B and NSE contents increase in patients with traumatic brain injury, and the increase is directly correlated with the oxidative stress and insulin resistance.

1. Introduction

Traumatic brain injury is a clinical typical emergency, patients are mostly with nerve injury and changes in contents of multiple neuron-specific indexes, including glial fibrillary acidic protein (GFAP), S100B protein (S100B), neuron-specific enolase (NSE) and so on, and their contents can objectively reflect the degree of brain injury[1,2]. Recent studies have shown that there are significant local and systemic oxidative stress and insulin resistance in acute stage of traumatic brain injury, they may be the important reasons for the secondary brain injury, and early judging its severity can provide the basis for selection of subsequent treatment options[3,4]. There is not much research at present about the internal relations of brain injury with oxidative stress and insulin resistance, the study focused on the differences in brain injury index contents between patients with brain injury and normal people, and the inner link of brain injury index contents with insulin resistance and oxidative stress was further analyzed, now reported as follows.

2. Information and methods

2.1 Case information

A total of 110 patients with traumatic brain injury who were treated in our hospital between January 2015 and December 2016 were collected as the observation group, and 60 healthy subjects who received physical examination in our hospital during the same period were collected as normal control group, and family

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members of observation group/normal control group themselves signed informed consent. Observation group included 59 male cases and 51 female cases that were 23-68 years old; normal control group included 32 male cases and 28 female cases that were 25-69 years. The gender and age distribution of the two groups were not significantly different, and the research was approved by the hospital ethics committee.

2.2 Serum GFAP, S100B and NSE

Immediately after admission, 3.0 mL of cubital venous blood was extracted from the two groups, anti-coagulated and then centrifuged at low speed to get supernatant liquid, and enzyme-linked immunosorbent assay (ELISA) was used to measure glial fibrillary acidic protein (GFAP), S100B protein (S100B) and neuron-specific enolase (NSE) levels.

2.3 Oxidative stress

Immediately after admission, serum was obtained from the two groups in the same way, and ELISA was used to detect the contents of oxidative stress indicators, including malondialdehyde (MDA), myeloperoxidase (MPO), lipid peroxide (LPO), superoxide dismutase (SOD) and total antioxidant capacity (TAC).

2.4 Insulin resistance indexes

Immediately after admission, serum was obtained from the two groups in the same way, and radioimmunoassay was used to detect glucose (GLU) and insulin (INS) levels, and assess the insulin resistance index (HOMA-IR).

2.5 Statistical processing

Statistical software was SPSS 23.0. GFAP, S100B, NSE, oxidative stress indexes, insulin resistance indexes and other measurement data were in terms of mean ± standard deviation, and the comparison between groups was by grouping t test. Correlation analysis was by Pearson test. $P<0.05$ indicated statistical significance in differences.

3. Results

3.1 Serum GFAP, S100B and NSE

Immediately after admission, comparison of serum GFAP (ng/L), S100B (μg/L) and NSE (μg/L) contents between two groups of subjects was as follows: serum GFAP, S100B and NSE contents of observation group were significantly higher than those of normal control group. Differences in serum GFAP, S100B and NSE contents were statistically significant between two groups of subjects ($P<0.05$), shown in Table 1.

3.2 Oxidative stress indexes

Immediately after admission, comparison of serum oxidative stress indexes MDA (nmol/mL), MPO (mg/L), LPO (μmol/L), SOD (U/L) and TAC (μmol/L) contents between two groups of subjects was as follows: serum MDA, MPO and LPO contents of observation group were significantly higher than those of normal control group while SOD and TAC contents were lower than those of normal control group. Differences in serum oxidative stress indexes MDA, MPO, LPO, SOD and TAC contents were statistically significant between two groups of subjects ($P<0.05$), shown in Table 2.

3.3 Insulin resistance indexes

Immediately after admission, comparison of serum insulin resistance indexes GLU (mmol/L), INS (mU/L) and HOMA-IR levels between two groups of subjects was as follows: serum GLU, INS and HOMA-IR levels of observation group were significantly higher than those of control group. Differences in serum insulin

Table 1.
Comparison of serum GFAP, S100B and NSE contents between two groups of subjects.

Groups	*n*	GFAP (ng/L)	S100B (μg/L)	NSE (μg/L)
Control group	60	0.48±0.06	0.14±0.03	0.76±0.08
Observation group	110	5.43±0.69	0.38±0.05	4.51±0.59
T		12.193	8.261	10.831
P		<0.05	<0.05	<0.05

Table 2.
Comparison of serum oxidative stress index contents between two groups of subjects.

Groups	*n*	MDA (nmol/mL)	MPO (mg/L)	LPO (μmol/L)	SOD (U/L)	TAC (μmol/L)
Control group	60	1.81±0.25	0.65±0.08	5.17±0.64	16.05±2.94	6.21±0.75
Observation group	110	4.29±0.61	1.98±0.25	8.92±0.96	9.71±0.98	2.79±0.35
T		9.092	7.143	8.498	12.476	8.497
P		<0.05	<0.05	<0.05	<0.05	<0.05

Table 3.
Comparison of serum insulin resistance index levels between two groups of subjects.

Groups	*n*	GLU (mmol/L)	INS (mU/L)	HOMA-IR
Control group	60	4.83±0.59	14.19±1.86	4.82±0.69
Observation group	110	10.27±1.65	32.47±4.51	10.37±1.76
T		12.871	15.436	10.928
P		<0.05	<0.05	<0.05

resistance indexes GFAP, S100B and NSE levels were statistically significant between two groups of subjects ($P<0.05$), shown in Table 3.

3.4 Correlation analysis

Analysis of the correlation of serum GFAP, S100B and NSE contents in patients with traumatic brain injury with oxidative stress and insulin resistance was as follows: serum GFAP, S100B and NSE contents were positively correlated with oxidative stress indexes MDA, MPO and LPO contents, and negatively correlated with SOD and TAC contents; they were positively correlated with insulin resistance indexes GFAP, S100B and NSE levels ($P<0.05$).

4. Discussion

There are different levels of neurological impairment in patients with traumatic brain injury. In addition to imaging findings, there is the change in the contents of various nerve injury markers in serum[5,6]. GFAP belongs to astrocytes intermediate filament and constitutes the skeleton of nerve cells, the current study shows that it belongs to cell damage indicator, and its content increases after brain injury and is highly consistent with trauma severity[7]. S100B is the most deeply studied nerve injury marker, and it is widely distributed in nerve tissue under physiological status and involved in the regulation of various calcium-dependent intracellular function. After nerve damage, the S100B is released by the damaged glial cells, and enters the blood circulation via the damaged blood-brain barrier[8,9]. NSE is the key enzyme of glycolytic pathway, it is specifically located within the neurons, the NSE levels in the circulating blood is extremely low under normal state, and it is massively leaked out from the neurons after nerve injury and enters into the cerebrospinal fluid and blood through the blood brain barrier[10]. In the study, the nerve damage index contents in serum were compared between patients with traumatic brain injury and healthy subjects, and it was found that compared with normal control group, the observation group were with higher serum GFAP, S100B and NSE contents, indicating from serology that there is substantial neuronal damage in patients with traumatic brain injury.

In the process of secondary brain injury caused by craniocerebral trauma, stress stimuli can cause strong excitement of sympathetic - adrenaline system, and the released various chemotactic active substances can attract and activate neutrophils, produce a large number of oxygen free radicals, and further lead to intracranial local and systemic oxidative stress reaction[11,12]. Oxidative/antioxidant imbalance is the direct cause of oxidative stress response. MDA, MPO and LPO are typical lipid oxidation products, and their overexpression can directly damage tissue viscera; SOD is an antioxidant substance that can neutralize oxygen free radicals and oxidative products and reduce stress damage. TAC can objectively reflect the antioxidant capacity[13]. In the study, serum contents of oxidative stress indexes were compared between the two groups, and it was found that compared with normal control group, the observation group were with higher serum MDA, MPO and LPO contents, and lower SOD and TAC contents, showing that there is indeed systemic oxidative stress response in patients with traumatic brain injury. Further Pearson test showed that serum GFAP, S100B and NSE contents in patients with traumatic brain injury were positively correlated with oxidation indexes MDA, MPO and LPO contents, and negatively correlated with anti-oxidation indexes SOD and TAC contents, confirming that the oxidative stress damage is one of the direct causes of secondary brain injury in patients.

Increase in blood sugar in patients with traumatic craniocerebral trauma is one of the important factors that affect the prognosis. With the deepening of the animal experiment and clinical research, it is found that there is the simultaneous increase in blood glucose and insulin levels after craniocerebral trauma, which is speculated to be associated with the body's resistance to insulin[14,15]. Insulin resistance is the decrease of systemic insulin sensitivity and reactivity, which leads to the glucose uptake and utilization disorder, and directly causes the energy supply disturbance of brain tissue. Excessive blood glucose in the cerebral ischemic lesion can aggravate local edema and lactic acidosis, and cause the area of ischemic injury to increase[16]. In the study, the levels of serum insulin resistance indexes were compared between the two groups, and it was found that compared with normal control group, the observation group were with higher serum GLU, INS and HOMA-IR levels, confirming that craniocerebral trauma can lead to insulin resistance in patients. Further Pearson test showed that serum GFAP, S100B and NSE levels in patients with traumatic brain injury were positively correlated with insulin resistance indexes GLU, INS and HOMA-IR levels, indicating that craniocerebral trauma can cause insulin resistance, and continuous insulin resistance may further

aggravate the degree of craniocerebral injury.

Above all, it can be concluded that serum GFAP, S100B and NSE contents are higher in patients with traumatic brain injury, and the specific contents are closely related to the degree of oxidative stress and insulin resistance.

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