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Change and significance of serum inflammatory factors, NSE, S100 protein and stress hormone levels in patients with craniocerebral injury

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ABSTRACT

Objective: To investigate the change and significance of serum inflammatory factors, neuron specific enolase (NSE), S100 protein and stress hormone levels in patients with brain diseases. **Methods:** A total of 115 patients with craniocerebral injury were selected as the observation group, according to the Glasgow Coma Scale (GCS), they were divided into light-sized group (n=38), middle-sized group (n=40) and severe-sized group (n=37), at the same time the other 120 healthy subjects were selected as the control group. The levels of serum inflammatory cytokines [tumor necrosis factor alpha (TNF-α) and procalcitonin (PCT)], neuron specific enolase (NSE), S100 protein and the stress hormone cortisol [(COR), adrenocorticotropic hormone (ACTH), β-endorphin (β-EP)] of both groups were compared. **Results:** The levels of TNF-α, PCT, NSE, S100, COR, ACTH and β-EP in the observation group were (145.73±19.24) ng/L, (2.41±0.64) ng/mL, (38.11±12.28) ng/mL, (0.87±0.32) μg/L, (818.87±121.14) nmol/L, (107.38±13.94) ng/L, (126.74±39.04) ng/mL, which were significantly higher than control group, the difference was statistically significant; Comparison of indexes among the observation group, NF-α, PCT, NSE, S100, COR, ACTH and β-EP levels in the middle-sized group and severe-sized group were significantly higher than those in the light-sized group, and the levels in the severe-sized group were significantly higher than those of the middle-sized group, the difference was statistically significant. **Conclusion:** The levels of Serum inflammatory factors, NSE, S100 protein and stress hormone were significantly increased in patients with craniocerebral injury, the level was related to the degree of traumatic brain injury, which could be used as an important indicator to assess the severity of the disease.

1. Introduction

Craniocerebral trauma was a common traumatic disease in neurosurgery, often resulted from traffic accident, occupational injury, crash and direct strike by blunt. Its occurrence usually accompanied with general inflammatory reaction and multiple organ injury, disability rate and death rate have been the worldwide public health and social economic problem[1,2]. At present, evaluation of this disease mainly used Glasgow Coma Scale (GCS) and CT, MRI and other iconography examination, there was still many deficiency in the severe degree and prognosis evaluation[3]. Biochemical marker related to brain injury was research hot in recent. This research was aimed to clear out the change and significance of indexes, through analyzing serum inflammatory factors, neuron specific enolase (NSE), S100 protein and stress hormone levels.

2. Material and method

2.1. General data

A total of 115 cases of patients with craniocerebral injury admitted in our medical center from November 2011 to June 2017 were

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selected as research subjects (observation group), all subjects were conformed to selection criteria established by this research, 73 males, 42 females, aged from 29-68 years old; injury reasons: 65 cases of traffic accidents, 28 cases of falling accidents, 13 cases of crush-related injury , 9 cases of strike injury; types of disease injury: 37 cases of skull fracture, 31 cases of epidural hematoma, 24 cases of cerebral contusion, 11 cases of subdural hematoma, 7 cases of intracranial hematoma, 5 cases of diffusive dendrite injury; according to GCS, they were divided into light craniocerebral injury 38 cases (light-group, GCS grading 13-15 grade); moderate craniocerebral injury 40 cases (moderate-group, GCS grading 9-12 grade); severe craniocerebral injury 37 cases (severe-group, GCS grading 3-8 grade); meanwhile selected 120 healthy persons as control group, 75 males, 45 females, aged from 30-69 years old. This research was conformed to ethics committee of hospital.

2.2 Selection criteria

Inclusion criteria: (1) all of patients with history of typical craniocerebral trauma, diagnosed by craniocerebral CT, MTRI examination, accorded with related criteria of craniocerebral injury[4]; (2) injury time was less than 12 h; (3) with complete clinical data.

Exclusion criteria: (1) accompanied with severe heart, pulmonary, hepatic and renal dysfunction, acute infective disease and malignant tumor; (2) with severe periphery neural disease, severe spine injury; (3) patients with shock; (4) deal with hormone specially; (5) with surgery and other trauma in recent.

2.3 Observation index

Extracted fasting periphery venous blood of whole subjects, respectively after admission (injury in 12 h) or at examination, water bath, following by centrifuge and collected supernatant in EP tube, stocked at -70 ℃ freezer for detection. Observation index including: (1) inflammatory factors: tumor necrosis factor-α (TNF-α) and procalcitonin (PCT), TNF-α was measured by ELISA, kits were provided from Beijing Jingmei bio-engineering Co. Ltd; fluorescence immunoassay was applied to detect PCT, its coresponding kits were purchased from Shanghai Meilian biotechnoloy Co., Ltd. (2) neuron specific enolase (NSE), detected by ELISA, NSE ELISA kits were provided by Shanghai Meilian biotechnoloy Co., Ltd. (3) S100 protein, detected by electrochemiluminescence, detection kits were provided from Roche diagnostic product Co., Ltd (Shanghai). (4) stress hormone: cortisol (COR), adrenocorticotrophic hormone (ACTH), β-endorphin (β-EP), detected by chemiluminescence with Roche electrochemistry luminescence immunity analyzer. All of operations were strictly accorded with introduction of measurement kits.

2.4 Statistical analysis

Statistical Software SPSS 17.0 was used for all raw data processing and analyzing, inflammatory factors, NSE, S100 protein and oxidative stress were conformed to normal distribution and represented by Mean ± SD, one-way analysis of variance was used for comparison of indexes level among multiple groups, SNK-q test was applied to comparison of intra-group, $P<0.05$ indicated the difference was statistical significant.

3. Results

3.1. Comparison of inflammatory factors level

Results of serum TNF-α and PCT level of all groups were shown in Table1. Compared with control group, TNF-α and PCT level in observation group were significantly decreased [(145.73±19.24) ng/L, (2.41±0.64) ng/mL], the difference was significant ($P<0.05$). In observation group, TNF-α and PCT level of light group, moderate group and severe group were compared and difference was significant ($P<0.05$); compared with light group, TNF-α and PCT level of moderate and severe group was obviously increased, moreover, severe group [(173.97±22.68) ng/L, (3.19±1.11) ng/mL] were higher than moderate group [(139.17±17.16) ng/L, (1.82±0.45) ng/mL], difference was significant ($P<0.05$).

Table1.

Comparison of inflammatory factors level.

Group	*n*	TNF-α (ng/L)	PCT (ng/mL)
Control group	120	94.10±12.02	0.29±0.05
Observation group	115	145.73±19.24[a]	2.41±0.64[a]
Light group	38	109.75±13.55	0.64±0.27
Moderate group	40	139.17±17.16[b]	1.82±0.45[b]
Severe group	37	173.97±22.68[bc]	3.19±1.11[bc]

Note: compared with control group, [a]$P<0.05$; compared with light group, [b]$P<0.05$; compared with moderate group, [c]$P<0.05$.

3.2. Comparison of serum NSE and S100 protein level

Results of NSE and S100 protein level were shown in Table 2. NSE and S100 protein level in observation group were (38.11±12.28) ng/mL and (0.87±0.32) μg/L, which was obviously higher than control group, the difference was significant ($P<0.05$). In observation group, NSE and S100 protein level of light group, moderate group and severe group were respectively (18.43±6.98) ng/mL, (0.51±0.26) μg/L, (32.66±11.32) ng/mL, (0.67±0.24) μg/L, (62.95±15.04) ng/mL and (1.26±0.37) μg/L, compared these levels, the difference in three groups was statistical significantly ($P<0.05$), moreover, moderate

and severe group were obviously higher than light group, moderate group was lower dramatically than severe group, difference was statistical significantly (P<0.05).

Table 2.

Comparison of serum NSE and S100 protein level.

Group	n	NSE (ng/mL)	S100 pro (μg/L)
Control group	120	9.26±2.04	0.23±0.11
Observation group	115	38.11±12.28[a]	0.87±0.32[a]
Light group	38	18.43±6.98	0.51±0.26
Moderate group	40	32.66±11.32[b]	0.67±0.24[b]
Severe group	37	62.95±15.04[bc]	1.26±0.37[bc]

Note: compared with control group, [a]P<0.05; compared with light group, [b]P<0.05; compared with moderate group, [c]P<0.05.

3.3 Comparison of stress hormone level

Results of stress hormone level were shown in Table 3. COR, ACTH and β-EP level in observation group were (818.87±121.14) nmol/L, (107.38±13.94) ng/L and (126.74±39.04) pg/mL, it was higher than control group, the difference was significant (P<0.05); whereas compared with light group, COR, ACTH and β-EP level in moderate and severe group were increased obviously, moreover, severe group was higher than moderate group, the difference was significant (P<0.05).

4. Discussion

Craniocerebral injury was a common kind of trauma in clinic, its occurrence was only less than limbs trauma, in all parts injury of whole body, its disability rate and death rate was the highest, and its occurrence rate was in increasing trend[5]. It often accompanied with other parts injury and severely threatened life of patients and brought heavy burden about family and society. The early and accurate diagnosis of craniocerebral injury was key for enhancing efficacy and improving prognosis[6]. In recent, a lot of researches proved that brain injury related biochemical indexes could sensitively and effectively reflect illness condition and prognosis of craniocerebral injury[7,8]. This research was aimed to define the change in different course of disease and clinical significance of all these indexes through analyzing inflammatory factors, NSE, S100 and stress hormone.

Along with the research about pathogenesis of craniocerebral injury becoming more and more deeply, related study pointed out that inflammatory factors played critical role in development of craniocerebral injury, which was thought as the important consisting factor in progress of physiopathologic change[9,10]. Researches have demonstrated that secondary cerebral neuron injury after craniocerebral injury and multiple organ injury were closely related to inflammatory oxidative stress, and oxidative stress was one of important reasons that resulted in state of craniocerebral injury aggregated and patients died[11,12]. As a typical pro-inflammatory factor TNF-α mainly generated by astrocyte and nerve cell, played critical role in maintaining nerve tissue develop and nervous signal transmission[13]. PCT was precursor of calcitonin, produced by follicular thyroid cell, rapidly generated through inflammatory factor and bacterial endotoxin inducing, its sensitivity was higher than C reaction protein, was early marker of inflammatory reaction[14]. Research found that serum TNF-α and PCT level of patients were increased when there was injury and inflammatory reaction[15,16]. This research showed that compared with healthy people, TNF-α and PCT level of patients with craniocerebral injury were increased significantly, moreover along with aggregation of illness condition, the increasing range was more obvious, the difference was significant. Research revealed that there was remarked inflammatory stress in patients with craniocerebral injury, TNF-α and PCT were related to severe degree of craniocerebral injury, which could used as critical indexes that evaluated severe degree of illness condition.

NSE and S100 protein were brain injury related indexes that studied in recent, its content in living organism was able to sensitively and reliably evaluate prognosis and illness condition[17,18]. Under normal condition, NSE only existed in neurons, entered into blood only neuron died, it was critical detected indexes of nerve injury and necrosis. S100 protein was a kind of neurotrophic factor, special protein of nervous system, participated in proliferation, differentiation, apoptosis of neurons mainly through regulating hormone secretion, inhibiting signal transmission. Its overexpression could aggregate inflammatory stress of nervous system, cause neural dysfunction[19,20]. This paper found NSE and S100 level in patients with craniocerebral injury were obviously higher than healthy people, and both level gradually increased in light group, moderate

Table 3.

Comparison of stress hormone level.

Group	n	COR (nmol/L)	ACTH (ng/L)	β-EP (pg/mL)
Control group	120	370.59±58.97	37.59±9.92	43.35±7.11
Observation group	115	818.87±121.14[a]	107.38±13.94[a]	126.74±39.04[a]
Light group	38	680.68±80.92	75.57±12.63	70.98±11.60
Moderate group	40	834.11±119.88[b]	115.74±15.27[b]	92.26±14.98[b]
Severe group	37	988.37±151.73[bc]	173.64±30.31[bc]	152.49±50.29[bc]

Note: compared with control group, [a]P<0.05; compared with light group, [b]P<0.05; compared with moderate group, [c]P<0.05.

group, severe group. Research results was accorded with previous report[21], further demonstrated both were important to evaluate degree of craniocerebral injury and prognosis.

In addition to cranial pathological injury, craniocerebral injury also caused hypothalamus-pituitary gland-adrenal gland (HPA) axis change, hence generated a series of inflammatory reaction and general injury, thereby aggregated illness condition and affected prognosis[22]. Stress hormone was HPA axis related hormone, with important effect on neuroendocrine regulation, proper level was better to recovery whereas over-expression and low-expression could result in metabolism disorder, inhibit immune function and indicate bad prognosis[23]. This research pointed that COR, ACTH and β-EP level in patients with craniocerebral injury were obviously increased, the illness condition was more severe, the level increased more obviously, it revealed serum stress hormone level was related to severe degree of craniocerebral injury, as sensitive index of craniocerebral injury.

In conclusion, inflammatory stress, NSE, S100 protein and stress hormone level was abnormally increased in patients with craniocerebral injury, change of all indexes was closely related to severe degree of illness condition. Monitoring change of inflammatory stress, NSE, S100 protein and stress hormone level was critical to evaluate illness condition.

Reference

[1] Huang Chengya, Liang Chunyan, Zhong Jiandong. Risk factor analysis of secondary traumatic epilepsy in patients with craniocerebral injury. *Clin Neurosurg J* 2017; **14**(3): 182-185.

[2] Dutra VC, Caregnato RCA, Figueiredo MRB. Craniocerebral trauma in motorcyclists: relation of helmet use and trauma severity. *Acta Paulista de Enfermagem* 2014; **27**(5): 485-491.

[3] Xu G, Hu B, Chen G. Analysis of blood trace elements and biochemical indexes levels in severe craniocerebral trauma adults with glasgow coma scale and injury severity score. *Biol Trace Element Res* 2015; **164**(2): 192-197.

[4] Liu Ning, Zhang Yan. *Surgery*. The sixth edition. Beijing: People's Education Press; **2012**, p. 286-287.

[5] Jiang X, Suo L, Liu LJ. Investigation on operation timing of limb fractures combined with severe craniocerebral trauma in children. *China J Orthopaedics Traumatol* 2014; **27**(6): 486-490.

[6] Song Maifen, Wang Xusheng, Wan Jie. Relationship dynamic change of tongue and prognosis evaluation in patients with craniocerebral injury. *Beijing Tradit Med* 2016; **35**(1): 6-8.

[7] Zetterberg H, Smith DH, Blennow K. Biomarkers of mild traumatic brain injury in cerebrospinal fluid and blood. *Nature Rev Neurol* 2013; **9**(4): 201-210.

[8] Papa L, Ramia MM, Edwards D. Systematic review of clinical studies examining biomarkers of brain injury in athletes after sports-related concussion. *J Neurotrauma* 2015; **32**(10): 661-673.

[9] Abdul-Muneer PM, Chandra N, Haorah J. Interactions of oxidative stress and neurovascular inflammation in the pathogenesis of traumatic brain injury. *Mol Neurobiol* 2015; **51**(3): 966-979.

[10]Luan Lei. Change of inflammatory stress and metabolism in perioperative period of standard craniotomy in patients with severe craniocerebral injury. *J Hainan Med Coll* 2016; **22**(14): 1541-1543.

[11]Zhang Junfeng. Clinical analysis of IL-6, BNP, CRP expression in brain blood in patients with craniocerebral trauma. *J Hainan Med Coll* 2015; **21**(9): 1219-1221.

[12]Corps KN, Roth TL, McGavern DB. Inflammation and neuroprotection in traumatic brain injury. *JAMA Neurol* 2015; **72**(3): 355-362.

[13]Zelova H, Hosek J. TNF-α signalling and inflammation: interactions between old acquaintances. *Inflammation Res* 2013; **62**(7): 641-651.

[14]Koerdt S, Rommel N, Rohleder NH. Perioperative serum levels of procalcitonin, C-reactive protein, and leukocytes in head and neck free flaps. *Int J Oral Maxillofacial Surg* 2017; **46**(6): 699-705.

[15]Zhang Mingxia, Zhao Ruiqing, Li Qingxia. Effect of premature rupture of membrane on bacterial infection in utero of fetal and its relevance with IL-6, PCT, CRP, TNF-α in umbilical cord blood. *Chin Hosp Infection J* 2016; **26**(21): 4968-4970.

[16]Wu Biao, Ai Rong, Yang Xiaozhi. Detection value of MMPs and TIMP and PCT and TNF-α indexes in serum and cerebrospinal fluid in child with viral encephalitis. *Chin Hosp Infect J* 2017; **27**(9): 2118-2121.

[17]Krohn M, Drebler J, Bauer M. Immunohistochemical investigation of S100 and NSE in cases of traumatic brain injury and its application for survival time determination. *J Neurotrauma* 2015; **32**(7): 430-440.

[18]Olivecrona Z, Bobinski L, Koskinen LOD. Association of ICP, CPP, CT findings and S-100B and NSE in severe traumatic head injury. Prognostic value of the biomarkers. *Brain Injury* 2015; **29**(4): 446-454.

[19]Rodriguez-Rodriguez A, Egea-Guerrero JJ, Gordillo-Escobar E. S100B and neuron-specific enolase as mortality predictors in patients with severe traumatic brain injury. *Neurological Res* 2016; **38**(2): 130-137.

[20]Wolf H, Frantal S, Pajenda G. Analysis of S100 calcium binding protein B serum levels in different types of traumatic intracranial lesions. *J Neurotrauma* 2015; **32**(1): 23-27.

[21]Chen Jinjing, Zhang Yang, Zhu Chunran. Significance of serum S100B and NSE combined detection in prognosis estimation of patients with craniocerebral injury. *Modern Med* 2016; **44**(11): 1602-1604.

[22]Lan Zhan, Qiu Hong, Zhang Chuandong. Relevant research between insulin resistance and brain injury, stress reaction. *J Hainan Med Coll* 2017; **23**(7): 943-945.

[23]Liu Chaoyuan, Pang Hailing, Huang Huaizhong. Effect of mouse nerve growth factor combined with early low temperature treatment on inflammation and oxidative stress and brain protection. *J Hainan Med Coll* 2017; 23(7): 958-961.