

## Relationship between CT features and serum GFAP, NSE and S100B protein in patients with severe traumatic brain injury.

Qiaoke Li\*, Qi Zhou

Department of Critical Care Medicine, Sichuan Provincial Crops Hospital of Chinese People's Armed Police Force, Leshan, Sichuan, PR China

### Abstract

**Objective:** To investigate the relationship between CT features and serum GFAP, NSE and S100B protein in patients with severe traumatic brain injury.

**Methods:** 80 patients with traumatic brain injury admitted in our hospital from January 2016 to January 2017 were selected and divided into mild (n=31), medium (n=28) and severe (21) according to their CT scores. The level difference between the three kinds of serum CFAP and between NSE and S-100B proteins, changes of three kinds of serum protein before and after treatment in patients with severe, and the relationship between the brain CT score and serum CFAP, NSE and S-100B protein analysis.

**Results:** The serum levels of CFAP, NSE and S-100B were significantly different in patients with different types of traumatic brain injury ( $P<0.05$ ); the difference of CFAP, NSE and S-100B protein levels in patients with severe disease before and after treatment was statistically significant ( $P<0.05$ ); by correlation analysis, the head CT score of patients with traumatic brain injury was positively correlated with CFAP, NSE and S-100B protein.

**Conclusion:** In patients with traumatic brain injury by CT score and serum CFAP, NSE, S-100B protein level has a positive correlation, which has a certain guiding significance of changes of serum CFAP, NSE, S-100B protein level identification and prognosis of patients with traumatic brain injury.

**Keywords:** Brain injury, Cranial CT, GFAP, NSE, S100B protein.

Accepted on October 18, 2017

### Introduction

Cerebral trauma onset is acute. The injury mechanism is complicated. It belongs to common diseases and frequently-occurring disease in clinic. But at present, for injury degree of cerebral injury diagnosis, except disease history, there are data of iconography and GCS only, but it is short of objective evaluation indexes of experiments [1,2]. Therefore, finding objective indexes for judging craniocerebral injury degree and prognosis has become hotspot problems of this field. In recent years, people find that Glial Fibrillary Acidic Protein (GFAP), Neuron Specific Enolase (NSE) and S100B protein after cerebral injury, their level has obvious changes [3]. Therefore, this study explores CFAP, NSE and S-100B protein conditions of critical patients after cerebral injury, and analyses its relations with craniocerebral CT. Now the detail content is reported as follows.

### Materials and Methods

#### Clinical data

This study selected 80 patients with traumatic brain injury admitted in our hospital from January 2016 to January 2017.

They were divided into mild (n=31), medium (n=28) and severe (21) according to their CT scores. 80 patients, of whom, there were 52 male cases and 28 female cases. The age was from 17 to 82 y old. The average age was  $37 \pm 5.3$  y old. General data of all patients were as followed in Table 1.

**Table 1.** Statistical table of basic data of patients. Comparison of sex attribution, age and injury reasons of patients in three groups, there were no statistical differences ( $P>0.05$ ).

Items		
Sex	Male (n)	52
	Female (n)	28
Age	Age range (years old)	17~82
	Average age (years old)	$37 \pm 5.3$
Injury reason	Car accident (n)	56
	Fall injury (n)	12
	Hit of hard substance (n)	7

### Exclusive criteria

Patients who met one of items in the following should be excluded in this study [4]: first, except cerebral injury, patients had severe compound injury of other systems and organs; second, patients who had neurological tumor, infectious diseases; third, injury before one month, patients were given major surgery or severe trauma history; fourth, patients with severe diabetes; fifth, patients who admitted into hospital beyond 24 h after injury.

### Methods

**CT evaluation methods:** All patients admitted into hospital, given cerebral CT scanning within 24 h. Two experienced senior imaging doctors evaluate cerebral CT image. The details of scores were as following: first, the third ventricle of cerebrum, the scores were from 0 to 3: no changes were 0, diminish were 1 to 2, complete disappear was 3; second, structure shift of center line were 0 to 4: no changes were 0, shifting equal to or less than 0.5 cm, it was 0, 0.6 to 1.0 cm shifting were 2, 1.1 to 1.5 cm shifting were 3, shifting over 1.5 were 4; third, lateral ventricle were 0 to 3: no changes were 0, unilateral transformation was 1, bilateral transformation was 2, bilateral disappear was 3; fourth, quadrigeminal cistern, interpeduncular cistern and ambient cistern were 0 to 2: no changes were 0, diminish was 1, complete disappear was 2, the scores were 0 to 15. The higher the scores, more severe the conditions and injury. The score equal to or less than 5, it was slight type; the scores were 6 to 10, it was moderate type; scores equal to or more than 11, it was severe type.

**Treatment methods:** After all patients admitted into hospital, given treatment of smooth respiratory tract, oxygen intake, cerebral tension lowering, anti-infection, cerebral cells nutrition and prevention for further injury. If patients had surgical indications, they should be given surgical treatment timely. The treatment time was half month.

**Detection methods of CFAP, NSE and S-100B proteins:** After patients admitted into hospital within 24 h, 5 ml venous blood was extracted under fasting. It was placed at room temperature for 0.5 h. Serum was separated centrifugally at low temperature and placed at -20°C refrigerator for detection. CFAP, NSE and S-100B reagents all were bought from American R&D Company. Operation was completed by detecting physicians in our hospital. Operation procedures followed guide of kits. After treatment of patients, CFAP, NSE and S-100B were detected again according to methods above.

**Statistical methods:** This study adopted SPSS 18.0 to do data statistics and analysis. Continuous variables used  $\bar{x} \pm s$ . Classified variable used percentage or frequent number. Comparison between groups used F or t-test. Classified variable used  $\chi^2$  test.  $P < 0.05$ , there were statistical differences. At the same time, it used spearman relevance analysis to analyse the correlations between CT scores and CFAP, NSE and S-100B level.

## Results

### Differences of CFAP, NSE and S-100B expressions of patients in three groups when admitted into hospital

When admitted into hospital, slight and moderate patients compared with severe patients, there were obvious statistical differences in CFAP, NSE and S-100B ( $P < 0.05$ ). Details seen in Table 2.

**Table 2.** Conditions of CFAP, NSE and S-100B expression of patients in three groups when admitted into hospital.

CT image scores	n (case)	MBP (µg/L)	NSE (mg/L)	S100B (µg/L)
slight (5 points)	31	2.85 ± 0.57	26.95 ± 4.72	1.17 ± 0.34
moderate (6~10points)	28	4.01 ± 0.83	39.68 ± 7.42	2.35 ± 0.66
severe (11 points)	21	6.32 ± 1.04	58.25 ± 9.76	5.15 ± 1.02
F value		8.152	9.024	7.97
P value		0.014	0.0084	0.019

### Comparison of MBP, NSE and S100B expression before and after treatment in severe patients

There were obvious statistical differences in MBP, NSE and S100B expression before and after treatment in severe patients ( $P < 0.05$ , Table 3).

**Table 3.** Conditions of CFAP, NSE and S-100B expressions before and after treatment in severe patients.

Time	MBP (µg/L)	NSE (mg/L)	S100B (µg/L)	CT scores
Before treatment	6.32 ± 1.04	58.25 ± 9.76	5.15 ± 1.02	12.5 ± 0.42
After treatment	3.53 ± 0.98	29.48 ± 6.32	1.74 ± 0.45	6.82 ± 0.47
T value	5.827	5.932	5.096	4.398
P value	0.016	0.011	0.021	0.032

### Relations between CT image scores and MBP, NSE and S100B expressions

Through Spearman grade correlation analysis, CT scores had positive correlations with NSE ( $P < 0.05$ ). CT scores had positive correlations with MBP expressions ( $r_s = 0.635$ ,  $P < 0.05$ ). CT scores had positive correlations with S100B protein expressions ( $r_s = 0.863$ ,  $P < 0.05$ ).

## Discussion

Cerebral trauma is the emergency treatment of cerebral surgical department, it has features of acute onset, high death rate and disability rate and so on. Patients often have consciousness dysfunction [5]. After cerebral injury, it produces injury on cerebral tissue immediately. But because of limited medical level, it is still unclear about cerebral injury

mechanism. Therefore, combining with features of cerebral injury, we should monitor disease changes frequently after injury of patients, positively prevent complications and secondary cerebral injury [6]. From the above, we can see the key of cerebral injury treatment lies in diagnosis of conditions and prognosis of prognosis. But at present, judgment of cerebral injury conditions mainly relies on manifestations of iconography and GCS. Though iconography data and GSC have a certain effects on judgment of conditions, its objectivity is relatively strong, it is difficult to reflect injury degree on cerebral cells because of objective indexes shortage [7]. Therefore, establishing high sensitivity, specificity and reliable cerebral injury serum markers, quantitative evaluation of cerebral injury degree after acute craniocerebral injury, early evaluation of prognosis have been taken seriously by research and clinical study [8,9].

At present, serum indexes of evaluating acute craniocerebral injury are plentiful, of which, the common indexes have NSE, MBP, S100B proteins, Nogo-A protein and so on. Its theoretical basis is the detection in serum increase when cellular factors in cytoplasm are released into cerebrospinal fluid and serum after neurological cell injury.

In normal conditions, the main specificity of NSE locates in neuron and neuroendocrine cells, it is soluble antigen. The percentage of it in neurological cells is higher. Cytoplasm in cerebral gray has high-concentration NSE because of neuron. When patients affect with cerebral trauma, especially gray, NSE released by neurological cells will enter into blood, which will cause it increase in serum expression [10,11]. In this study, according to CT scores, they are divided into slight, moderate and severe cerebral injury patients. There is obvious differences in NSE level ( $P<0.05$ ). From that, we can see, NSE expression increases obviously after cerebral injury, at the same time, it has a certain positive correlations with injury degree. MBP is a kind of membrane protein with strong alkalinity synthesized by oligo dendrocytes in nervous system and peripheral nerve sheath cells, often locating in serosal surface of myelin, it combines with lipid of myelin, which not only can maintain stability of structure and function of nervous system, also has launching function in the formation of myelin. When cerebral tissue has amyelination injury, it will increase MBP expression. Cerebral trauma will cause cerebral swelling, amyelination and so on [12,13]. Therefore, the studies show that MBP expression of slight and severe cerebral trauma patients is high, at the same time, with the aggravation of injury degree, its MBP expression increases ( $P<0.05$ ). S100 is a kind of calcium-binding protein. It has wide biological activity. It will participate in cell proliferation, differentiation, muscle contraction, gene expression and cell apoptosis and so on [14,15]. S100B protein molecule cannot enter into blood brain barriers under the normal conditions, but after cerebral injury, cerebral tissue injury will cause damage of cerebral cells and BBB. S100B protein will increase rapidly. Like secondary injury, BBB will be damaged furtherly. Damage of gliocyte will induce overflow of S100B, its level changes have close relations with clinical symptoms, signs and iconography changes, and it is good index for judging cerebral injury degree

[16,17]. Therefore, in this study, it is found that S100B protein expression of slight and moderate cerebral trauma is high, at the same time, with the aggravation of injury degree, its S100B protein expression increases ( $P<0.05$ ).

There are studies which show that [18,19] after treatment of cerebral trauma, serum level of three indexes above decrease obviously. This study selects severe patients, at the same time, compared with SE, MBP and S100B protein, CT scores before and after treatment, the results show that CT scores decrease after treatment, which is generally meet manifestations of slight injury patients. It accompanied by decrease of SE, MBP and S100B protein level. In the analysis of correlations between CT scores and three indexes find that CT scores have positive correlations with these three indexes.

In conclusion, cerebral CT scores of cerebral trauma have correlations with SE, MBP and S100B protein level in serum. SE, MBP and S100B protein level changes in serum have significant guidance for identify and prognosis of cerebral trauma patients. In clinic, we can combine with CT scores, GCS, CFAP, NSE and S-100B protein level to judge and formulate corresponding strategies for conditions and prognosis of cerebral trauma patients.

## References

1. Wang W, Li Y, Ren J. Hydrogen rich saline reduces immune-mediated brain injury in rats with acute carbon monoxide poisoning. *Neurol Res* 2012; 34: 1007- 1015.
2. Papa L, Ramia MM, Kelly JM. Systematic review of clinical research on biomarkers for pediatric traumatic brain injury. *J Neurotrauma* 2013; 30: 324-338.
3. Sandler SJ, Figaji AA, Adelson PD. Clinical applications of biomarkers in pediatric traumatic brain injury. *Childs Nerv Syst* 2010; 26: 205-213.
4. Yordan T, Erenler AK, Baydin A, Aydin K, Cokluk C. Usefulness of S100B protein in neurological disorders. *J Pak Med Assoc* 2011; 61: 276-281.
5. Liu Y, Liu LP, Liu AD. Relations between CT scores of senile cerebral injury patients and myelin alkaline protein in serum, enolase of neurological specificity, A100B protein expression. *Chinese J Gerontol* 2015; 4: 2124-2126.
6. Honda M, Tsuruta R, Kaneko T. Serum glial fibrillary acidic protein is a highly specific biomarker for traumatic brain injury in humans compared with S-100B and neuron-specific enolase. *Trauma* 2014; 69: 104-109.
7. Wolf H, Frantal S, Pajenda GS. Predictive value of neuromarkers supported by a set of clinical criteria in patients with mild traumatic brain injury: S100B protein and neuron-specific enolase on trial: clinical article. *J Neurosurg* 2013; 118: 1298-1303.
8. Zhang WQ, Zheng P, Xu P. Influence of temperature control on serum neuron specific enolase and Tau protein levels in patients with severe craniocerebral injury and its significance. *J Chinese Pract Diagn Ther* 2016; 30: 389-390.

9. Fei Y, Wang P C, Chen B Z. Clinical trial of ganglioside injection in the treatment of patients with severe craniocerebral injury. *Chinese J Clin Pharmacol* 2017.
10. Zurek J, Fedora M. The usefulness of S100B, NSE, GFAP, NF- H, secretagogin and Hsp70 as a predictive biomarker of outcome in children with traumatic brain injury. *Acta Neurochir (Wien)* 2012; 154: 93-103.
11. Zurek J, Fedora M. The usefulness of S100B, NSE, GFAP, NF-H, secretagogin and Hsp70 as a predictive biomarker of outcome in children with traumatic brain injury. *Acta Neurochirurgica* 2012; 154: 93.
12. Jiang W, Xia F, Han J. Patterns of Nogo-A, NgR, and RHoA expression in the brain tissues of rats with focal cerebral infarction. *Transl Res* 2014; 154: 40-48.
13. Deng JP, Sun XC, Liu K. Combination detecting the diagnosis and prognosis meaning of serum S-100B protein, enolase of neurological specificity, GFAP on severe cerebral injury. *J Traum Surg* 2012; 14: 494-497.
14. Costine BA, Quebede- Clerkin PB, Dodge CP. Neuron-specific enolase, but not S100B or myelin basic protein, increases in peripheral blood corresponding to lesion volume after cortical impact in piglets. *J Neurotrauma* 2012; 29: 2689-2695.
15. Esnafoglu E, Ayyildiz S N, Cirrik S. Evaluation of serum Neuron-specific enolase, S100B, myelin basic protein and glial fibrillary acidic protein as brain specific proteins in children with autism spectrum disorder. *Neurosci Off J Int Soc Develop Neurosci* 2017; 61: 86.
16. Li JJ, Luo GD, Cao YB. Relationships among CT imaging features, intracranial pressure and prognosis after moderate or severe traumatic brain injury. *Chinese J Minim Invas Neurosurg* 2013; 18: 307-309.
17. Rundhaug NP, Moen KG, Skandsen T. Moderate and severe traumatic brain injury: effect of blood alcohol concentration on Glasgow coma scale score and relation to computed tomography findings. *J Neurosurg* 2015; 122: 1-8.
18. Zhong L, Lin J. Level change of serum neuron specific enolase, Nogo-a protein and myelin basic protein from patients with acute craniocerebral injury. *China Med Herald* 2013; 10: 120-122.
19. Chang T, Wang L, Zhao XP. Relationship of Nogo-A gene expression in serum and cerebrospinal fluid with nerve injury and inflammatory factor levels in patients with craniocerebral trauma. *J Hainan Med Univ* 2017; 23.

**\*Correspondence to**

Qiaoke Li

Department of Critical Care Medicine

Sichuan Provincial Crops Hospital of Chinese People's Armed Police Force

PR China