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Original Article

Correlation between platelet parameters, platelet/lymphocyte ratio, the severity and prognosis of patients with traumatic brain injury

Hao Liu[1], Xianjiang Zhang[2]

Departments of [1]Emergency, [2]Critical Care Medicine, Xuzhou Central Hospital, Xuzhou, Jiangsu Province, China

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Abstract: Objective: To investigate the correlation between platelet parameters, platelet/lymphocyte ratio (PLR), disease severity and prognosis of patients with traumatic brain injury (TBI). Methods: This retrospective study recruited 102 patients with TBI and they were divided into severe group (n=36), moderate group (n=45) and mild group (n=21) according to their Glasgow Coma Scale (GCS) score. Meanwhile, 23 healthy subjects were selected as the control group. The differences in platelet parameters, PLR, neuron-specific enolase (NSE), and high-sensitivity C-reactive protein (hs-CRP) levels among the enrolled subjects on the day of admission were compared, and the correlation between the above indicators and the severity and prognosis of TBI patients was analyzed. Results: There were significant differences in blood platelet (PLT) level and PLRs among the four groups (all P<0.05). Compared with the control group, TBI patients had significantly lower PLT level, but significantly higher PLR and serum levels of NSE and hs-CRP (all P<0.05). Spearman correlation analysis showed that PLT level was positively correlated with GCS score (r=0.586, P<0.05), while PLR, NSE and hs-CRP levels were negatively correlated with GCS score (r=-0.374, P<0.01; r=-0.320, P<0.05; r=-0.705, P<0.05). Multivariate binary logistic regression showed that PLT level was negatively correlated with poor prognosis (OR=0.746, P<0.05), while PLR, NSE, hs-CRP levels were positively correlated with poor prognosis (OR=2.774, 1.840, 1.968, all P<0.05). Conclusion: For TBI patients at the early stage, decrease of PLT counts and increased serum levels of PLR, serum NSE and hs-CRP may suggest severe disease condition and poorer prognosis.

Keywords: Platelet counts, platelet/lymphocyte ratio, traumatic brain injury, condition, prognosis

Introduction

Traumatic brain injury (TBI) refers to brain tissue damage caused by various traumas. Accounting for about 15% cases, severe TBI has rapid disease progression and high mortality, which can lead to various complications in patients after surgery [1, 2]. The Glasgow Coma Scale (GCS) is the most popular index to evaluate the coma degree of patients in terms of language response, eye opening response and limb movement score. Lower GCS score suggests more severe coma degree of patients. The external force on cranium can cause inner wall injury and rupture or vasospasm of cerebral vessel. As a result, the count, morphology and function of platelets change are closely related to the disease development such as secondary brain injury, ischemic hypoxic encephalopathy and cerebral infarction, and patient's prognosis [3-5]. Therefore, the detection of platelet parameters and other laboratory indicators for disease indication can be effective. It can not only greatly reduce the economic burden and time cost of the patient, but also increase the accuracy of the assessment by combining with some traditional assessment methods.

Recent studies found that the platelet/lymphocyte ratio (PLR) is a new predictor of inflammation. PLR is closely related to diabetic microvascular complications and cancer [6-8]. Moreover, high PLR often indicates a poor prognosis of patients with acute cerebral infarction [9]. Some studies have found that craniocerebral injury can induce an inflammatory response within 15 min in the body, leading to the corresponding changes in platelet count and function [10]. A variety of inflammatory cytokines, such as high-sensitivity C-reactive protein (hs-CRP) and tumor necrosis factor α (TNF-α), are involved in secondary inflammatory responses after craniocerebral injury, indicating a certain relationship with the occurrence and development of secondary brain injury [11]. Some scholars tracked the changes of neuron-specific enolase (NSE) levels in TBI patients, and found that serum NSE level increased significantly after injury. Therefore, they believed that NSE can be used as a predictive indicator for the postoperative outcome of patients with brain injury [6]. However, the sensitivity of NES in disease evaluation remains unclear.

Therefore, this study explored the correlation between platelet parameters, PLR, NSE, hs-CRP and the severity of TBI patients, and their predictive value in patient's prognosis.

Materials and methods

General information

Information of 102 patients with TBI who were treated in Xuzhou Central Hospital from August 2017 to October 2019 as well as 23 healthy people who received physical examination at the same period were retrospectively analyzed. TBI patients were divided into severe group (GCS score 3-8, n=36), moderate group (GCS score 9-12, n=45) and mild group (GCS score 13-15, n=21) according to their GCS scores. The 23 healthy people were enrolled in the control group. This study was approved by the Ethics Committee of Xuzhou Central Hospital.

Inclusion criteria: Patients with a confirmed history of brain traumas; patients who diagnosed as TBI (skull fracture, brain contusion, epidural hematoma, intracranial hematoma etc.) and confirmed by CT or MRI; patients with GCS score from 3 to 15; patients who received standard large flap decompression or conventional bone flap craniotomy and other surgical treatment; patients who can cooperate with consults and examination; patients whose family members signed the informed consent after understanding the experimental purpose of this study.

Exclusion criteria: Patients with primary brain stem injury; patients with multiple injuries; patients who died on the spot; patients with hypoimmunity caused by malignant tumors and other reasons; pregnant and lactating patients; patients who were transferred to other hospital or their family members abandoned treatment for other reasons.

Methods

Approximately 5 mL of venous blood was collected from TBI patients on the day of admission, in which 2 mL of whole blood was anticoagulated with EDTA-K2 (Shanghai Haling Biotechnology Co., Ltd., origin: Shanghai, China) for blood routine test within 60 min. And the remaining of blood was centrifuged at 2500 r/min for 10 min to collect serum for later use. The blood samples of the control group were taken on the day of the physical examination and prepared in the same way.

The blood routine test was performed by using a fully automatic biochemical analyzer (AU-5800, Beckman Coulter company, USA), and platelet parameters such as platelet count (PLT), platelet distribution width (PDW), and mean platelet volume (MPV) were recorded, and PLT/lymphocyte (L) (PLR) was calculated.

Serum NSE level was detected by enzyme-linked immunosorbent assay method (kit: hj-C5926, Shanghai Lanpai Biotechnology Co., Ltd., China). Serum hs-CRP level was detected by immunoturbidimetry method (kit: Y70105-1, Zhejiang Yili Kang Biotechnology Co., Ltd., China). All procedures were operated by qualified technical personnel in accordance with the instruction of kits.

The TBI patients came to the hospital for further consultation or followed up by tele-visit 3 months after surgery. According to the condition of patients, Glasgow Outcome Scale (GOS) was filled by themselves or by the clinician to evaluate the prognosis of patients. GOS 4-5 indicted a good prognosis while GOS 1-3 indicated a poor prognosis. The mortality of patients was calculated.

Statistical analysis

Data analysis was performed by SPSS 20.0. Enumeration data were shown as cases/percentage (n/%) and the comparison between groups was performed by χ^2 test. Measurement

Table 1. General data of four groups (n, $\bar{x}$ ± sd)

Groups	Severe group (n=36)	Moderate group (n=45)	Mild group (n=21)	Control group (n=23)	χ^2/F	P
Gender (n)					1.256	0.522
Male	19	26	10	13		
Female	17	19	11	10		
Age (year)	42.3±2.5	43.1±3.1	43.6±2.9	42.9±3.2	0.975	0.407
BMI (kg/m^2)	22.83±1.42	23.12±1.29	23.40±1.57	22.57±1.10	1.700	0.171
Time from injury to admission (h)	2.45±1.04	2.14±0.87	1.93±0.70		2.408	0.095
Underlying diseases (n)					0.679	0.712
Hypertension	5	6	3	0		
Hyperlipemia	4	4	3	0		
Diabetes	2	1	1	0		
GCS score at admission (points)	4.78±0.98	10.45±1.70	13.55±2.28		218.703	<0.001

Note: BMI: body mass index; GCS: glasgow coma scale.

Table 2. Comparison of platelet parameter levels in four groups of patients ($\bar{x}$ ± sd)

Groups	PLT (*10^9/L)	PDW (fL)	MPV (fL)	PLR
Severe group (n=36)	107.56±18.19$^{**,\#\#,\Delta\Delta}$	16.08±2.54	10.47±1.10	234.38±43.90$^{**,\#\#,\Delta\Delta}$
Middle group (n=45)	128.95±24.32$^{**,\#}$	16.04±2.11	10.60±0.94	201.40±28.57$^{**,\#\#}$
Mild group (n=21)	141.09±21.40**	15.50±2.40	10.24±1.77	180.40±20.70**
Control group (n=23)	184.39±30.88	15.74±2.35	11.15±1.54	110.43±17.56
F	50.988	2.331	2.116	76.189
P	<0.001	0.078	0.102	<0.001

Note: PLT: platelet count; PDW: platelet distribution width; MPV: mean platelet volume; PLR: platelet/lymphocyte ratio. Compared with the control group, **P<0.01; compared with the mild group, $^{\#}$P<0.05, $^{\#\#}$P<0.01; compared with the moderate group, $^{\Delta\Delta}$P<0.01.

data were expressed as mean ± standard deviation ($\bar{x}$ ± sd). One-way ANOVA test was used for comparison among multiple groups, and post hoc analysis adopted LSD method. Spearman correlation analysis was used to analyze the correlation between platelet parameters, NSE, hs-CRP levels and GCS scores. Multivariate logistic regression analysis was performed by using platelet parameters, PLR, NSE, and hs-CRP as independent variables, and the prognosis of patients as the dependent variable. The difference was statistically significant when P<0.05.

Results

General data of four groups

There were no significant differences in gender, age, body mass index (BMI), and underlying diseases among the four groups (P>0.05). There was no significant difference in the time from injury to admission among the three groups of patients (P>0.05). But the GCS scores among the three groups of patients were statistically significant at admission (P<0.001). See **Table 1**.

Comparison of platelet parameter levels in four groups

The PLT levels and PLRs of the four groups were significantly different. Compared with the control group, TBI patients had significantly lower PLT level, but significantly higher PLR (both P<0.001). There was no significant difference in PDW and MPV among the four groups (P>0.05). See **Table 2**.

Comparison of serum NSE levels in four groups

The serum NSE level in the control group was 6.70±1.08 μg/L, which in the mild, moderate

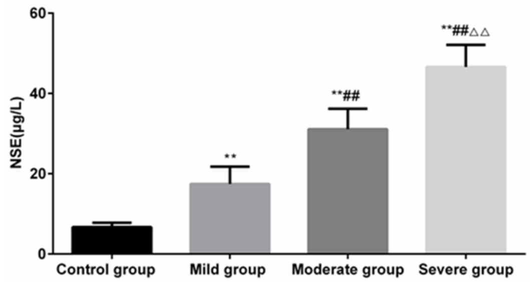

Figure 1. Comparison of serum NSE levels in four groups. NSE: neuron-specific enolase. Compared with the control group, **P<0.01; compared with the mild group, ##P<0.01; compared with the moderate group, △△P<0.01.

Table 3. Comparison of serum hs-CRP levels in four groups ($\bar{x}$ ± sd)

Groups	hs-CRP (mg/L)
Severe group (n=36)	49.75±5.80**,##,△△
Middle group (n=45)	33.08±5.26**,##
Mild group (n=21)	18.80±4.47**
Control group (n=23)	2.10±0.66
F	503.464
P	<0.001

Note: hs-CRP: high-sensitivity C-reactive protein. Compared with the control group, **P<0.01; compared with the mild group, ##P<0.01; compared with the moderate group, △△P<0.01.

Table 4. Spearman correlation analysis of preoperative platelet parameters, NSE, hs-CRP levels and GCS scores

Index	GCS scores	
	r	P
PLT	0.586	0.013
PDW	0.493	0.171
MPV	-0.184	0.223
PLR	-0.374	0.009
NSE	-0.320	0.018
hs-CRP	-0.705	0.030

Note: PLT: platelet count; PDW: platelet distribution width; MPV: mean platelet volume; PLR: platelet/lymphocyte ratio; NSE: neuron-specific enolase; hs-CRP: high-sensitivity C-reactive protein; GCS: Glasgow coma scale.

and severe groups were 17.47±4.29 μg/L, 31.09±5.10 μg/L, and 46.60±5.50 μg/L, respectively. There was a significant difference in serum NSE level among the four groups (P<0.01) and compared with the control group, the serum NSE level of TBI patients was significantly higher (P<0.01). See **Figure 1**.

Comparison of serum hs-CRP levels in four groups

There was a significant difference in serum hs-CRP level among the four groups (P<0.001). Compared with the control group, the serum hs-CRP level of TBI patients was significantly higher (all P<0.01). See **Table 3**.

Correlation between preoperative platelet parameters, NSE, hs-CRP levels and GCS scores

Spearman correlation analysis showed that PLT level was positively correlated with GCS scores (P=0.013), while PLR, NSE, and hs-CRP levels were negatively correlated with GCS scores (all P<0.05). PDW and MPV were not correlated with GCS scores (all P>0.05). See **Table 4**.

Predictive value of platelet parameters, NSE and hs-CRP levels before surgery on poor prognosis of patients 3 months after surgery

Three months after surgery, there were 65 patients with good prognosis and 37 patients with poor prognosis, including 4 deaths. Multivariate logistic regression analysis showed that PLT level was negatively correlated with poor postoperative prognosis (P=0.023), while PLR, NSE, hs-CRP levels were positively correlated with poor postoperative prognosis (all P<0.05). See **Table 5**.

Discussion

Based on the GCS scores of TBI patients, this study divided them into mild, moderate and severe groups. By comparison, the results showed that TBI patients had significantly lower PLT level but significantly higher PLR than the healthy subjects, especially those in the severe group with more obvious differences. These results indicated that PLT level and PLR were abnormal in patients with craniocerebral trauma, which was related to the severity of injury. After craniocerebral trauma, a large number of platelets are adhered to the constricted vessels and aggregated to participate in the coagulation, finally inducing thrombus [12]. Therefore, we speculate that the low PLT level in TBI patients may be caused by the heavy consumption of platelets in the body.

Table 5. Multivariate logistic regression analysis of patients with poor postoperative prognosis

Factor	Estimate of parameter	Standard error	Wald	P	OR	95% CI
PLT	-0.463	0.096	8.096	0.023	0.746	0.364-0.975
PDW	0.635	0.108	10.484	0.108	0.464	0.210-1.347
MPV	0.847	0.304	13.274	0.124	0.747	0.314-1.249
PLR	0.464	0.105	8.484	0.016	2.774	1.876-4.010
NSE	0.426	0.143	5.580	0.033	1.840	1.567-3.305
hs-CRP	0.590	0.294	7.609	0.041	1.968	1.776-4.394

Note: PLT: platelet count; PDW: platelet distribution width; MPV: mean platelet volume; PLR: platelet/lymphocyte ratio; NSE: neuron-specific enolase; hs-CRP: high-sensitivity C-reactive protein; OR: odd ratio; CI: confidence interval.

Normally, NSE is only expressed in neuronal cytoplasm and it accounts for about 40% to 65% of all enolase in human cerebral cortex [13]. Craniocerebral injury damages the integrity of the patient's nerve cell membrane. Afterwards, NSE can be released into the blood circulation via the damaged blood-brain barrier [14]. Therefore, high level of NSE can be detected in the serum and may be a predictor for the prognosis of patients with craniocerebral injury [15]. Some studies have pointed out that serum NSE level can increase sharply within 24 hours after craniocerebral injury, and reach a peak on the third day, and generally begin to decrease after 7 days [16]. Other studies also found that the serum level of NSE can reflect the damage range and severity to brain neurons, that is, high level of serum NSE indicates a severe brain tissue damage [17]. In addition, trauma is a kind of stress response, in which many inflammatory cytokines are involved and play important roles. Hs-CRP, a sensitive inflammatory marker, can be quickly synthesized and secreted in the liver, and largely released into the blood in the early stages of tissue damage. Hence, hs-CRP is also considered as an early marker of tissue damage, and its level is not changed by drugs, hormones, etc. [18]. Several studies have shown that serum hs-CRP levels have increased dramatically in posttraumatic patients [19, 20]. Our results were consistent with above studies. We found that compared with healthy subjects, TBI patients had significantly higher serum levels of NSE and hs-CRP, and the severe cases had highest level, indicating that the NSE and hs-CRP were released into the blood after brain injury, which may be sensitive markers to evaluate the condition of TBI patients.

Therefore, we then used Spearman correlation analysis to further explore the correlation between the above indicators and TBI disease progression. Our results showed that the PLT level was positively correlated with GCS scores, and PLR, NSE, and hs-CRP levels were negatively correlated with GCS scores, suggesting that PLT, PLR, NSE, and hs-CRP were closely related to the severity of TBI disease. These results are consistent with the findings of Galvagno et al [21]. Furthermore, we also analyzed the relationship between the above indicators and the patient's prognosis by multivariate logistic regression analysis. We found that PLT level was negatively correlated with poor postoperative prognosis, and PLR, NSE, hs-CRP levels were positively correlated with poor postoperative prognosis. The results indicated that TBI patients with low PLT level or high level of PLR, serum NSE, or serum hs-CRP before operation are in great possibility to have poor prognosis after operation. However, the research indicators were not sufficiently analyzed as we only evaluated one inflammatory factor. Moreover, the related mechanisms haven't been explored. Therefore, further studies are needed to verify our findings.

In conclusion, TBI patients with low PLT level and high levels of PLR, serum NSE and serum hs-CRP are regarded to be in severe condition and have poorer prognosis.

Disclosure of conflict of interest

None.

Address correspondence to: Xianjiang Zhang, Department of Critical Care Medicine, Xuzhou Central Hospital, No. 199 Jiefang South Road, Xuzhou 221002, Jiangsu Province, China. Tel: +86-0516-80812338; Fax: +86-0516-80812338; E-mail: zhangxianjiang6u8x@tom.com

References

[1] Edlow BL, Chatelle C, Spencer CA, Chu CJ, Bodien YG, O'Connor KL, Hirschberg RE, Hochberg LR, Giacino JT, Rosenthal ES and Wu O.

Early detection of consciousness in patients with acute severe traumatic brain injury. Brain 2017; 140: 2399-2414.

[2] Stocchetti N, Carbonara M, Citerio G, Ercole A, Skrifvars MB, Smielewski P, Zoerle T and Menon DK. Severe traumatic brain injury: targeted management in the intensive care unit. Lancet Neurol 2017; 16: 452-464.

[3] Przybycien-Szymanska MM, Yang Y and Ashley WW. Microparticle derived proteins as potential biomarkers for cerebral vasospasm post subarachnoid hemorrhage. A preliminary study. Clin Neurol Neurosurg 2016; 141: 48-55.

[4] Glass HC. Hypoxic-Ischemic encephalopathy and other neonatal encephalopathies. Continuum (Minneap Minn) 2018; 24: 57-71.

[5] Jing LU, Zou Z and Zhuang G. Comparison on thromboelastography and conventional coagulation tests for evaluating blood coagulation function in elderly patients with asymptomatic cerebral infarction. Lab Med 2017; 32: 663-667.

[6] Srinivas B, Maldar A, Bellad A and Mukhi N. Relation of neutrophilic lymphocyte ratio to microvascular complications of diabetes mellitus. IJHSR 2015; 5: 34-38.

[7] Hsueh C, Tao L, Zhang M, Cao W, Gong H, Zhou J and Zhou L. The prognostic value of preoperative neutrophils, platelets, lymphocytes, monocytes and calculated ratios in patients with laryngeal squamous cell cancer. Oncotarget 2017; 8: 60514-60527.

[8] Gao Y, Wang WJ, Zhi Q, Shen M, Jiang M, Bian X, Gong FR, Zhou C, Lian L, Wu MY, Feng J, Tao M and Li W. Neutrophil/lymphocyte ratio is a more sensitive systemic inflammatory response biomarker than platelet/lymphocyte ratio in the prognosis evaluation of unresectable pancreatic cancer. Oncotarget 2017; 8: 88835-88844.

[9] Zhai MM, Wang JP, Yu L, Fu XJ and Li LY. Neutrophil and lymphocyte ratios for the predictive analysis of the prognosis in patients with acute cerebral infarction. Chin J Cerebrovasc Dis 2017; 14: 82-86.

[10] Ponschab M, Schlimp CJ, Zipperle J, Gabriel C, Sussner S, Cadamuro J, Gratz J, Redl H and Schochl H. Platelet function in reconstituted whole blood variants: an observational study over 5 days of storage time. J Trauma Acute Care Surg 2015; 79: 797-804.

[11] Juengst SB, Kumar RG, Failla MD, Goyal A and Wagner AK. Acute inflammatory biomarker profiles predict depression risk following moderate to severe traumatic brain injury. J Head Trauma Rehabil 2015; 30: 207-218.

[12] Hayon Y, Shai E, Varon D and Leker RR. The role of platelets and their microparticles in rehabilitation of ischemic brain tissue. CNS Neurol Disord Drug Targets 2012; 11: 921-925.

[13] Liu XH, Zhang Y and Liu CK. Expression of neuron-specific enolase and synaptophysin in esophageal development of human embryos. Zhejiang Da Xue Xue Bao Yi Xue Ban 2015; 44: 184-188.

[14] Pratamastuti D, Indra Gunawan P and Saharso D. Serum neuron specific enolase is increased in pediatric acute encephalitis syndrome. Korean J Pediatr 2017; 60: 302-306.

[15] Wiberg S, Kjaergaard J, Kjaergaard B, Moller B, Nornberg B, Sorensen AM, Hassager C and Wanscher M. The biomarkers neuron-specific enolase and S100b measured the day following admission for severe accidental hypothermia have high predictive values for poor outcome. Resuscitation 2017; 121: 49-53.

[16] Mokhtari M, Nayeb-Aghaei H, Kouchek M, Miri MM, Goharani R, Amoozandeh A, Akhavan Salamat S and Sistanizad M. Effect of memantine on serum levels of neuron-specific enolase and on the glasgow coma scale in patients with moderate traumatic brain injury. J Clin Pharmacol 2018; 58: 42-47.

[17] Liu YY, Ma JJ, Li J and Jia RC. The relationship between neuron-specific enolase and prognosis of patients with acute traumatic brain injury. Chin J Contemp Neurol Neurosurg 2015; 15: 235-239.

[18] Hod K, Dickman R, Sperber A, Melamed S, Dekel R, Ron Y, Halpern Z, Berliner S and Maharshak N. Assessment of high-sensitivity CRP as a marker of micro-inflammation in irritable bowel syndrome. Neurogastroenterol Motil 2011; 23: 1105-1110.

[19] Chen W, Tan Y, Ge Y, Chen Y and Liu X. The effects of levetiracetam on cerebrospinal fluid and plasma NPY and GAL, and on the components of stress response system, hs-CRP, and S100B protein in serum of patients with refractory epilepsy. Cell Biochem Biophys 2015; 73: 489-494.

[20] Wang J, Chen C and Zhao L. Effects of propofol combined with remifentanil on the levels of MBP,NSE and S100B protein, D-D and inflammatory factors in patients with acute craniocerebral trauma. J Hainan Med Univ 2017; 23: 63-66.

[21] Galvagno SM Jr, Fox EE, Appana SN, Baraniuk S, Bosarge PL, Bulger EM, Callcut RA, Cotton BA, Goodman M, Inaba K, O'Keeffe T, Schreiber MA, Wade CE, Scalea TM, Holcomb JB and Stein DM. Outcomes after concomitant traumatic brain injury and hemorrhagic shock: a secondary analysis from the pragmatic, randomized optimal platelets and plasma ratios trial. J Trauma Acute Care Surg 2017; 83: 668-674.