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

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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 cranio-cerebral injury can induce an inflammatory response within 15 min in the body, leading to the corre-
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Responding 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 NSE 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 consultation 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 χ² test. Measurement
data were expressed as mean ± standard deviation (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 trauma to admission among the three groups of patients (P>0.05). 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...
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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, and 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.
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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.

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

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

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.

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.

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