Analysis of Risk Factors of Intracranial Infection After Traumatic Brain Injury Surgery

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Background: Craniocerebral operation is the main method for the treatment of traumatic brain injury. However, it is very easy to be complicated with intracranial infection after operation, which affects the surgical efficacy and patient's prognosis. It is also the main cause of surgical failure. It may also cause patient's death for some patients with serious diseases. It is found that the infection after craniocerebral operation is often accompanied with abnormal changes of body-related treatment, in which the changes of serological indicators are more significant. Therefore, it is helpful to provide guidance for the prevention and judgment of patient's postoperative infection by analyzing the patient's serological indicators.

Objective: To investigate the risk factors of intracranial infection and the levels of serum procalcitonin (PCT) and endothelin-1 (ET-1) in patients after traumatic brain injury.

Methods: From January 2018 to January 2021, 58 patients with intracranial infection after traumatic brain injury (infection group) were selected, and 116 patients without intracranial infection after traumatic brain injury (non-infection group) were selected. The difference of clinical data between the two groups was analyzed. Serum PCT and ET-1 levels were measured in the two groups.

Results: In the infection group, admission GCS scoring <8 points, operation time ≥ 4h, indwelling time of drainage tube ≥ 2d, preoperative ALB <35g/ L, mechanical ventilation and cerebrospinal fluid leakage were 63.79%, 72.41%, 43.10%, 68.97%, 32.76% and 68.97% respectively, which were obviously higher than those in the non-infection group (P<0.05). Logistic regression analysis results showed that admission GCS scoring, operation time, indwelling time of drainage tube, preoperative ALB, mechanical ventilation and cerebrospinal fluid leakage were the influencing factors of intracranial infection after traumatic brain injury (OR = 0.712, 1.556, 1.451, 0.641, 1.954 and 1.667, P<0.05); serum PCT and ET-1 in the infection group were (0.83 ± 0.20) mg/L and (0.87 ± 0.23) ng/L, respectively, which were significantly higher than those in the non-infection group (P<0.05); serum PCT and ET-1 in patients with different sex, age and pathogen had no significant difference (P>0.05); serum PCT and ET-1 area under ROC curve were 0.828 and 0.751, respectively P<0.05.

Conclusion: The intracranial infection of patients with traumatic brain injury are affected by many factors including, admission GCS scoring, operation time, and so on, the levels of serum PCT and ET-1 in patients with intracranial infection are increased, which may be useful in predicting intracranial infection.

Keywords: Traumatic brain injury; Intracranial infection; Risk factors; Procalcitonin; Endothelin-1
Tob Regul Sci.™ 2021;7(5-1): 3161-3167
DOI: doi.org/10.18001/TRS.7.5.1.88

Procalcitonin (PCT), which has good stability and is not easy to degrade, can be easily detected and secreted without the influence of various hormones in the body. It is now recognized as a marker of inflammatory reaction caused by bacterial infection

and has been widely used in the diagnosis of bacterial infectious diseases with high sensitivity and specificity [1-2]. Endothelin-1 (ET-1), which is mainly derived from vascular endothelial cells, participates in the occurrence and development of cardio-cerebral vascular injury by mediating the release of multiple inflammatory mediators, and is the most persistent and intense vasoconstrictor known at present [3]. This study discusses the risk factors, serum PCT, ET-1 level and significance of intracranial infection in patients after traumatic brain injury (TBI) surgery. The aim of this study is to provide new ideas for the prevention and evaluation of intracranial infection in patients after TBI surgery.

DATA AND METHODS

General data

From January 2018 to January 2021, 58 patients with intracranial infection after traumatic brain injury surgery (infection group) were selected and 116 patients without intracranial infection after traumatic brain injury surgery (non-infection group) were selected; inclusion criteria: (1) Craniotomy was performed in our hospital; (2) Intracranial infection met the criteria in "Diagnostic Criteria for Nosocomial Infection" [4]; (3) There was a definite history of traumatic injury; (4) The patients were older than 18 years; (5) The time from injury to admission was <24h; (6) The clinical data were kept intact. Exclusion criteria: (1) Patients who gave up treatment; (2) Patients with infection at other sites before operation; (3) Patients with malignant tumor, liver and kidney dysfunction and immune system disease. There was no significant difference in gender, age and body mass index between infection group and non-infection group (P>0.05). See Table 1.

Test method

Fasting venous blood was collected from all patients on postoperative day 1, and serum was separated after centrifugation at 3000 r/min. Serum PCT levels were measured and compared by quantitative immunoassay. Serum ET-1 levels were measured by enzyme-linked immunosorbent assay (ELISA). Enzyme-labeled analyzer was purchased from GE Inc., and relevant kits were provided by Shanghai Institute of Materia Medica.

Statistical processing

SPSS 22.0 software was used for data analysis. Normal distribution measurement data was expressed as ($\bar{\chi} \pm s$), and t test was used for comparison between groups. Count data was expressed as frequency or percentage, and χ^2 test was used for comparison between groups. Logistic regression analysis was used for multi-factor analysis, and ROC curve was used for prediction value. P<0.05 indicates that the difference is statistically significant.

RESULTS

Single factor analysis of infection group and non-infection group

In the infection group, the proportion of patients with admission GCS scoring < 8 points, operation time ≥ 4h, indwelling time of drainage tube ≥ 2d, preoperative ALB <3 5g/L, mechanical ventilation and cerebrospinal fluid leakage was significantly higher than that in the non-infection group (P<0.05). See Table 2.

Single factor analysis

Logistic regression analysis was performed with the above mentioned statistically significant indicators as independent variables and whether intracranial infection occurred OR not as dependent variables. The results showed that: admission GCS scoring, operation time, placing time of drainage tube, preoperative ALB, mechanical ventilation and cerebrospinal fluid leakage were the influencing factors of postoperative complicated intracranial infection after traumatic brain injury surgery (OR = 0.712, 1.556, 1.451, 0.641, 1.954 and 1.667, P <0.05), see Table 3.

Comparison of serum PCT and ET-1 between the infection group and the non-infection group

Serum PCT and ET-1 in the infection group were significantly higher than those in the non-infection group (P<0.05). See Table 4.

Comparison of serum PCT and ET-1 levels in patients with infection of difference gender, age and pathogen

There was no significant difference in serum PCT and ET-1 between patients with different gender, age and pathogens (P>0.05). See Table 5.

Value of serum PCT and ET-1 in predicting intracranial infection

The area under the ROC curve of PCT and ET-1 in predicting intracranial infection were 0.828 and 0.751, respectively (P<0.05). See Figure 1. See Table 6 for specific parameters.

DISCUSSION

After craniocerebral injury, pathogenic bacteria can enter the skull and cause intracranial infection, which is a common way of intracranial infection. There are four main ways to cause intracranial infection [5-8]: (1) Direct infection, which refers to the direct opening of the brain to the outside world due to external causes, which causes the bacteria to enter the skull and cause intracranial infection; (2) Iatrogenic infection, if the patient's skull is opened during the surgery, the disinfection is not strict or iatrogenic treatment causes the patient's intracranial infection; (3) The infection at the adjacent site spreads, such as otitis media, sinusitis has acute infection, the bacteria will spread to the intracranial and cause the infection; (4) The blood-borne infection, if the bacteria are more virulent and the patient's resistance is poor, the bacteria will enter the intracranial infection through the blood circulation, causing the intracranial infection, both of them can seriously affect the effect and prognosis of surgical treatment. The results of this study showed that the proportion of patients with admission GCS scoring < 8 points, operation time ≥ 4h, indwelling time of drainage tube ≥ 2d, preoperative ALB <3 5g/L, mechanical ventilation and cerebrospinal fluid leakage was significantly higher than that in the non-infection group. The results also suggested that patients with long-term craniocerebral operation had more influencing factors of craniocerebral infection. Therefore, the treatment and prognosis of intracranial infection after craniocerebral injury are crucial to reduce the incidence of complications and improve the quality of life of patients.

Further factor analysis showed that admission GCS scoring, operation time, placing time of drainage tube, preoperative ALB, mechanical ventilation and cerebrospinal fluid leakage were the influencing factors of intracranial infection after traumatic brain injury surgery. The prolonged exposure time of brain tissue caused by prolonged operation time may increase the bacterial infection rate; the admission GCS scoring and the ALB before operation are the important indexes to evaluate the patient's status and immune function; the patients with poor body state and immune ability are more likely to have intracranial infection; the clinical application of ventilator is more likely to increase the possibility of nosocomial infection of patients receiving invasive mechanical ventilation, so the possibility of intracranial infection of patients is also significantly increased; cerebrospinal fluid leakage can severely impair the patient's blood-brain barrier, resulting in a significantly increased risk of bacterial invasion [9-13]. According to the risk factors of intracranial infection, the author thinks that it is necessary to take corresponding prevention and treatment strategies in time: (1) To improve the quality and success rate of operation as much as possible, shorten the operation time and avoid secondary operation; (2) To strengthen the monitoring of cerebrospinal fluid during operation; (3) To avoid invasive ventilation and strengthen the prevention of complications such as cerebrospinal fluid leakage according to the patient's specific condition.

PCT is rapidly synthesized and secreted when severe bacterial, fungal and parasitic infections and multi-organ failure occur in the body, whereas PCT levels are not elevated when allergic and autoimmune and viral infections occur, and therefore have high PCT for bacterial infections [14-15]. ET-1 is a marker of impaired endothelial function that is synthesized and released during tissue ischemia-hypoxia and endothelial injury. Since intracranial infections often cause cerebrovascular dysfunction, ET-1 has the potential to assess and diagnose intracranial infections [16]. The results of this study showed that the serum PCT and ET-1 levels in the infection group were

significantly higher than those in the non-infection group, but there were no significant differences in the serum PCT and ET-1 levels among the patients of different genders and ages. These results suggest that there is a significant increase of PCT and vascular endothelial function in intracranial infection, which may be caused by the injury of blood-brain barrier and cerebral blood vessel in severe patients caused by intracranial infection and intracranial injury, which promotes the entry of PCT and the secretion of ET-1. In addition, craniocerebral injury is a condition in which ET-1 further stimulates the secretion of ET-1 by vascular endothelial cells from the spilled, ischemic and hypoxic cerebral vessels, resulting in an increase in serum ET-1 levels in intracranial infections [17-18,21].

The area under value ROC curve where serum PCT and ET-1 predicting intracranial infection was 0.828 and 0.751. These results suggested that serum PCT and ET-1 had high clinical value in predicting intracranial infection, with specificity and sensitivity. The prevention and treatment of intracranial infection in craniocerebral injury surgery is an important direction for clinical treatment. Similar study aimed at the dynamic monitoring of cerebrospinal fluid PCT level in patients with intracranial infection found that the level of cerebrospinal fluid PCT gradually decreased in patients with better control of infection, while the treatment PCT was still at a higher level than that in patients with difference of treatment effect. This result was also consistent with the results of this study.

In conclusion, the intracranial infection of patients with traumatic brain injury are affected by many factors including, admission GCS scoring, operation time, and so on, the levels of serum PCT and ET-1 in patients with intracranial infection are increased, which may be useful in predicting intracranial infection.

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Table 1.
Comparison of General Data for Infection and Noninfection groups

Group	cases	male/female	age（year）	Body mass index（kg/m²）
Infection group	58	33/25	59.64±6.63	22.24±2.61
Non infection group	116	75/41	58.03±7.12	22.10±2.34
t/c^2		0.989	1.438	0.358
P		0.32	0.152	0.721

Table 2.
Single factor analysis of infection groups and infection - free groups

Clinical data	Infection group（n=58）	Non infection group（n=116）	t/c^2	*P*
GCS score on admission				
≥8 points	21(36.21)	85(73.28)	22.317	0.000
＜8 points	37(63.79)	31(26.72)		
operation time				
＜4h	16(27.59)	79(68.1)	25.607	0.000
≥4h	42(72.41)	37(31.9)		
Intraoperative blood loss				
＜100ml	27(46.55)	57(49.14)	0.104	0.748
≥100ml	31(53.45)	59(50.86)		
Indwelling time of drainage tube				
＜2d	33(56.9)	101(87.07)	19.883	0.000
≥2d	25(43.1)	15(12.93)		
Preoperative Hb				
＜110g/L	21(36.21)	38(32.76)	0.205	0.651
≥110g/L	37(63.79)	78(67.24)		
Preoperative ALB				
＜35g/L	40(68.97)	45(38.79)	14.088	0.000
≥35g/L	18(31.03)	71(61.21)		
Mechanical ventilation				
Yes	19(32.76)	14(12.07)	10.770	0.001
No	39(67.24)	102(87.93)		
Cerebrospinal fluid leakage				
Yes	40(68.97)	47(40.52)	12.517	0.000
No	18(31.03)	69(59.48)		
complications				
diabetes	10(17.24)	15(12.93)	0.584	0.445
hypertension	22(37.93)	38(32.76)	0.458	0.499

Table 3.
Multi - factor analysis results

Factor	b	SE	Walds	*P*	OR (95%CI)
GCS score on admission	-0.340	0.112	9.216	0.000	0.712（0.571～0.886）
operation time	0.442	0.124	12.706	0.000	1.556（1.220～1.984）
Indwelling time of drainage tube	0.372	0.101	13.566	0.000	1.451（1.190～1.768）

Preoperative ALB	-0.445	0.143	9.684	0.000	0.641（0.484～0.848）
Mechanical ventilation	0.670	0.211	10.083	1.000	1.954（1.292～2.955）
Cerebrospinal fluid leakage	0.511	0.154	11.010	2.000	1.667（1.233～2.254）

Table 4.
Serum PCT、ET-1 Comparison among Infection and Infection - free Groups

Group	cases	PCT（mg/L）	ET-1（ng/L）
Infection group	58	0.83±0.20	0.87±0.23
Non infection group	116	0.61±0.19	0.70±0.19
t		7.075	5.179
P		0.000	0.000

Table 5.
Serum PCT、ET-1 comparison of people infected with different gender, age and pathogens

Group	**cases**	**PCT（mg/L）**	**ET-1（ng/L）**
Sex			
Male	33	0.82±0.14	0.86±0.18
Female	25	0.84±0.13	0.88±0.20
t		-0.555	-0.399
P		0.581	0.691
Age			
＜60 years	27	0.85±0.18	0.89±0.14
≥60 yesrs	31	0.81±0.13	0.85±0.16
t		0.979	1.006
P		0.332	0.319
Pathogenic bacteria			
Staphylococcus aureus	22	0.82±0.16	0.85±0.18
pneumococci	19	0.83±0.14	0.89±0.21
other	17	0.84±0.15	0.87±0.17
F		1.022	0.782
P		0.544	0.821

Table 6.
ROC Curve Parameters

Index	**Area under curve**	***P***	**Cutoff value**	**sensitivity（%）**	**specificity（%）**
PCT	0.828	0.000	0.78 mg/L	82.50%	66.00%
ET-1	0.751	0.000	0.82 ng/L	52.50%	86.00%

Figure 1.
ROC Curve Drawing