

Original Article

Study on risk factors and preventive measures regarding intracranial infection in patients with traumatic brain injury

Shenghong Ding, Jianyue Huang

Department of Neurosurgery, Yiwu Central Hospital, Yiwu City, Zhejiang Province, China

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Abstract: Objective: The present study was designed to investigate the incidence and risk factors for postoperative intracranial infection after traumatic brain injury (TBI), with the aim of providing some theoretical bases for the preventive measures against this infection. Methods: The study retrospectively analyzed the clinical data of a total of 500 patients with TBI who received treatment in the department of neurosurgery in our hospital from January 2011 to July 2017. The clinical data of patients with or without intracranial infection (infection group vs. non-infection group) were collected and analyzed, which included age, gender, cause of TBI, preoperative Glasgow coma score (GCS), admission diagnosis, and type of organism causing the intracranial infection, for the purpose of determining the risk factors for postoperative intracranial infection after TBI. Results: A total of 30 patients (6.00%, 30/500) were diagnosed with postoperative intracranial infection, most of which occurred between 4th and 10th day after operation. Factors including advanced age, preoperative GCS \geq 8, open TBI, cerebrospinal fluid (CSF) leakage, multiple craniotomies were all correlated with the infection (all $P < 0.05$). The logistic regression analysis showed that CSF leakage was an independent risk factor for postoperative intracranial infection after TBI. Conclusion: Intracranial infection is considered as one of the serious complications of TBI, while patients with CSF leakage are at the greatest risk of being infected. Therefore, it is important to take effective preventive measures for this group of patients in order to avoid intracranial infection.

Keywords: Traumatic brain injury, intracranial infection, risk factors, prevention

Introduction

Traumatic brain injury (TBI) is a global public health issue [1]. Due to the advances in medical technology and standardized treatment, the prognosis of this disease has been improved significantly. However, intracranial infections including meningitis, encephalitis, and brain abscesses are still common complications after TBI. The infection needs to be treated in a timely and effective manner; otherwise it could seriously affect the prognosis of TBI, prolong hospital length of stay, increase psychological and financial burden on patients and their families, and even endanger patients' lives [2-7].

Although the progress of surgical techniques and the implementation of standardized preventive measures have brought about a reduction in the incidence of intracranial infection

after TBI, researchers in neurosurgery are still exploring ways to further reduce this incidence. Therefore, the present study retrospectively analyzed the clinical data of a total of 500 patients with TBI, in an effort to explore the risk factors for postoperative intracranial infection after craniocerebral trauma, provide theoretical bases for the preventive measures against this infection, and find ways to reduce the infection incidence.

Materials and methods

Patients

The study protocol was reviewed and approved by the Ethics Committee of Yiwu Central Hospital. Informed consents were obtained from all participants. A total of 500 patients with TBI who received treatment in the depart-

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Table 1. Demographic information and clinical characteristic of patients with TBI

Variable	
Age (years), range (mean \pm sd)	16-75 (43.8 \pm 8.4)
Gender, n (%)	
Male	340 (68.0)
Female	160 (32.0)
Causes of TBI, n (%)	
MVA	355 (71.0)
Fall	75 (15.0)
Assault	30 (6.0)
Others	40 (8.0)
Preoperative GCS, n (%)	
3-5	120 (24.0)
6-8	215 (43.0)
9-12	110 (22.0)
13-15	55 (11.0)
Admission diagnoses, n (%)	
Intracerebral hematoma	235 (47.0)
Subdural hematoma	155 (31.0)
Epidural hematoma	60 (12.0)
Others	50 (10.0)

Note: TBI, traumatic brain injury; MVA, motor vehicle accident; GCS, Glasgow coma score.

ment of neurosurgery in our hospital from January 2011 to July 2017 were recruited for the study. Inclusion criteria were as follows: patients aged 18 years and above; patients with TBI were admitted within 24 hours; patients had no serious complications, such as cardiac, pulmonary, hepatic or kidney dysfunction. Exclusion criteria were: patients had multiple injuries; patients had contraindications for craniotomy; patients had infectious diseases, including hepatitis B, hepatitis C, syphilis and HIV infection.

Diagnostic criteria for intracranial infection

The diagnostic criteria for intracranial infection were based on the literature by Kourbeti et al., which were as follows: 1) patients had postoperative symptoms including fever, headache, nausea, vomiting, loss of consciousness, and meningeal irritation signs; 2) leukocyte count in cerebrospinal fluid (CSF) $\geq 1.0 \times 10^6/L$, in which neutrophil $< 50\%$, and peripheral blood leukocyte count $\geq 1.0 \times 10^9/L$; 3) CSF protein quantification > 450 mg/L, and glucose quantification < 400 mg/L; 4) CSF bacterial culture was positive [8].

CSF bacteria culture

CSF samples were collected and placed in two culture tubes which contained Todd-Hewitt broth (Oxoid, Hampshire, United Kingdom) and were supplemented with gentamicin (8 $\mu\text{g/mL}$) and nalidixic acid (15 $\mu\text{g/mL}$). After being incubated at 33-37°C for 18 to 24 h in a 5% CO_2 atmosphere, the cultures were streaked on 5% sheep blood agar plates and then being incubated again in the same environment for the same period of time.

Statistical analysis

SPSS 17.0 statistics software was applied for the data analysis. All measurement data were expressed as mean \pm standard deviation and the categorical data as ratio or percentage. Differences in measurement data between groups were compared by paired t test, while differences in categorical data were compared by χ^2 test. Multiple logistic regression analysis was conducted to evaluate possible risk factors for intracranial infection. $\alpha=0.05$ was set as the statistical significance level.

Results

Demographic information and clinical characteristic of patients with TBI

There were 340 (68.0%) male patients and 160 (32.0%) female patients, who were aged between 16-75 years (43.8 \pm 8.4 years). The causes of TBI were motor vehicle accident (MVA), fall, assault, etc. The most common cause was MVA, which accounted for 71.0% (355/500). Admission diagnoses included intracerebral hematoma, subdural hematoma, epidural hematoma, etc. The intracerebral hematoma was the most common diagnosis, which accounted for 47.0% (235/500). The demographic information and patients' characteristics can be seen in **Table 1**.

Incidence of intracranial infection

Among all the 500 patients, 30 patients (6.00%, 30/500) were diagnosed with postoperative intracranial infection. It can be seen from **Figure 1** that most of the infections occurred between 4th and 10th day after operation, while the last occurrence of intracranial infection was on the 15th day.

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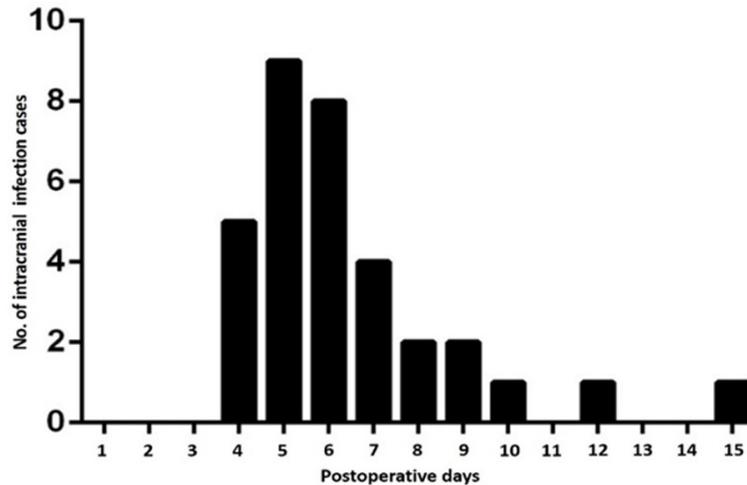


Figure 1. Postoperative incidence of intracranial infection among patients with TBI. TBI, traumatic brain injury.

Table 2. Bacterial species which caused intracranial infection

Organism	n	Percentage (%)
Gram-positive		
Staphylococcus aureus	11	36.7
Staphylococcus epidermidis	4	13.3
Enterococcus	3	10.0
Others	2	6.7
Gram-negative		
Escherichia coli	6	20.0
Klebsiella Pneumoniae	3	10.0
Enterobacter aerogenes	1	3.3
Others	1	3.3

Bacterial species which caused intracranial infection

As shown in **Table 2**, the most common gram-positive bacteria that caused the intracranial infection were *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Enterococcus*, whereas the most common gram-negative bacteria were *Escherichia coli*, *Klebsiella Pneumoniae*, and *Enterobacter aerogenes*.

Univariate analysis of risk factors

The following items were included as possible risk factors for the univariate analysis, which were age, preoperative Glasgow coma score (GCS), open TBI, CSF leakage, number of craniotomy, and postoperative albumin level. The result showed that factors such as advanced age, preoperative GCS \geq 8, open TBI, CSF leak-

age, and multiple craniotomies were all correlated with the postoperative intracranial infection (all $P < 0.05$, **Table 3**).

Multivariate logistic regression analysis of risk factors

As shown in **Table 4**, the multivariate logistic regression analysis demonstrated that CSF leakage (OR=2.077, $P=0.007$) was independent predictor of intracranial infection. The analysis found no association between intracranial infection and advanced age, preoperative GCS, open TBI, and multiple craniotomies (all $P > 0.05$).

Discussion

The postoperative intracranial infection among patients with TBI can be classified into two types: infective and non-infective infection. For the former one, the primary infectious agents are bacteria, whereas the latter one is mainly caused by patient's own inflammation or autoimmune response [9]. Postoperative intracranial infection can result in poor clinical outcomes, cognitive dysfunction, and high mortality [10, 11]. Therefore, it would be of great significance to study on the risk factors and preventive measures regarding this type of infection.

The present study showed that the incidence of postoperative intracranial infection was 6.00%. This result was consistent with previous studies which reported an incidence rate of postoperative intracranial infection from 0.8% to 7% in various neurosurgical procedures in which patients received preoperative antibiotics prophylactically [12-14]. In the present study, we found that *Staphylococcus aureus* was the most common pathogen, which caused 36.7% cases of intracranial infection. The result was similar to those in previous research, which documented that *Staphylococcus aureus* accounted for approximately 50% cases of infection [15-18]. The slight variation might be due to the differences in the types of surgical procedure and institutions. For example, the infection discussed in the study by Apisarnthanarak et al. was related to the spine surgery [15]. All previous studies were conducted in western

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Table 3. Univariate analysis of risk factors for intracranial infection

Risk factors	Infection group (n=30)	Non-infection group (n=470)	X ²	P
Age (years)			47.550	0.000
<60	14	426		
≥60	16	44		
Preoperative GCS			5.968	0.015
<8	14	321		
≥8	16	149		
Open TBI			0.450	0.502
Yes	10	130		
No	20	340		
CSF leakage			17.910	0.000
Yes	10	38		
No	20	432		
Number of craniotomy (n)			130.300	0.000
Single	3	420		
Multiple	27	50		
Postoperative albumin level (g/L)			7.386	0.007
<25	4	12		
≥25	26	458		

Note: TBI, traumatic brain injury; GCS, Glasgow coma score; CSF, cerebrospinal fluid.

Table 4. Multivariate logistic regression analysis of risk factors for intracranial infection

Risk factors	B value	OR value	95% CI	P value
Age	2.950	1.795	0.732-3.325	0.785
Preoperative GCS	1.315	1.525	0.765-2.677	0.315
Open TBI	1.077	0.997	0.133-2.135	0.917
CSF leakage	1.456	2.077	1.557-4.567	0.009
Number of craniotomy	1.011	1.745	0.745-2.768	0.877

Note: TBI, traumatic brain injury; GCS, Glasgow coma score; CSF, cerebrospinal fluid; CI, confidence interval.

countries, whereas our research was performed in China.

The study showed that patients with intracranial infection were much older than those without infection. The immune systems in patients who are advanced in age are usually more weakened, resulting in increased susceptibility to invasive organisms [19]. The preoperative GCS in patients with intracranial infection was significantly lower than that in patients without infection. GCS is indicative of the severity of brain injury. The more severe the brain injury, the more significantly the immune capacity declines, causing patients to be vulnerable to pathogen invasion, and increasing the probability

of concurrent intracranial infection [20, 21]. In addition, the incidence of open TBI in patients with intracranial infection was significantly higher than that in patients without infection. Open TBI can create access for pathogens from outside to enter cranial cavity, thus increasing the incidence of intracranial infection. CSF leakage indicates the existence of connectivity between external environment and cranial cavity, which can harm body's physiological barrier, and increase the chance of infection [22]. The study showed that the number of craniotomy among patients with intracranial infection was significantly higher than that in patients without infection. Complications related to the craniotomy include retention of fluid and later swelling of the brain tissue. Some studies found that patients who underwent more craniotomies

would have higher chances of getting intracranial infection [23, 24]. The serum albumin level in patients with intracranial infection after operation was significantly lower than that in patients without infection. Previous research has demonstrated that the nutritional status determined by serum albumin levels was important for immune functions [25]. Therefore, malnutrition can contribute to the decline of immune response, which increases the probability of infection.

The multivariate logistic regression analysis displayed that CSF leakage was an independent predictor of intracranial infection in patients with TBI. Therefore, in order to prevent

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intracranial infection, the following preventive measures would be necessary: 1) signs and symptoms of intracranial infection should be closely monitored, such as fever, purulent drainage, mental status change, headache, swelling, and seizure; 2) aseptic protocols and procedures should be strictly followed; visits should be limited in order to prevent and control the occurrence of cross infection; 3) pressure bandage needs to be applied to control CSF leakage; 4) perioperative antibiotics need to be used prophylactically; 5) malnutrition should be treated with nutritional support.

There were still some limitations in the present study. For example, the study was conducted at only one hospital, which meant that multi-centered studies may be needed to verify the results. Besides, the data regarding the follow-up were not collected for studying the short-term and long-term prognosis. Thus, further studies would be necessary for further verification.

In conclusion, intracranial infection is considered as a serious complication after TBI, while patients with CSF leakage are at the greatest risk of being infected. Therefore, effective preventive measures should be taken for this group of patients to avoid the infection.

Disclosure of conflict of interest

None.

Address correspondence to: Shenghong Ding, Department of Neurosurgery, Yiwu Central Hospital, No. 699 Jiangdong Road, Yiwu City 322000, Zhejiang Province, China. Tel: +86-0579-8520-9811; Fax: +86-0579-85209811; E-mail: dingshenghong2337@163.com

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