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Original Article

Risk factors and nursing strategies for multidrug-resistant organism infections in craniocerebral injury complicated with pulmonary infection

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Abstract: Objective: To explore the risk factors and nursing strategies for multidrug-resistant organism (MDRO) infection in craniocerebral injury complicated with pulmonary infection. Methods: A total of 112 patients with craniocerebral injury complicated with pulmonary infection in the ICU were selected for this prospective study, including 39 patients with MDRO infection and 73 patients with non-MDRO infection. The white blood cell count, serum procalcitonin (PCT), C-reactive protein levels and the distribution of MDRO in different years were determined and the risk factors associated with MDRO infection were investigated. Results: The PCT and C-reactive protein in the MDRO infection group were higher than those in the non-MDRO infection group (all $P < 0.05$). At the same time, there were differences in the distribution of MDRO pathogenic bacteria in different years ($P < 0.05$). Multivariate regression analysis found that age, invasive procedures before infection, multiple injuries, open injury, smoking history and elevated PCT were independent risk factors for MDRO infection in patients with craniocerebral injury complicated with pulmonary infection ($P < 0.05$). Conclusion: The pathogenic bacteria of MDRO occurring from craniocerebral injury complicated with pulmonary infection were mainly carbapenem-resistant acinetobacter baumannii and carbapenem-resistant enterobacteriaceae. The distribution of infectious bacteria differed from year to year. Age, invasive operation before infection, multiple injuries, open injury, smoking history and elevated PCT were the independent risk factors for MDRO infection in patients with malignancy.

Keywords: Craniocerebral injury, pulmonary infection, multidrug-resistant organism, distribution characteristics, risk factors

Introduction

Craniocerebral injury is an injury to the skull and brain caused by external violence. If the injury makes the patient unconscious for more than 6 hours, it is clinically regarded as a severe craniocerebral injury [1, 2]. As a critical illness with a high mortality and disability rate, severe craniocerebral injury often requires surgical intervention and it is a common condition that is seen in the intensive care unit (ICU) [3, 4]. Craniocerebral injury is often caused by trauma, and clinical treatment often includes surgical intervention, which increases the risk of infection in patients. At the same time, because the injured part, the brain, is a central part of the human body, patients need to stay in bed for a long time during the treatment process, which increases the chance of lung infection and leads to a poor prognosis [5, 6]. Patients in the ICU are all critically ill, and the use of invasive procedures and immunosuppressive agents such as glucocorticoids to inhibit the secretion of inflammatory factors

after trauma is higher than that of other medical departments, resulting in an increased risk of multidrug-resistant organism (MDRO) infections [7, 8]. The clinical abuse of antibiotics in the ICU also indirectly leads to the mutation of bacteria and increases the risk of MDRO infection [9]. Studies have unveiled that MDRO infection in patients with craniocerebral injury can cause rapid disease progression and a significant increase in mortality [10]. The poor efficacy of antibiotic use after MDRO infection improves the difficulty of clinical treatment and also increases the economic burden of patients [11]. Therefore, research on the distribution characteristics and related risk factors of the microflora of MDRO in craniocerebral injury complicated with pulmonary infection is conducive to the early intervention, prevention and disease control in patients. Based on the research findings, we analyzed the MDRO infection rates and related infection indicators in patients with craniocerebral injury complicated with pulmonary infection in The People's Hospital of Linqing, so as to provide clinical reference for the prevention and control of multidrug resistant bacteria in patients with craniocerebral injury complicated with pulmonary infection.

Materials and methods

Clinical data

We enrolled 112 patients admitted to The People's Hospital of Linqing from January 2017 to December 2019 with craniocerebral injury complicated with pulmonary infection for this prospective study. Among them, 39 were MDRO-infected patients and 73 were non-MDRO-infected patients. All patients were 23-74 years old, with an average age of 64.8±7.6 years. Informed written consent was obtained from all the patients and this study was approved by the Ethics Committee of The People's Hospital of Linqing.

Inclusion and exclusion criteria

Inclusion criteria were listed as follows: Patients who met the diagnostic criteria for craniocerebral injury [2]; patients who met the diagnostic criteria for pulmonary infection [12]; patients who were aged between 18-75 years old; and patients whose blood culture or urine culture or secretion bacterial culture were positive. Exclusion criteria were as follows: Patients with immunodeficiency; patients with multibacterial infection; and patients with pulmonary infection before craniocerebral injury.

Methods

Bacterial culture: The blood, urine, and secretions (sputum, pus, pleural or abdominal effusion, etc.) of the included patients were collected and submitted for inspection after infection. Routine inspection was carried out once a day for three consecutive days. The specimen collection standards were in accordance with the national clinical laboratory procedures [13]. MDROs diagnostic criteria were made according to the description of the types of MDROs and the diagnostic criteria in "Multidrug-resistant, extensively drug-resistant and pan drug-resistant bacteria: An international expert proposal for interim standard definitions for acquired resistance" [14]. The main types of MDRO included carbapenem-resistant enterobacteriaceae (CRECO), carbapenem-resistant pseudomonas aeruginosa (CRPA), carbapenem-resistant acinetobacter baumannii (CRAB), carbapenem-resistant klebsiella pneumonia (CRKP), methicillin-resistant staphylococcus aureus (MRSA) and vancomycin-resistant enterococcus faecium (VREFM). The operating instrument was Walk A-way40 automatic microbial identification instrument (Siemens, Japan).

Markers of blood infection: Two 5 mL tubes of blood from the elbow vein were collected from each patient after the occurrence of infection. The collected blood samples were stored in sterile ethylenediaminetetraacetic acid tubes. After storage at 4°C for 15 min in the refrigerator, serum and plasma were separated using a centrifuge with a centrifugal force of 1106.8 (xg) and stored in a freezer at -80°C. The white blood cell count was measured using the Coulter LH750 automatic blood cell analyzer (Beckman Coulter, USA). The enzyme-linked immunosorbent assay was used to determine serum procalcitonin (PCT) and C-reactive protein (CRP) in the serum through an automatic immunoassay analyzer (Siemens, Germany). The above kits were all from Shanghai Enzyme Linked Biology Co., Ltd. (China).

Table 1. Comparison of general information of patients (n, %) (x ± sd)

Items	MDRO infection group (n = 39)	Non-MDRO infection group (n = 73)	χ^2/t	P
Gender (male:female)	23:16	43:30	0.000	0.994
Age (years)	64.9±9.5	59.2±8.2	3.297	0.001
BMI (kg/m^2)	23.45±3.73	23.23±3.72	0.298	0.766
Invasive procedure before infection	18 (46.15)	19 (26.03)	4.665	0.031
Invasive procedure after infection	7 (17.95)	13 (17.81)	0.001	0.985
Complicated multiple injuries	24 (61.54)	30 (41.10)	4.225	0.039
Open injury	25 (64.10)	32 (43.84)	4.178	0.041
Comorbidity				
Hypertension	18 (46.15)	32 (43.84)	0.055	0.814
Type 2 diabetes	15 (38.46)	29 (39.73)	0.017	0.896
Heart coronary disease	12 (30.77)	20 (27.40)	0.142	0.707
Smoking history	21 (53.85)	19 (26.03)	8.568	0.003
Alcohol abuse history	16 (41.03)	32 (43.84)	0.082	0.775

Note: MDRO: multidrug-resistant organism; BMI: Body Mass Index.

Table 2. Comparison of related indicators after infection (x ± sd)

Items	MDRO infection group (n = 39)	Non-MDRO infection group (n = 73)	t	P
Length of hospitalization (d)	16.33±4.92	12.34±3.24	5.208	< 0.001
Days of fever (d)	10.70±6.51	7.20±4.23	3.451	< 0.001

Note: MDRO: multidrug-resistant organism.

Outcome measures

The WBC, PCT and CRP values of the two groups of patients after infection were compared. The distributions of MDRO in different years were observed. In addition, multivariate logistic regression was used to analyze the risk factors of craniocerebral injury with pulmonary infection MDRO.

Statistical analysis

SPSS 17.0 statistical software was used to analyze the data. Continuous variables were presented as mean ± standard deviation (x ± sd), and M (P25, P75) were used to represent data in a non-normal distribution. The variables conforming to normal distribution and equal variance were analyzed by independent-sample t-test, represented by t. Otherwise, rank-sum test was applied, represented by χ^2. Furthermore, the count data were analyzed using Pearson's chi-square test and expressed in chi-square. The occurrence of MDRO infection was taken as the dependent variable, and factors with differences in single-factor comparison were selected as independent variables. The forward stepwise entry method was used to construct a multi-factor Logistic regression model with a variable entry criterion of 0.05 and an exclusion level of 0.10. The difference was statistically significant when $P < 0.05$.

Results

Comparison of general information and post-infection-related information

There was no statistical difference between the two groups of patients in gender, body mass index (BMI), hypertension, type 2 diabetes and coronary heart disease, invasive procedures after infection, and alcohol abuse history (all $P > 0.05$). The age, length of hospitalization, days of fever, invasive procedures before infection and the proportion of smoking history in the MDRO infection group were significantly higher than those in the non-MDRO infection group (all $P < 0.05$), as shown in **Tables 1** and **2**.

Table 3. Comparison of infection-related blood indicators

Items	MDRO infection group (n = 39)	Non-MDRO infection group (n = 73)	t	P
PCT (μg/L)	0.93±0.61	0.49±0.29	5.177	< 0.001
CRP (mg/L)	63.71±28.83	17.63±9.71	12.441	< 0.001
WBC ($\times 10^9$/L)	9.78±4.21	9.54±4.73	0.082	0.775

Note: MDRO: multidrug-resistant organism; PCT: serum procalcitonin; CRP: C-reactive protein; WBC: white blood cell count.

Table 4. Comparison of the number of MDRO infection cases in different years

Items	2017	2018	2019	χ^2	P
MDRO infection cases (n)	16	13	10	2.369	0.306
Non-MDRO infection cases (n)	21	24	28		

Note: MDRO: multidrug-resistant organism.

Table 5. Comparison of the composition of MDRO infection strains in different years (n, %)

Items	2017	2018	2019	χ^2	P
CRECO	2 (12.50)	5 (38.46)	2 (20.00)	22.404	0.015
CRPA	1 (6.25)	3 (23.08)	4 (40.00)		
CRAB	10 (62.50)	2 (15.39)	1 (10.00)		
CRKP	1 (6.25)	1 (7.69)	1 (10.00)		
MRSA	1 (6.25)	1 (7.69)	1 (10.00)		
VREFM	1 (6.25)	1 (7.69)	1 (10.00)		

Note: CRECO: carbapenem-resistant Enterobacteriaceae; CRPA: carbapenem-resistant pseudomonas aeruginosa; CRAB: carbapenem-resistant bowman kinetobacter; CRKP: carbapenem-resistant klebsiella pneumonia; MRSA: methicillin-resistant staphylococcus aureus; VREFM: vancomycin-resistant enterococcus faecium; MDRO: multidrug-resistant organism.

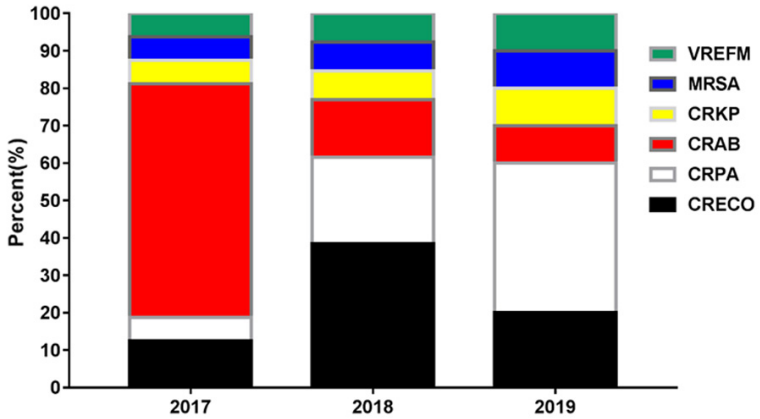

Figure 1. Comparison of the composition of MDRO infection strains in different years. VREFM: vancomycin-resistant enterococcus faecium; MRSA: methicillin-resistant staphylococcus aureus; CRKP: carbapenem-resistant klebsiella pneumonia; CRAB: carbapenem-resistant bowman kinetobacter; CRPA: carbapenem-resistant pseudomonas aeruginosa; CRECO: carbapenem-resistant Enterobacteriaceae; MDRO: multidrug-resistant organism.

Comparison of infection-related blood indicators

The PCT and CRP of the MDRO infection group were higher than those of the non-MDRO infection group (all P < 0.001). There was no significant difference in WBC between the two groups (P > 0.05), as shown in **Table 3**.

Comparison of the composition of MDRO infection strains in different years

MDRO infections in patients with craniocerebral injury complicated with pulmonary infection were mainly CRAB and CRECO. The distribution of MDRO infection strains in different years were statistically different (P < 0.05), as shown in **Tables 4**, **5** and **Figure 1**.

Multivariate logistic regression analysis of MDRO infection in patients with malignant tumors

Multivariate regression analysis found that age, invasive procedures before infection, complicated multiple injuries, open injuries, smoking history, and elevated PCT were independent risk factors for MDRO infection in patients with malignant tumors (all P < 0.05), which is shown in **Tables 6** and **7**.

Discussion

The gold standard of MDRO diagnosis is still bacterial culture, but it was found that the positive rate of bacterial culture was relatively low, which was only about 15% [15]. This leads to delays in the diagnosis of, and medication for MDRO. In addition, MDRO-

Table 6. Assignment table of independent variables of MDRO risk factors in 112 patients with craniocerebral injury complicated with pulmonary infection

Factors	Independent variables	Assignment
Age	X1	Age > 50 = 1, Age ≤ 50 = 0
Length of hospitalization	X2	≥ 15 days = 1, < 15 = 0
Days of fever	X3	≥ 10 days = 1, < 10 = 0
Complicated multiple injuries	X4	Yes = 1, no = 0
Open injury	X5	Yes = 1, no = 0
Smoking history	X6	Yes = 1, no = 0
PCT	X7	> 0.5 μg/L = 1, ≤ 0.5 μg/L = 0
CRP	X8	> 8 mg/L = 1, ≤ 8 mg/L = 0

Note: MDRO: multidrug-resistant organism; PCT: serum procalcitonin; CRP: C-reactive protein.

infected patients are more resistant to antibiotics and often need to be treated for the specific pathogenic bacteria of MDRO to control the disease [16-19]. The delay in diagnosis and effective medication has adverse effects on the prognosis of patients. Therefore, the selection of relevant infection markers for early MDRO judgment has become the direction of clinical research.

White blood cell count (WBC) is the most commonly used clinical indicator to respond to infection. However, due to its many influencing factors, high volatility, and being elevated in most patients with bacterial infection, it is suggested that WBC alone is not effective in identifying MDRO infection. It was discovered in this study that WBC was elevated in both MDRO-infected and non-MDRO-infected patients, and there was no statistical difference between the two, which is consistent with previous studies [20]. Therefore, other infection-related indicators are selected for further research. C-reactive protein (CRP) is synthesized in the liver under the mediated action of interleukin-6 and other inflammatory factors, and it is a commonly used clinical test index [21]. However, clinical studies discovered that CRP was not only increased in infections, but also increased in oxidative stress or body damage [22, 23], which leaded to its poor specificity in diagnosing infection. However, it was also proved that there was a positive correlation between CRP and the severity of infection [24]. Procalcitonin (PCT) is a more specific indicator of bacterial infection [25], and an increase in PCT indicates the presence of bacterial infection. In this study, the increase in PCT after MDRO infection was found to be more obvious, suggesting that MDRO infection was a more severe bacterial infection. At the same time, CRP and PCT increased significantly in patients with MDRO infection, which may be related to the severity of MDRO infection and poor treatment effect.

An increase in antibiotics will lead to an increase in MDRO infections [26, 27]. The ICU often treats severe or post-surgery patients, so antibiotics are often used for treatment. In addition, due to the small space of the ICU, the distance between beds is small, and the resistance of ICU patients is lower than that of ordinary patients, so the spread of MDRO is easy among patients [28]. A study on the distribution of strains of MDRO-infected patients found that the ICU was dominated by CRAB and CRECO infections, which was consistent with previous findings [29]. CRAB is the most common MDRO strain in ICU patients, and CRAB has high drug resistance due to its own characteristics [30]. In recent years, with the development of infection control for MDRO, the incidence of CRAB is still high but shows a decreasing trend. As for CRECO, the incidence of it shows an increasing trend, whether it is related to the unreasonable use of antibiotics and the introduction of community infections still needs further research to strengthen the related monitoring and management.

Further study of factors associated with increased risk of infection revealed that older age of the patient, having had invasive procedures such as tracheal intubation and gastric intubation, combination of multiple injuries, open injury and elevated PCT are independent risk factors for MDRO infection in patients with craniocerebral injury complicated with pulmonary infection. It is suggested that for elderly patients with invasive procedures, multiple injuries, open injuries, poor systemic symptoms and decreased body resistance, the risk of infection will increase, which is consistent with previous studies [31, 32]. This study also

Table 7. Multivariate logistic regression analysis of MDRO infection in patients with malignant tumors

Factors	β	SE	Wald Value	OR (95% CI)	P
Age (years)	1.346	0.452	8.421	3.032 (1.154-4.483)	0.024
Length of hospitalization (d)	0.346	0.382	0.821	1.132 (0.957-1.432)	0.687
Days of fever (d)	0.069	0.029	0.712	1.019 (0.978-1.081)	0.715
Invasive procedure before infection	1.421	0.571	12.439	3.123 (2.931-7.565)	< 0.001
Complicated multiple injuries	2.103	0.543	15.733	8.230 (2.981-20.232)	< 0.001
Open injury	2.213	0.412	16.933	8.482 (3.923-21.932)	< 0.001
Smoking history	1.234	0.413	11.214	2.841 (2.741-7.123)	< 0.001
PCT (μg/L)	0.906	0.269	4.165	2.164 (1.315-3.743)	0.022
CRP (mg/L)	0.071	0.038	0.714	1.016 (0.958-1.074)	0.721

Note: PCT: serum procalcitonin; CRP: C-reactive protein; OR: odds ratio; CI: confidential interval; MDRO: multidrug-resistant organism.

suggested that patients with a history of smoking were more susceptible to MDRO infection. Long-term smoking affects lung function and increases the risk of lung infection. Patients with craniocerebral injury often have symptoms of coma that slow down blood flow and weaken respiratory function, which also increases the risk of aspiration pneumonia and MDRO infection [33, 34].

There are several nursing countermeasures to prevent the occurrence of MDRO for craniocerebral injury complicated with pulmonary infection. For patients with brain injury, the airway should be kept unobstructed, which can reduce the secondary injury under cerebral ischemia and hypoxia. In addition, the unobstructed airway can facilitate lung ventilation and ventilation function and reduce the chance of lung infection; promote the excretion of sputum in patients. Patients with brain injury are prone to sputum blockage symptoms. After blockage, respiratory dysfunction is likely to occur, which can cause aggravation of cerebral ischemia and hypoxia, and also increase the risk of MDRO infection. Therefore, it is necessary to promptly help patient to excrete sputum. Turning over patients and patting them on the back to promote sputum excretion, and perform sputum suction or tracheotomy when necessary; patients should also keep their head high and the feet low to prevent the backflow of blood from the bleeding site of intracranial injury to decrease the risk of infection.

However, there were still several shortcomings in this study. The sample size in this study was small, and a multi-center study can be carried out to expand the sample size. Moreover, relevant intervention measures for MDRO in craniocerebral injury complicated with pulmonary infection weren't carried out in this study, and further intervention measures can be performed to study the prevention methods of MDRO infection.

In summary, CRAB and CRECO are the main causative organisms for MDRO in craniocerebral injury complicated with pulmonary infection, and the distribution of infectious organisms varies from year to year. Age, invasive procedure, complicated with multiple injuries, open injury, smoking history and elevated PCT are independent risk factors for MDRO infection in patients with pulmonary infection.

Disclosure of conflict of interest

None.

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