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Journal of Advances in Medicine Science
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Risk Factors and Distribution of Pathogens for Pulmonary Infection in Patients with Severe Acute Pancreatitis

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ARTICLE INFO

Article history
Received: 7 January 2021
Revised: 14 January 2021
Accepted: 24 January 2021
Published Online: 31 January 2021

Keywords:
Pulmonary infections
Severe acute pancreatitis
Risk factors
Distribution of pathogens

ABSTRACT

Objective: To investigate risk factors and distribution of pathogens for pulmonary infection in patients with severe acute pancreatitis. **Methods:** The clinical data of 285 patients with severe acute pancreatitis were retrospectively analyzed. Sputum specimens of patients with lung infections were studied. Univariate analysis and logistic regression were performed to screening the factors correlating to lung infections. **Results:** Gram-negative bacilli were the principal microorganisms isolated from those lung infections, and these bacterial pathogens demonstrated a marked pattern of antibiotic resistance. It was identified that age (OR 1.05, 95% CI 1.01-1.09, p=0.01), Ranson scores (OR 3.01 , 95% CI 1.13-8.03, p = 0.03) and surgical treatment (OR4.27, 95% CI 1.03-17.65, p = 0.04)were independent risk factors of lung infections in patients with severe acute pancreatitis. **Conclusion:** Analysis of pathogen spectrum and drug sensitivity will contribute to choosing antibiotics empirically. And preventive measures aimed at risk factors could help reduce the incidence of lung infections in patients with severe acute pancreatitis.

1.Introduction

Acute pancreatitis (AP) is a common acute abdomen, the incidence of AP in the world is 10~80 cases /100000 people, the overall mortality in clinic is 5%~10%, and the mortality in severe cases can be as high as 30%[1-2]. The common causes include drinking alcohol and gallstones[3]. 15-20% of which are severe acute pancreatitis (SAP). SAP progresses rapidly with many complications, making it difficult to treat[4]. Since there is damage to acinar cells in the AP, it may cause multiple organ dysfunction syndrome (MODS)[5] in the acute phase of the disease, while in the middle and late stage of the disease, the extra-pancreatic tissue infection is caused by the displacement of intestinal bacteria (Extrapancreaticinfec-tions, EPI) [6].With the progress of SAP treatment, the number of early deaths due to organ dysfunction has gradually decreased. Infection-related complications have become the main cause of death in SAP patients. The results of many retrospective studies show that the clinical mortality of infected patients is significantly different from that of those with no infection, so infection has a great influence on the prognosis of AP patients, especially SAP patients[7-9]. Among them, lung infection is a common infection-related complication, whose incidence is as high as 11%

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 DOI: https://doi.org/10.30564/jams.v4i1.2848

-30%[10], seriously affecting the treatment and prognosis of SAP patients[11]. The reason why SAP is prone to lung infection may be related to decreased immunity and the damage of endothelial cells and alveolar epithelial cells caused by excessive activation of inflammatory molecules[12]. SAP patients' lung infections are mostly hospital-acquired pneumonia, and prevention should be stressed. Finding out the risk factors of lung infection will help us to take targeted preventive measures to reduce the occurrence of it. Understanding the distribution of pathogenic bacteria in lung infections complicated by SAP is of great significance to the empirical medication of lung infections.

This paper conducts a retrospective analysis of 285 SAP patients in the Second Affiliated Hospital of Kunming Medical University from June 1992 to June 2017, aiming to provide constructive opinions for future clinical practice and better prevent and deal with SAP patients' lung infections.

2.Materials and Methods

2.1 Research Object

285 SAP patients in the Second Affiliated Hospital of Kunming Medical University from June 1992 to June 2017 were selected. The diagnostic criteria for SAP are based on the "Guidelines for the Diagnosis and Treatment of Acute Pancreatitis in China (2013, Shanghai)" by the Pancreatic Disease Group of the Chinese Medical Association Digestive Disease Branch [13]. The diagnostic criteria for lung infection adopt the "Diagnostic Criteria for Nosocomial Infection" approved by the Chinese Lung Infection Administrative Association [14]. Patients with incomplete clinical data were excluded.

2.2 Research Method

① Summarize the incidence of lung infection and its mortality among the included cases. ② Bacterial spectrum analysis: The strains were derived from the sputum culturing results of the included patients with lung infection, and were identified by the French Mérieux Vitek 32 automatic bacterial identification instrument. For drug susceptibility testing, the K-B disc method was used. As for the diagnostic criteria for drug resistance, the standards of the National Committee for Clinical Laboratory Standardization (NCCLS) were adopted. ③ Analyze the risk factors of lung infection in the patients. 52 of the 285 SAP patients had lung infection, and they made up the case group. The control group, consisting of 52 cases without lung infection, were randomly selected from the rest 233 patients. 16 risk factors were chosen based on relevant literature reports and clinical experience: gender, age, body mass index (BMI), Ranson score at admission, history of smoking (smoking for more than 10 years), history of drinking (drinking every day for more than 5 years), history of chronic obstructive pulmonary disease (COPD), history of hypertension, history of diabetes, blood amylase level at admission, urea nitrogen level at admission, albumin level at admission, ventilator treatment, indwelling gastric tube for more than 10 days, surgical treatment, and hormone therapy. SPSS13.0 software was applied to statistical analysis. Measurement data was expressed as mean plus or minus standard deviation, and counting data was expressed as percentage. Measurement data and counting data respectively used t test and $\chi 2$ test to compare the differences between the case group and the control group, looking for factors related to infection. Single-factor analysis of statistically significant risk factors was followed by logistic regression analysis, and then multi-factor analysis was used to further find independent risk factors related to lung infection.

3.Results

3.1 Incidence and Mortality of SAP Patients' Lung Infection

Lung infection occurred in 52 of the 285 SAP patients, with an incidence rate of 18.25%. There were 11 deaths among patients with lung infection, with a mortality rate of 21.15%. Among the 233 SAP patients without lung infection, 24 died, with a mortality rate of 10.30%. The difference between the two groups was statistically significant ($P < 0.05$).

3.2 Distribution and Drug Sensitivity of Pathogenic Bacteria in SAP Patients' Lung Infection

A total of 56 pathogens were isolated from the sputum samples of 45 out of 52 patients with lung infections. One pathogen was found in 30 patients, and mixed infection of two or more pathogens was found in 15 patients (33.33%). Among them, gram-negative bacteria, gram-positive bacteria and fungi respectively accounted for 80.36% (45/56), 12.50% (7/56) and 7.14% (4/56). The common pathogens of gram-negative bacteria are Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Acinetobacter and Enterobacter cloacae in sequence; the pathogens of gram-positive bacteria are staphylococcus aureus and coagulase-negative staphylococci; fungal pathogens are Candida albicans and Candida glabrata. For details see Table 1.

DOI: https://doi.org/10.30564/jams.v4i1.2848

Table 1. Distribution and constituent ratio of pathogens of pulmonary infection in patients with severe acute pancreatitis (%)

Pathogens	Number of plants	Composition ratio
Gram-negative bacterium	45	80.36
Escherichia coli	14	25.00
Pseudomonas aeruginosa	11	19.64
Klebsiella pneumoniae	10	17.86
Acinetobacter	7	12.50
Enterobacter cloacae	2	3.75
Bacillus maltophilia	1	**1.79**
Gram-positive bacteria	7	12.5
Staphylococcus aureus	5	8.93
Coagulase-negative staphylococci	2	3.57
Fungi	4	7.14
Candida albicans	3	5.36
Candida smooth	1	**1.79**

The isolated common pathogens were tested for antibiotic sensitivity, and the results are shown in Table 2. Gram-negative bacteria are resistant to common antibiotics to varying degrees. Pseudomonas aeruginosa is the most resistant, showing a certain degree of resistance to imipenem.

Table 2. Resistant rates of major gram-negative bacteria to antimicrobial agents(%)

Antibacterial drugs	Escherichia coli (n=14)		Pseudomonas aeruginosa (n=11)		Klebsiella pneumoniae (n=10)	
	Number of plants	Resistance rate	Number of plants	Resistance rate	Number of plants	Resistance rate
Ampicillin	14	100.00	11	100.00	10	100.00
Piperacillin/tazobactam	3	21.43	7	63.64	5	50.00
Amikacin	4	28.57	7	63.64	6	60.00
Ciprofloxacin	9	64.29	10	90.90	7	70.00
Cefazolin	10	71.43	11	100.00	8	80.00
Ceftazidime	7	50.00	8	73.73	6	60.00
Cefoperazone/Subactam	2	14.29	6	54.55	4	40.00
Imipenem	0	0.00	5	45.45	2	20.00

3.3 Analysis of Risk Factors for Lung Infection in SAP Patients

In order to determine the risk factors of lung infection in SAP patients, we selected 16 relevant factors for statistical comparison and analysis between the control group and the case group. There were statistical differences in 7 variables, namely age, ventilator treatment, Ranson score at admission, surgical treatment, indwelling nasogastric tube for more than 10 days, urea nitrogen level at admission and albumin level at admission. The results are shown in Tables 3 and 4. In order to exclude relevant risk factors, variables were included in a multivariate logistic regression analysis, and three variables were determined to be independent risk factors for lung infection in SAP patients. The results are shown in Table 5, which are respectively age (OR 1.05, 95% CI 1.01 -1.09, p = 0.01), Ranson score (OR3.01, 95% CI 1.13-8.03, p = 0.03) and surgical treatment (OR4.27, 95% CI 1.03-17.65, p = 0.04).

Table 3. Univariate analysis of risk factors of pulmonary infection in patients with severe acute pancreatitis (quantitative variables)

	Infection group (n=52)		Control group (n=52)		t value	*P value*
	Average	SD	Average	SD		
Age (years)	50.98	14.62	41.38	14.13	3.403	0.00
BMI (kg/m2)	25.51	3.05	25.11	3.33	0.645	0.52
Ranson score (score)	4.35	0.68	3.75	0.65	4.550	0.00
Blood amylase (U/L)	780.77	327.11	762.88	366.25	0.263	0.79
urea nitrogen (mmol/L)	7.12	1.76	6.27	2.00	2.314	0.02
Albumin (g/L)	37.36	5.00	39.69	6.00	-2.151	0.03

Table 4. Risk factors and infection rates(%) of pulmonary infection in patients with severe acute pancreatitis (categorical variables)

	Factors	Number of cases investigated	Number of cases of infection	Infection rates	χ^2 value	*P value*
Gender	Male	59	31	52.54	0.35	0.69
	Female	45	21	46.67		
COPD	Yes	11	7	63.64	0.92	0.53
	No	93	45	48.39		
History of smoking	Yes	32	19	59.38	1.63	0.29
	No	72	33	45.83		
History of drinking	Yes	29	13	44.83	0.43	0.66
	No	75	37	46.67		
History of hypertension	Yes	19	12	63.16	1.61	0.31
	No	85	40	47.59		
Diabetes history	Yes	14	8	57.14	0.33	0.78
	No	90	44	48.89		
Ventilator therapy	Yes	31	21	67.74	5.56	0.03
	No	73	31	42.47		
Surgical treatment	Yes	21	17	80.95	10.08	0.00
	No	83	35	42.17		
Retention of gastric tube(d >10)	Yes	52	32	61.54	5.54	0.03
	No	52	20	38.46		
Hormone use	Yes	19	11	57.89	0.58	0.61
	No	85	41	48.24		

DOI: https://doi.org/10.30564/jams.v4i1.2848

Table 5. Logistic regression analysis of risk factors for pulmonary infection in patients with severe acute pancreatitis

	β	SE	Wald/χ^2	*p value*	OR	95%*CI*
Age	0.05	0.02	6.67	0.01	1.05	1.01-1.09
Ranson score	1.10	0.50	4.86	0.03	3.01	1.13-8.03
Surgical treatment	1.45	0.72	4.02	0.04	4.27	1.03-17.65

4. Discussion

SAP is a serious disease with high prevalence and mortality. It is prone to multiple organ complications, among which the incidence of pulmonary complications is as high as 68.1% [15]. Lung infection is the main pulmonary complication of SAP and an important cause of death in SAP patients. The incidence of lung infection in our group of cases was as high as 18.25%. The mortality rate of patients with lung infection was 21.15%, which was higher than that of the non-infected group. Therefore, active treatment and prevention of lung infection are beneficial to reduce the mortality of SAP.

Lung infections of SAP patients are mostly hospital-acquired. Empirical initial antibiotic treatment for hospital-acquired infections is the main factor determining the prognosis of patients. And bacterial resistance testing is an important basis for empirical initial antibiotic treatment. In etiology, the proportion of Gram-negative bacteria was relatively high, which was consistent with that of Chen Zhongjian[16]. This study has found that the bacterial spectrum of the case group has the following characteristics: ① The pathogenic bacteria are mainly gram-negative bacteria, and the infection of gram-negative bacteria may be related to endogenous infections such as bacterial translocation and inhalation of oropharyngeal secretions. ② The detection rate of multi-drug resistant bacteria is high. Also, the distribution ratio of Pseudomonas aeruginosa is high, showing strong antibiotic resistance. ③ The proportion of mixed infections is high, and about 1/3 of patients have two or more bacterial infections. SAP complicated by lung infection is prone to complications such as metabolic disorders and respiratory failure; the disease progresses fast with high mortality rate; there are a number of risk factors for multidrug-resistant bacteria infection with high infection rate. Considering the above points, it is appropriate to employ broad-spectrum antibiotic therapy, targeted at multi-drug resistant bacteria, for empirical initial antibiotic treatment. According to bacterial distribution characteristics and guidelines for hospital-acquired infection, antibiotics can be selected from third-generation or fourth-generation cephalosporins (cefoperazone, ceftazidime, cefepime) or β-lactams/β-lactamase inhibitors (cefoperazone/sulbactam, piperacillin/tazobactam). And if necessary, carbapenems (imipenem, meropenem) can be chosen.[17-18]

Prevention is the emphasis of hospital-acquired infection. Based on clinical experience and related literature reports, 16 possible risk factors were included in this study. Given the possible mutual influence among these risk factors, single factor analysis was followed by multi-factor analysis to screen independent risk factors. The study has found that age, Ranson score and surgical treatment are three independent risk factors for SAP complicated by lung infection. First, as the patient ages, his/her immune globulin level and cellular immunity decline, resulting in decreased systemic resistance to infection. In addition, elderly patients' capacity of sputum excretion weakens after operation. These systemic and local factors can make postoperative patients vulnerable to lung infections. Hence, elderly SAP patients should be the key population that needs to prevent lung infections. Second, Ranson score is a scoring standard that reflects the severity of pancreatitis recommended by most guidelines. The scoring system includes 5 clinical indicators at admission and 6 indicators in 48 hours. A score greater than 3 indicates severe pancreatitis, and the score is highly accurate in predicting organ failure and death. Our study has found that an increase in the Ranson score also means an increased risk of lung infection in SAP patients. Third, surgical debridement plays an important role in the treatment of SAP, but due to the patient's systemic inflammatory response syndrome and the body's poor state, there are various surgical complications and high mortality[19]. Abdominal incisions after debridement surgery can lead to difficulty in expectorating sputum and decreased breathing ability, which may give rise to lung infection. In recent years, minimally invasive debridement surgery of SAP has been valued. The progressive treatment of puncture, endoscopy, laparoscopy, and laparotomy can reduce postoperative complications and lower the lung infection rate from 50% to 27%[20].

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 DOI: https://doi.org/10.30564/jams.v4i1.2848