Risk Factors and Distribution of Pathogens for Pulmonary Infection in Patients with Severe Acute Pancreatitis

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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 (OR 4.27, 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 (Extrapancreatic infections, 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%
Analyze the risk factors of lung infection in the patients. 52 of the 285 SAP patients had lung infection, and they made up 23.15% (52/225) of the total SAP patients. Among patients with lung infection, 24 died, with a mortality rate of 10.30%. The mortality among the included cases.

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.
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 pneumonia (n=10) |
|---------------------|-------------------------|-------------------------------|----------------------------|
|                     | Number of plants | Resistance rate | Number of plants | Resistance rate | Number of plants | Resistance rate |
| Amoxicillin         | 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 |
| Cefazidime/Cefoperazone/ Zobactam | 7  | 50.00 | 8 | 73.73 | 6 | 60.00 |
| Imipenem            | 2  | 14.29 | 6 | 54.55 | 4 | 40.00 |

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)

| Factors                        | Infection group (n=52) | Control group (n=52) | t value | P value |
|--------------------------------|------------------------|----------------------|---------|---------|
| Age (years)                    | Average | SD     | Average | SD     |         |         |
| 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  | 327.1 | 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 | χ² value | P value |
|--------------------------------|-----------------------------|------------------------------|----------------|----------|---------|
| Gender                         | Male                        | 59                           | 52.54           | 0.35     | 0.69    |
|                               | Female                      | 45                           | 46.67           |          |         |
| COPD                           | Yes                         | 11                           | 63.64           | 0.92     | 0.53    |
|                               | No                          | 93                           | 48.39           |          |         |
| History of smoking             | Yes                         | 32                           | 59.38           | 1.63     | 0.29    |
|                               | No                          | 72                           | 45.83           |          |         |
| History of drinking            | Yes                         | 29                           | 44.83           | 0.43     | 0.66    |
|                               | No                          | 75                           | 46.67           |          |         |
| History of hypertension        | Yes                         | 19                           | 63.16           | 1.61     | 0.31    |
|                               | No                          | 85                           | 47.59           |          |         |
| Diabetes history               | Yes                         | 14                           | 57.14           | 0.33     | 0.78    |
|                               | No                          | 90                           | 48.89           |          |         |
| Ventilator therapy             | Yes                         | 31                           | 67.74           | 5.56     | 0.03    |
|                               | No                          | 73                           | 42.47           |          |         |
| Surgical treatment             | Yes                         | 21                           | 80.95           | 10.08    | 0.00    |
|                               | No                          | 83                           | 42.17           |          |         |
| Retention of gastric tube(>10)  | Yes                         | 52                           | 38.46           | 5.54     | 0.03    |
|                               | No                          | 52                           | 48.24           |          |         |
| Hormone use                    | Yes                         | 19                           | 57.89           | 0.58     | 0.61    |
|                               | No                          | 85                           | 48.24           |          |         |
The pathogenic bacteria are mainly gram-negative. The proportion of mixed infections is high, and about 95% 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/sublactam, 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].

### References

1. Velusamy RK, Tamizhselvi R. Protective effect of methylsul-Fonylmethane in caerulein-induced acute pancreatitis and asso- Ciated lung in jury in mice[J]. J Pharm Pharmacol,2018,70 (9):1188-1199.

2. Zhang WF,Li ZT,Fang JJ,et al.Effect of mannose on the Lung function of rats with acute pancreatitis[J].J Biol Regul Homeost Agents,2018,32(3):627-633.

3. Choi SB,Bae GS,Jo IJ,et al.Effects of Berberine on acute ne- Crotizing pancreatitis and associated lung
injury[J]. Pancreas, 2017, 46(8): 1046-1055.

[4] Raghu M, Wig J, Kochhar R, et al. Lung complications in acute pancreatitis. JOP : Journal of the pancreas. 2007; 8(2): 177-85.

[5] Restrepo R, Hagerott HE, Kulkarni S, et al. Acute pancreatitis in pediatric patients: demographics, etiology, and diagnostic imaging[J]. AJR Am J Roentgenol, 2016, 206(3): 632 -644.

[6] Majidi S, Golembioski A, Wilson SL, et al. Acute pancreatitis: etiology, pathology, diagnosis, and treatment[J]. South Med J, 2017, 110(11): 727-732.

[7] Zhu R, Zhao Y, Li X, et al. Effects of penehyclidine hydrochloride on severe acute pancreatitis-associated acute lung injury in rats[J]. Biomed Pharmacother, 2018, 97: 1689-1693.

[8] Qin Li, Cao Jingli, Ge Libin, et al. Comparison of the value of the modified Atlanta classification standard and the determinant-based classification standard for the prognosis of acute pancreatitis [J]. Chinese Journal of Gastroenterology, 2019, 39(1): 52-55.

[9] Wu Dong, Lu Bo, Xue Huadan, et al. A comparative study of the modified Atlanta classification and determinants based classification of acute pancreatitis [J]. Chin J Med, 2017, 56 (12): 909-913.

[10] Liu WJ, Zhang Y, Lu B. Clinical analysis of 45 cases of severe pancreatitis with pulmonary infection. Chinese Journal of Lung Diseases. 2017; 10(06): 723-725.

[11] Hongzhang Cui, Shu Li, Caiming Xu, et al. Emodin alleviates severe acute pancreatitis-associated acute lung injury by decreasing pre-B-cell colony-enhancing factor expression and promoting polymorphonuclear neutrophil apoptosis. 2017, 16(4): 5121-5128.

[12] Huang L, Wang M, Yang X, et al. Acute lung injury in patients with severe acute pancreatitis. The Turkish journal of gastroenterology: the official journal of Turkish Society of Gastroenterology. 2013; 24(6).

[13] Wang X, Li Z, Yuan Y. Guidelines for the Diagnosis and Treatment of Acute Pancreatitis in China (Shanghai, 2013). Chinese Journal of Digestion. 2013(04): 217-220.

[14] Xu X, Wu A, Yi X. Clinical nosocomiology 1998-2001-06-28.

[15] Párniczky A, Kui B, Szentesi A, et al. Prospective, Multicentre, Nationwide Clinical Data from 600 Cases of Acute Pancreatitis. PloS one. 2016;11(10): e0165309.

[16] Chen Zhongjian, Gou Fei, Zhang Tianfeng, et al. Effects of pulmonary infection on respiratory function and peripheral blood inflammatory cytokines in patients with severe acute pancreatitis [J]. Chinese Journal of Nosocomiology, 2017, 27(9): 2050-2053.

[17] Li P, Shi Y. Interpretation of guidelines for diagnosis and treatment of nosocomial acquired pneumonia and ventilator-associated pneumonia. Chinese Journal of Evidence-Based Medicine. 2015; 15(07): 772-6.

[18] Wang L, Wang X, Huang X, et al. Ventilator-associated pneumonia pathogen spectrum literature analysis. Chinese Journal of Nosocomiology. 2013; 23(10): 2478-80.

[19] Gooszen H, Besselink M, van Santvoort H, et al. Surgical treatment of acute pancreatitis. Langenbeck's archives of surgery. 2013; 398(6): 799-806.

[20] Wang Z, Xu W, Teng B. Perioperative stress response and postoperative inflammatory response in the treatment of severe pancreatitis by minimally invasive surgery and open surgery. Journal of Applied Medicine. 2016; 32(12): 1997-8.