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# Effect of traditional Chinese preparation Xuebijing on inflammatory markers in patients with ventilator-associated pneumonia

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## ABSTRACT

**Objective:** To observe the effect of Xuebijing, a complex traditional Chinese preparation, on inflammation and prognosis of patients with pneumonia.

**Methods:** The patients with ventilator-associated pneumonia in the intensive care unit (ICU) were randomly divided into the control group and the treatment group with 35 cases in each group. Both groups were given routine treatment such as anti-inflammatory drugs, rehydration, expectorant, and nutritional support, while the treatment group was additionally given Xuebijing injection. Serum C-reactive protein (CRP), clinical pulmonary infection score (CPIS), acute physiology, and chronic health score II (APACHE II) were recorded before treatment, the 3rd and 7th day after treatment. The duration of antibiotic use, mechanical ventilation, ICU stay, and mortality during 28 days was recorded.

**Results:** There was no significant difference in CRP, CPIS, and APACHE II between the two groups before treatment ( $P>0.05$ ). The improvement of CRP, CPIS, and APACHE II in the treatment group was better than those in the control group on the 3 and 7 days after treatment, and the differences were statistically significant ( $P<0.05$ ). The duration of antibiotic use, mechanical ventilation, and ICU stay in the treatment group were less than those in the control group ( $P<0.05$ ). The 28-day mortality of the treatment group was lower than that of the control group, but the difference was not statistically significant ( $P>0.05$ ).

**Conclusions:** Xuebijing injection can improve the inflammatory indexes of patients with ventilator-associated pneumonia, and can partly improve the prognosis.

**KEYWORDS:** Xuebijing injection; Ventilator-associated pneumonia;

C-reactive protein; Clinical pulmonary infection score; APACHEII

## 1. Introduction

Mechanical ventilation (MV) is a key treatment in the treatment of acute and severe respiratory insufficiency. With the development of critical care medicine and population growth, more and more patients need MV. Despite the improvement of MV technology, the incidence and mortality of ventilator-associated pneumonia (VAP) remain high[1]. Once ventilator-associated pneumonia occurs in

### Significance

Ventilator-associated pneumonia (VAP) is one of serious complications mechanical ventilation. Once VAP occurs in patients, the risk of death will increase. Therefore, the use of effective medicine has great significance. Xuebijing injection is a traditional medicine, which can improve conditions of patients with severe respiratory diseases. In this study, we found that Xuebijing injection can improve the inflammatory indexes of patients with VAP, and can partly improve the prognosis.

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critically ill patients, it indicates that the condition is aggravated. Therefore, early treatment has practical significance in improving the survival rate.

Xuebijing injection is extracted from *Carthamus tinctorius*, Chishao, Chuanxiong, Danshen, Danggui, and other traditional Chinese medicine, which could antagonize endotoxin, regulate immune response, curb inflammatory cytokines, improve microcirculation, protect endothelial cells, and so on<sup>[2,3]</sup>. Xuebijing injection can improve conditions of patients with severe respiratory diseases and enhance the clinical cure rate<sup>[4,5]</sup>. In this study, we aim to determine the effect of Xuebijing injection on the inflammation and prognosis of patients with ventilator-associated pneumonia.

## 2. Patients and methods

### 2.1. Patients

This prospective study included patients with ventilator-associated pneumonia who were admitted to the intensive care unit of the Second Hospital of Tangshan from January 2016 to December 2020.

### 2.2. Ethical approval

The study protocol was approved by the Ethical Committee of the Second Hospital of Tangshan (Serial number: TSTRY-LL-2021042). Informed consent was obtained from all the patients before the research.

### 2.3. Inclusion and exclusion criteria

Inclusion criteria were according to the national infection surveillance system VAP diagnostic criteria<sup>[6]</sup>: MV for more than 48 h, and chest X-ray showed new or progressive infiltrating lesions in the lung, which could not be explained by other reasons. At the same time, patients should have two of the following manifestations: (1) Fever: Body temperature  $\geq 37.5^{\circ}\text{C}$  or body temperature  $1^{\circ}\text{C}$  higher than that before MV; (2) Peripheral blood leukocytes  $\geq 10.0 \times 10^9/\text{L}$ , or  $\leq 4.0 \times 10^9/\text{L}$ . Purulent airway secretion or secretion increased.

Exclusion criteria: (1) Patients with pneumonia before MV; (2) Before the diagnosis of VAP, the patients were treated with antibiotics, adrenocortical hormone, or immunosuppressant; (3) Patients with infection of other unspecific sites before tracheal intubation; (4) Patients with acquired immunodeficiency virus; (5) Patients with hyperthyroidism and epilepsy.

### 2.4. Treatment

All patients were given comprehensive treatment according to the guidelines<sup>[7]</sup>, including anti-inflammatory drugs, fluid infusion, expectorant, nutrition, oxygen inhalation, analgesia, and other

conventional treatment. There was no significant difference in comprehensive treatment between the two groups. The treatment group was additionally treated with Xuebijing injection (provided by Tianjin HongRi Pharmaceutical Group) 100 mL 0.9% sodium chloride solution + 50 mL Xuebijing injection intravenous drip, 60 min each time, twice a day, 7 d as a course of treatment.

### 2.5. Evaluation index

The serum C-reactive protein (CRP), clinical pulmonary infection score (CPIS)<sup>[8]</sup>, acute physiology, and chronic health score II (APACHE II)<sup>[9]</sup> were recorded before treatment, the 3rd and 7th day after treatment. The duration of antibiotic use, mechanical ventilation, ICU stay, and mortality during 28 days was recorded.

Serum CRP was detected by an automatic biochemical analyzer in the hospital laboratory center. CPIS score included body temperature, white blood cell count, tracheal secretion, oxygenation, chest X-ray, the progress of pulmonary infiltration shadow, and tracheal aspirate culture, with the highest score of 12. APACHE II score included three parts: Acute physiology score, age score, and chronic health score. The highest score is 71.

### 2.6. Statistical analysis

SPSS17.0 statistical software was used for statistical analysis. CRP, CPIS, APACHE II, duration of antibiotic use, mechanical ventilation, ICU stay, and other indicators were taken as measurement data, expressed as mean  $\pm$  standard deviation, and Student's *t*-test was applied to analyze these data. 28-day mortality and other indicators were taken as the count data, using *Chi*-square test to analyze. The significant level of the test was set at  $\alpha=0.05$ .

## 3. Results

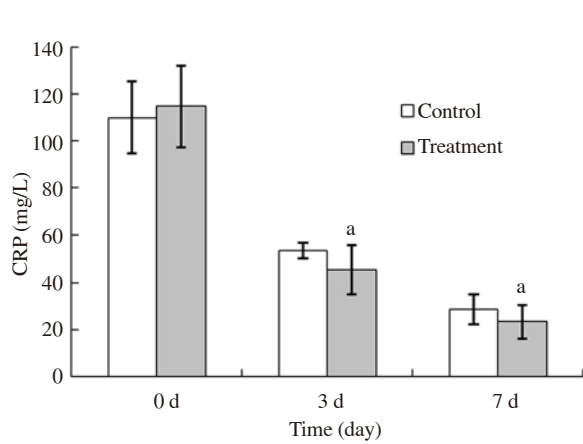
A total of 70 patients with VAP in ICU from January 2016 to December 2020 were selected, including 39 males and 31 females, ranging in age from 22 to 75 years old. All patients were randomly divided into the control group and the treatment group by random envelope method, with 35 cases in each group.

There was no significant difference in gender, age, weight, and primary disease between the two groups ( $P>0.05$ ). The duration of antibiotic use, mechanical ventilation, and ICU stay in the treatment group were lower than those of the control group, and the difference was statistically significant ( $P<0.05$ ). The mortality of 28 d of the two groups was 11.42% and 22.85%, respectively. The mortality of the treatment group was lower than that of the control group, but the difference was not statistically significant ( $P>0.05$ ) (Table 1).

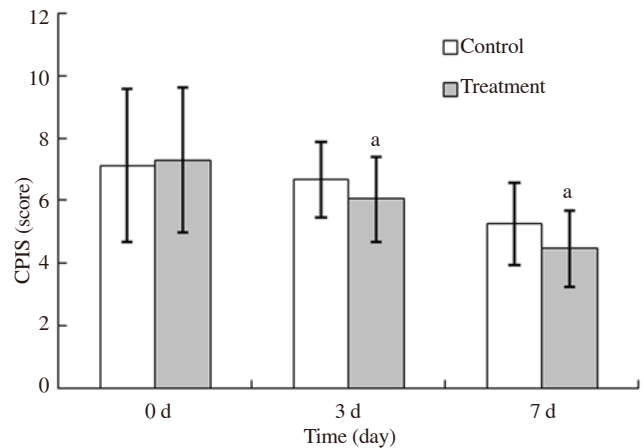
There was no statistical difference in CRP between the two groups before treatment ( $P>0.05$ ). On the 3rd and 7th day after treatment, the CRP in the treatment group was lower than those in the control

**Table 1.** Demographic and baseline information.

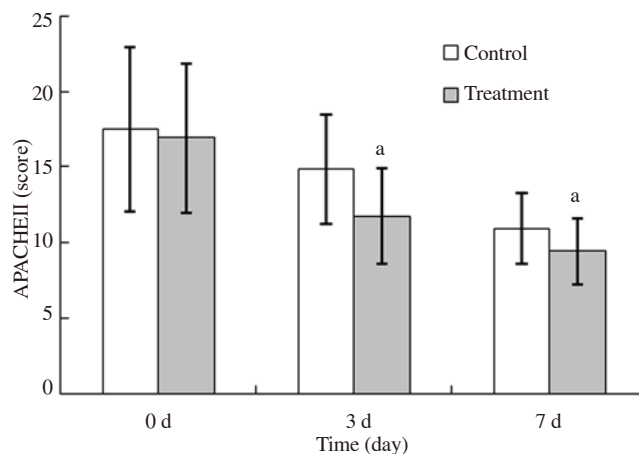
Variables	Treatment (n=35)	Control (n=35)	$\chi^2/t$	P
<b>Sex, n (%)</b>			2.611	0.106
Male	19 (54.29%)	20 (57.14%)	-	-
Female	16 (45.71%)	15 (42.86%)	-	-
<b>Age, years</b>	58.22±7.38	57.31±8.11	0.491	0.624
<b>Weight, kg</b>	67.57±11.24	65.48±10.38	0.808	0.423
<b>Primary disease, n (%)</b>			0.249	0.969
Stroke	11 (31.43)	12 (34.29)	-	-
Multiple injuries	11 (31.43)	10 (28.57)	-	-
Spinal cord injury	8 (22.86)	7 (20.00)	-	-
Chest injury	5 (14.29)	6 (17.14)	-	-
<b>Duration of antibiotic use, d</b>	9.04±2.70	10.84±2.56	2.862	0.005
<b>Duration of mechanical ventilation, d</b>	6.71±1.61	7.56±1.86	2.044	0.045
<b>Duration of ICU stay, d</b>	12.22±3.08	13.84±3.12	2.186	0.032
<b>28-day mortality, n (%)</b>	4 (11.43%)	8 (22.86%)	1.609	0.205



**Figure 1.** Comparison of C-reactive protein between the treatment group and the control group. a:  $P < 0.05$ . CRP: C-reactive protein.



**Figure 2.** Comparison of clinical pulmonary infection score between the treatment group and the control group. a:  $P < 0.05$ . CPIS: Clinical pulmonary infection score.



**Figure 3.** Comparison of acute physiology, and chronic health score II between the treatment group and the control group. a:  $P < 0.05$ . APACHEII: Clinical pulmonary infection score.

group, and these differences were statistically significant ( $P < 0.05$ ) (Figure 1).

There was no significant difference in CPIS between the two groups before treatment ( $P > 0.05$ ). On the 3rd and 7th day after treatment, the CPIS in the treatment group were lower than those in the control group, and these differences were statistically significant ( $P < 0.05$ ) (Figure 2).

There was no statistical difference in APACHE II between the two groups before treatment ( $P > 0.05$ ). On the 3rd and 7th day after treatment, the APACHE II in the treatment group was lower than those in the control group, and these differences were statistically significant ( $P < 0.05$ ) (Figure 3).

#### 4. Discussion

VAP refers to new infectious pulmonary parenchymal inflammation after tracheal intubation or tracheotomy and MV  $\geq 48$  hours. VAP is a common and serious complication in the process of MV. Once VAP occurs in patients, it is easy to cause offline difficulties, thus prolonging the length of hospital stay, increasing the cost of hospitalization, and even threatening the life of patients. Literature reported that the incidence of VAP in patients with MV was 20%-75%[10], and the mortality after VAP was as high as 20%-80%[11]. Although many scholars have proposed many different methods for the prevention and treatment of VAP, the overall incidence and mortality have not decreased significantly. Antibiotics are one of the chooses for the treatment of VAP, but single-use of antibiotics can not achieve ideal effect. The reason is that antibiotics can kill bacteria and promote the release of bacterial endotoxin. However, it has not been confirmed that some antibiotics can neutralize endotoxin. Studies have shown that the treatment of endotoxin is conducive to infection control and disease improvement[12].

The active ingredient of Xuebijing injection is extracted from Chinese herbals, which is a natural medicine with an antagonistic effect against endotoxin. The mechanism of its effective treatment of sepsis and other infectious diseases is to reduce the level of endotoxin, protect vascular endothelial cells, improve microcirculation, and then promote the absorption of inflammation so that the damaged tissues and organs can be repaired[13].

CRP is an acute-phase protein synthesized by hepatocytes when the body is stimulated by inflammation such as microbial invasion or tissue damage. The change of CRP is a very sensitive index to reflect tissue damage and infection. CRP is the most practical inflammatory marker for clinical evaluation of infection[14]. APACHE II score and CPIS are the most widely used indicators to evaluate the severity and prognosis of critically ill patients with respiratory infections, and they have high accuracy[15].

In this study, the treatment group was given Xuebijing injection, and the levels of CRP, CPIS, and APACHE II in the treatment group were significantly lower than those in the control group, indicating

that Xuebijing injection can effectively inhibit the inflammatory reaction and promote the absorption of inflammation by reducing endotoxin and improving microcirculation mechanism. It improved the patient's condition and prognosis, and ultimately shortened the duration of antibiotic use, mechanical ventilation and ICU stay. Therefore, this study confirmed that Xuebijing injection is an effective medicine in the treatment of VAP.

#### Conflict of interest statement

The authors report no conflict of interest.

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#### Authors' contributions

H.W.Z. wrote the first draft and analyzed the data. All authors contributed to the design and approved the final version of the article.

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