

ORIGINAL RESEARCH

Investigation of the Clinical Studies of Traditional Chinese Medicine and Western Medicine in the Treatment of Disorders Related to Ventilators

ChunYan Wu, MM; Dongmei Li, MD; Zhu Zeng, MD;
Youjian Yang, MD; Yunling Huang, MD; Xiaoyan Yao, MM

ABSTRACT

Objective • To observe the comprehensive treatment effect of Traditional Chinese Medicine on ventilator-related diseases.

Methods • From January 2021 to August 2022, a total of 80 patients with ventilator-associated pneumonia were selected and divided into a test group and a matched control group based on the random number table, with 40 cases in each group. The control group received traditional Western medical care, and all patients were given tigecycline intravenously. The patients in the test group were treated with integrated traditional Chinese and Western medicine, and all patients were given tigecycline for injection by intravenous drip combined with Qingfei Huatan decoction orally. The two groups' therapeutic outcomes were contrasted, namely: procalcitonin (PCT), tumor necrosis factor (TNF)- α , hypersensitive C-reactive protein (CRP), blood oxygen saturation (PaO₂), and white blood cell (WBC) count. Acute physiology and persistent

health scores, clinical lung infection score, mechanical ventilation time, body temperature recovery time, and hospitalization time were recorded.

Results • The effective Of cure in the test group was 37/40 (92.50%) and in the control group it was 30/40 (75.00%). The test group outperformed the control group by a considerable margin ($P < .05$). The levels of PCT, TNF- α , and hs-CRP were lower in the two groups, and the levels of TNF- α , PCT, and hs-CRP reduced with treatment ($P < .05$). The white blood cell and PaO₂ levels were lower in the experimental group. APACHE II and CPIS scores decreased ($P < .05$). two groups, Postoperative body temperature recovery time, mechanical ventilation time, and hospital stay were all shortened ($P < .05$).

Conclusion • The combination of traditional Chinese medicine and Western medicine has a positive clinical impact on ventilator-related diseases. (*Altern Ther Health Med.* 2023;29(8):286-291).

ChunYan Wu, MM; Xiaoyan Yao, MM; Department of Intensive Care Medicine, Shaoxing People's Hospital, Shaoxing, Zhejiang, China. **Dongmei Li, MD; Zhu Zeng, MD; Youjian Yang, MD; Yunling Huang, MD;** Respiratory Department, Hospital of Chengdu University of TCM, Chengdu, Sichuang, China.

Corresponding author: Xiaoyan Yao, MM
E-mail: hyl980823@163.com

INTRODUCTION

The most prevalent nosocomial infection among patients receiving mechanical ventilation in intensive care units is ventilator-associated pneumonia (VAP).¹ Studies have shown that the incidence of VAP in intensive care units is as high as 2.5% - 40.0%, and the case fatality rate is as high as 13.0% - 25.2%.^{2,3} Nosocomial infection pathogens are mainly Gram-negative bacteria, among which one of the more extensively found Gram-negative pathogens is drug-resistant

Acinetobacter baumannii,⁴ which is characterized by strong drug resistance and clonal transmission ability.

In recent years, it has become one of the most common pathogenic factors of VAP and may increase the risk of poor prognosis of VAP patients.⁵ It may cause severe respiratory dysfunction, systemic inflammatory response, and even important organ dysfunction. Thus, it is crucial to effectively treat VAP caused due to Gram-negative bacteria as soon as possible.⁶ Tigecycline is a glycylcycline antibiotic, which is mainly used to treat infections caused by sensitive bacteria. As a new broad-spectrum active antibiotic for intravenous injection, tigecycline exhibits effective antibacterial properties against Gram-positive, negative, and anaerobic microorganisms.⁷

Tigecycline is the first choice for patients with severe multi-drug-resistant bacterial infections. Tigecycline used over an extended period, however, is linked to several negative side effects and antibiotic resistance. TCM has a very long history of treating pneumonia.⁸ For example, Qingfei Huatan decoction is made from various medicinal materials such as *Ceanothus americanus*, *Isatis tinctoria*, and

Tian Zhu Huang (siliceous secretions of bamboo). Reed root can clear lung heat, generate saliva, and quench thirst, Banlangen can clear heat and detoxify, Tian Zhu Huang can clear heat and dissipate phlegm, and the dosage can be chosen based on the patient's health. The dosage can be changed, i.e., increased or decreased depending upon the patient's state. The entire recipe achieves the therapeutic effect of reducing lung qi and eliminating phlegm heat.⁹ Moreover, as an auxiliary treatment for pneumonia, patients' levels of inflammatory factors can be raised by using Qingfei Huatan decoction, which has a definite therapeutic impact.¹⁰

Nowadays, the practical use of TCM and Western medicine has had obvious positive benefits in the treatment of various diseases,^{11,12} however, research on the management of ventilator-associated pneumonia is scant. Considering this, assessing the medical effectiveness of integrating TCM and Western medicine in the treatment of ventilator-associated diseases could be beneficial. This research seeks to provide a scientific and trustworthy clinical reference basis for the treatment and recovery of patients with ventilator-associated diseases (e.g., ventilator-associated pneumonia).

PATIENTS AND METHODS

Basic Information

Between January 2021 and August 2022, data on 80 individuals with ventilator-associated pneumonia were gathered. They were split into two groups using the random number table method: the test group and the control group, 40 each. (1) There were 23 men and 17 women in the test group, with ages ranging from 55 to 83 years and a mean of (64.21 ± 2.04) years. The average duration of the diseases was 14.45 days, ranging from 6 to 22 days. (2) Control group: 24 men and 16 women; the age is between 56 and 82 years, with a mean of 64.55 ± 2.24 years. The average onset time of disease in patients (14.05 ± 1.17) days. There is no statistical difference in general data between the two groups ($P > .05$). This study was approved by the Ethics Committee of Shaoxing People's Hospital (Grant No:20210256).

Inclusion

(1) See the "Guidelines for the Diagnosis and Treatment of Hospital-Acquired Pneumonia and Ventilator-Associated Pneumonia in Chinese Adults" for information on the diagnosis and treatment of ventilator-associated pneumonia and hospital-acquired pneumonia (2018 Edition), the diagnostic criteria for VAP were discussed,¹³ which meet any of the following 1) and 2) and 3) to 8): 1) mechanical ventilation time ≥ 48 hours; 2) new or progressive patchy and patchy infiltrative shadows with or without pleural effusion on chest X-ray;¹⁴ 3) new fever, body temperature $>38^{\circ}\text{C}$, or 1°C higher than basal body temperature; 4) purulent secretions in the trachea; 5) pulmonary consolidation characteristics and/or moist rales heard on pulmonary auscultation; WBC count $> 10 \times 10^9/\text{L}$ or $< 4 \times 10^9/\text{L}$ in peripheral white blood cells, with or without left shift of the nucleus; 7) positive endotracheal aspirate culture; 8) blood

culture or pleural effusion culture is the same as the pathogen cultured from endotracheal secretions. (2) Complete clinical data. (3) Strong compliance and good communication with medical staff. (4) Patients' families also signed informed consent forms.

Exclusion Standards

(1) Hospital acquired pneumonia (HAP); (2) those suffering from systemic infectious illnesses; (3) patients with severe disturbance of consciousness or mental disorders; (4) patients during pregnancy or lactation; (5) patients suffering from severe liver, renal, and cardiac dysfunction; and (6) patients with severe malignant tumors.

Method

Individuals in the control group received standard Western medical care, including an intravenous drip of the antibiotic tigecycline (strength: 50 mg, Guoyao Zhunzhi: H20133165, production batch number: 180424, manufacturer: Nanjing Haichen Pharmaceutical Company Limited, Nanjing), 50 mg/12 h; The treatment was continued for 14 days. The control group was treated with a combination of TCM and Western medicine. The patients in the test group received Qingfei Huatan decoction. The composition of the prescription was: 15 g each of Tian Zhu Huang, Houptuynia cordata, and Isatis indigotica, 12 g each of Huangling, asters, Coltsfoot flowers, reed roots, yam, and lentils, 10 g each of Fritillaria thunbergii, fried bitter almonds, tangerine peels, and licorice, 1 dose per day, decocted twice, and about 300 mL of the two decoctions were mixed and treatment was continued for 14 days.

Outcome Measures

(1) To compare the clinical effectiveness of the two patient groups. Criteria for efficacy:¹⁵ (i) Recovered: Clinical symptoms such as cough, difficulty breathing, and wet wheezing in the lungs have been alleviated, and chest X-ray shows that lung infiltration has been alleviated or the area has reached over 90%, and the efficacy index reached at least 90%. (ii) Obviously effective: the patient's clinical symptoms such as cough, dyspnea, and moist lungs were improved, the disappearance rate of lung infiltration in chest X-ray examination was between 60% and 90%, and the efficacy index was between 60% and 90%. (iii) Effective: clinical symptoms improved, pulmonary infiltrates disappeared between 30% and 60%, and the performance index achieved was between 30% and 60%. (iv) Ineffective: no improvement in clinical symptoms, disappearance of pulmonary infiltrates less than 30%, performance index less than 30%, or further deterioration of the condition. The efficacy index, or overall treatment response rate, is calculated as follows: (Recovery + Excellent + Effective) cases/total cases, multiplied by 100%.

(2) Serum inflammatory factors, including serum tumor necrosis factor- α (TNF- α), procalcitonin (PCT), and high-sensitivity C-reactive protein (hs-CRP): measured before treatment and after 14 days of treatment. Five milliliters of

cubital venous blood from each patient was drawn and spun using a medical low-speed centrifuge for 15 minutes at 3000 rpm (model: TDZ4-WS, manufacturer: Changsha Xiangzhi Centrifuge Instrument Company Limited, Changsha, Hunan). After serum separation, various liver function parameters were measured using an automatic biochemical analyzer (model: cobas-6000, Roche Holding Ag, Basel). The aforementioned characteristics were ascertained using an enzyme-linked immunosorbent assay.

(3) Blood parameters, including oxygen saturation (PaO_2) and white blood cell (WBC) count: Before treatment and the morning following 14 days of treatment, five milliliters of cubital venous blood from the patients were drawn while they were fasting. The blood was then centrifuged using a medical low-speed centrifuge at 3000 rpm for 15 minutes. After serum separation, arterial blood count was measured using an automatic hematology analyzer (model: CT-3080, manufacturer: Shenzhen Kaike Biomedical Electronic Technology Company Limited). 1.0-1.5 mL of arterial blood was collected from the aortic site of the patient using a disposable preflush arterial blood gas needle (model: REF364314, manufacturer: Becton, Dickinson and Company, USA). If bleeding occurred during the puncture, the needle was stopped, and the syringe was rubbed with the palm for 5 seconds to thoroughly mix blood and heparin to prevent red blood cell aggregation. After the completion of the collection, the needle was immediately closed with a rubber plug, the air was closed, and the sample was sent for testing 15 minutes later. After the sample was evenly mixed, the first drop of blood was set in the machine, and an arterial blood gas analyzer (model: RAPID248/348, manufacturer: Siemens, Beijing) was used to read the test chip and the oxygen saturation was inserted and printed.

(4) Acute physiology and chronic health evaluation (APACHE II): scores for APACHE II scores for both groups of patients before and after treatment for 14 days The Clinical Pulmonary Infection Scale (CPIS) ¹⁶ was used to screen for pulmonary infection, along with other parameters such as the body temperature, white blood cell count, tracheal drainage, oxygen inhalation, and invasive chest radiography, with scores ranging from 0 to 12. Antibiotics were discontinued if the score was below 6. The APACHE II grading method was used to assess the severity of the systemic disease,¹⁷ with a maximum score of 71; with higher scores indicating greater severity of the disease.

(5) After the treatment, parameters such as hospital stays, mechanical breathing times, and body temperature recovery times were compared between the two groups.

Statistical Procedures

SPSS26.0 statistical software was used to examine all experimental data. Enumeration data were expressed as %, and the χ^2 test was used to compare the findings between the two groups. Measurement data with a normal distribution were expressed as ($\bar{x} \pm s$), and an independent t test was used to compare groups. $P < .05$ indicates that the difference was statistically significant.

Table 1. Contrast of Medical Effectiveness Between the Two Groups (n, %)

Group	Recovery	Excellent	Effective	Invalid	Total Effective Rate
Control group (n = 40)	8 (20.00)	10 (25.00)	12 (30.00)	10 (25.00)	30 (75.00)
Test group (n = 40)	16 (40.00)	14 (35.00)	7 (17.50)	3 (7.50)	37 (92.50) ^a
χ^2					4.501
P value					.034

^aCompared with the concurrent control group, $P < .05$.

RESULTS

Comparison of medical effectiveness between the two groups

There was a clear difference between the two groups, with the test group's total effective rate (92.50%, 37 out of 40 patients) being much higher than that of the control group (75.00%, 30 out of 40 patients) ($P > .05$). For information, refer to Table 1.

Comparison of serum inflammatory factor markers in the two groups before and after treatment

Compared with before treatment, PCT and TNF in both groups of patients- α The levels of hs CRP decreased after treatment. Compared with the control group, the TNF of the experimental group after treatment- α . The levels of PCT and hs CRP decreased ($P < .05$). However, there was no statistically significant difference before treatment ($P > .05$), as shown in Table 2.

Comparison of blood values between the two groups before and after treatment

There was no discernible difference in WBC count and PaO_2 levels before treatment between the two groups ($P > .05$). The WBC and PaO_2 levels in the two groups decreased after treatment in comparison to their levels before treatment. Compared to the control group, the values of PaO_2 and WBC count in the test group were significantly lower ($P < .05$), as shown in Table 3.

Comparison of CPIS and APACHE II scores between the two groups before and after treatment

Before treatment, there was no significant difference in APACHE II and CPIS scores between the two groups ($P > .05$). Compared with before treatment, the scores of both groups decreased significantly after treatment, and the APACHE II and CPIS scores of the experimental group were lower than those of the control group ($P < .05$), as shown in Table 4.

Comparison of hospital stays, body temperature recovery times, and mechanical ventilation times between the two groups

The postoperative body temperature recovery period, the length of mechanical ventilation, and the hospital stay in the test group were all significantly shorter than those of the control group ($P < .05$). For information, refer to Table 5.

Table 2. Contrast of Serum Inflammatory Factor Markers in the Two Groups Before and After Treatment ($\bar{x} \pm s$)

Group	PCT (ng/mL)				TNF- α (μ g/L)				hs-CRP (mg/L)			
	Before treatment	After treatment	<i>t</i>	<i>P</i> value	Before treatment	After treatment	<i>t</i>	<i>P</i> value	Before treatment	After treatment	<i>t</i>	<i>P</i> value
Control group (n = 40)	11.87 \pm 2.35	7.88 \pm 1.51 ^a	9.034	<.001	5.20 \pm 0.61	0.94 \pm 0.29 ^b	39.890	<.001	30.12 \pm 5.40	15.10 \pm 3.57 ^b	14.675	<.001
Test group (n = 40)	12.15 \pm 2.43	3.49 \pm 0.60 ^{a,b}	21.882	<.001	5.27 \pm 0.56	0.62 \pm 0.14 ^{a,b}	50.948	<.001	29.97 \pm 5.08	9.03 \pm 2.16 ^a	23.991	<.001
<i>t</i>	1.179	17.0888			0.535	6.285			0.128	23.991		
<i>P</i> value	.242	<.001			.594	<.001			.899	<.001		

^aCompared with the concurrent control group, *P* < .05^bCompared with that before treatment, *P* < .05**Abbreviations:** TNF- α , tumor necrosis factor- α ; PCT, procalcitonin; hs-CRP, high-sensitivity C-reactive protein.**Table 3.** Comparison of the Blood Values Between the Two Groups Before and After Treatment ($\bar{x} \pm s$)

Group	PaO ₂ (mmHg)				WBC count ($\times 10^9/L$)			
	Before treatment	After treatment	<i>t</i>	<i>P</i> value	Before treatment	After treatment	<i>t</i>	<i>P</i> value
Control group (n = 40)	70.10 \pm 1.67	86.95 \pm 2.18 ^a	38.807	<.001	14.17 \pm 1.01	10.05 \pm 0.73 ^a	20.909	<.001
Test group (n = 40)	70.25 \pm 0.72	98.78 \pm 0.81 ^{a,b}	166.497	<.001	14.04 \pm 0.98	8.02 \pm 0.52 ^a	34.319	<.001
<i>t</i>	0.522	32.172			0.584	14.325		
<i>P</i> value	.603	<.001			0.561	<0.001		

^aCompared with the concurrent control group, *P* < .05^bCompared with that before treatment, *P* < .05**Abbreviations:** PaO₂, blood oxygen saturation; WBC: white blood cell.**Table 4.** The Two Groups' Respective CPIS and APACHE II Scores Before and After Treatment ($\bar{x} \pm s$, points)

Group	CPIS				APACHE II			
	Before treatment	After treatment	<i>t</i>	<i>P</i> value	Before treatment	After treatment	<i>t</i>	<i>P</i> value
Control group (n = 40)	7.47 \pm 1.34	5.36 \pm 0.90	8.071	<.001	22.53 \pm 2.35	13.22 \pm 1.58	20.793	<.001
Test group (n = 40)	7.51 \pm 1.40	4.27 \pm 0.31	14.291	<.001	22.65 \pm 2.42	9.52 \pm 1.26	30.436	<.001
<i>t</i>	0.294	7.242			0.225	11.579		
<i>P</i> value	0.770	<.001			.823	<.001		

Abbreviations: CPIS: Clinical Pulmonary Infection Score; APACHE II: Acute Physiology and Chronic Health Evaluation II.**Table 5.** Contrast of the Two Groups' Hospital Stays, Body Temperature Recovery Times, and Mechanical Ventilation Times ($\bar{x} \pm s$)

Group	Mechanical ventilation time (d)	Temperature recovery time (h)	Length of stay (d)
Control group (n = 40)	11.43 \pm 1.79	6.88 \pm 1.46	15.52 \pm 3.42
Test group (n = 40)	8.16 \pm 1.47 ^a	3.65 \pm 1.22 ^a	10.60 \pm 1.45 ^a
<i>t</i>	8.929	10.737	8.377
<i>P</i> value	<.001	<.001	<.001

^aCompared with the concurrent control group, *P* < .05.

DISCUSSION

Patients are often needed to wear respirators for short durations before being asked to take them off once their condition improves. However, when patients are on prolonged mechanical ventilation, complications such as respiratory muscle fatigue, airway injury, and VAP, are common, with a potential incidence of up to 40%. VAP occurs when pathogens invade the distal bronchi and alveoli, break through the body's defense mechanisms, and multiply inside the lungs.^{18,19}

Intensive care unit (ICU) patients are often critically unwell when they are admitted. Hence, with rapid changes in the patient's condition and low immunity, nasal infections are likely to occur. VAP patients are directly affected by lower respiratory tract infections after endotracheal intubation, since the ability of cilia to fix the airway decreases, thus resulting in direct contact between the lower respiratory tract and the outside world. Tracheal intubation destroys the protective wall of respiratory tract, reduces the capacity of

capillary lumen, and then promotes the proliferation and colony formation of various bacteria at the injury/lesion site.²⁰ Clinical Western medicine often uses antibiotics to treat VAP patients, such as tigecycline, however, due to antibiotic resistance the drug fails to achieve the ideal therapeutic effect.²¹ Chinese medicine has achieved significant advancements in the treatment of COVID-19 in recent years, as well as in the integration of TCM and Western medicine.²² Furthermore, the treatment of VAP with Qingfei Huatan decoction has also produced clear outcomes in the field of Chinese medicine.²³

The results of this study showed that the total effective rate of treatment in the test group (92.50%) was substantially higher than that in the control group (75.00%) (*P* < .05). In Western medicine, tigecycline is effective for treating VAP; however, when coupled with Qingfei Huatan decoction, tigecycline had a more effective therapeutic effect than when administered alone. This is because Tian Zhu Huang, Huangling, asters, Coltsfoot flower, licorice, and other traditional Chinese medicinal materials contained in Qingfei Huatan decoction has the medicinal properties of moistening the lung, relieving cough, relieving fever, anti-virus, improving immune mechanism, and reducing phlegm, thereby improving the therapeutic effect of tigecycline on VAP patients.²⁴

The Chinese medicinal materials in Qingfei Huatan decoction, such as astragalus, contain chemically active ingredients that can enhance the patient's immune system and work together with tigecycline to effectively improve the

patient's clinical symptoms.²⁵ PCT is the main diagnostic indicator of fever caused by infection, which can accurately indicate the occurrence of bacterial infection,²⁶ while TNF- α is a natural factor produced by macrophages for specific infection or immunity, with high accuracy in evaluating bacterial inflammation.²⁷ The findings of the study show that after treatment, PCT, TNF- α , and hs-CRP levels decrease compared to the levels before treatment. Importantly, after treatment, the decrease in the levels of these serum inflammatory indicators was significantly more in the test group than in the control group ($P < .05$). The combination of TCM and Western medicine treatment for VAP can significantly reduce the inflammatory response in patients. Hs-CRP is a rapid measure of how much inflammation is present in the body and is useful in determining the status and prognosis of infection.²⁸ In this study, Tigecycline combined with Qingfei Huatan Decoction was used to treat VAP and inhibit the propagation of pathogenic bacteria. This helps to effectively block the pathway of pathogenic bacteria infecting target cells in patients with VAP, thereby enhancing their immune function and improving clinical symptoms. In Qingfei Huatan decoction, Tang, Poria cocos, Herba Pinelliae, and tangerine peel can invigorate the spleen and dry dampness; forsythia suspensa, honeysuckle, and houttuynia cordata can clear heat and detoxify; scallops, Trichosanthes kirilowii, and platycodon have the effect of broadening the chest and eliminating phlegm; anemarrhena asphodeloides and ophiopogon japonicus can moisten the lungs and relieve cough, clear heat, and nourish yin; and, licorice can harmonize the medicinal properties. Thus, administering a combination of the above drugs can further improve the therapeutic effect on VAP patients. The use of tigecycline and Qingfei Huatan decoction in this study which attempted to combine TCM and Western medicine has a positive synergistic effect on the therapy of VAP.

Compared to before treatment, both PaO₂ and WBC count decreased after treatment ($P < .05$), clearly indicating that the combination of tigecycline and Qingfei Huatan decoction could enhance the blood oxygen level of VAP patients, relieve their dyspnea, and reduce the body's inflammatory response.²⁹ The presence of a variety of TCM materials such as winter melon, tangerine peel, Trichosanthes kirilowii, and almond, which are associated with the effects of relieving cough and asthma, moistening lung, reducing phlegm,³⁰ improving the respiratory mechanics and blood gas parameters of VAP patients, reducing inflammatory factors, improving immune function, Qingfei Huatan decoction contributes to the rehabilitation of VAP patients.

Xue Ming et al.³¹ in their study highlighted the protective effects of Qingfei Huatan decoction on the pulmonary function and its therapeutic effect on the immune function in children with severe pneumonia. Their findings are consistent with those obtained in this study, thus demonstrating that tigecycline and Qingfei Huatan decoction together can lessen patients' inflammation reactions, reduce the inflammatory infiltration of lung tissue, control the pulmonary infection

caused by VAP, reduce multiple organ dysfunction, reduce the symptoms caused by pulmonary and even systemic infection, shorten the ventilation time, and further promote patient recovery. The test group's hospitalization time, body temperature recovery time, and artificial ventilation time were all significantly less than those of the control group ($P < .05$), indicating that the combined approach can improve the recovery of VAP patients and reduce the length of stay in the hospital.

Since the main pathological changes associated with VAP are inflammatory reactions caused by bacterial infection, the degree of changes in the inflammatory state is very critical for the treatment and recovery of VAP patients.³² Therefore, when using integrated traditional Chinese and Western medicine to treat VAP in clinical practice, more attention should be paid to the changes in various indicators/parameters indicating the patient's condition, and appropriate modifications should be made to the treatment plan to improve the patient's prognosis and recovery, and reduce research bias. However, further research is needed to validate and promote our findings in different populations.

CONCLUSION

In summary, the clinical outcome of combining TCM with Western medicine in the treatment of disorders linked to ventilators is favorable, which can potentially improve the respiratory function of patients, control their pulmonary infection, and reduce the inflammatory response. Therefore, it is worth considering its application in an open clinical environment.

FUNDING

No funding was received for the study

DATA AVAILABILITY

Data is available upon request to the corresponding author.

AUTHOR DISCLOSURE STATEMENT

There are no conflicts of interest in this study

REFERENCES

1. Ismaeil T, Alfunaysan L, Alotaibi N, Alkadi S, Othman F. Repositioning of endotracheal tube and risk of ventilator-associated pneumonia among adult patients: A matched case-control study. *Ann Thorac Med*. 2019;14(4):264-268. doi:10.4103/atm.ATM_26_19
2. Johnstone J, Meade M, Lauzier F, et al; Prevention of Severe Pneumonia and Endotracheal Colonization Trial (PROSPECT) Investigators and the Canadian Critical Care Trials Group. Effect of probiotics on incident ventilator-associated pneumonia in critically ill patients: a randomized clinical trial. *JAMA*. 2021;326(11):1024-1033. doi:10.1001/jama.2021.13355
3. Pulmonary Infections J-LL, Ventilator-Associated Pneumonia I. *Crit Care Nurs Clin North Am*. 2021;33(4):381-393. doi:10.1016/j.cnc.2021.08.002
4. Jung YJ, Kim EJ, Choi YH. Aerosolized antibiotics in the treatment of hospital-acquired pneumonia/ventilator-associated pneumonia. *Korean J Intern Med (Korean Assoc Intern Med)*. 2022;37(1):1-12. doi:10.3904/kjim.2021.277
5. Saipriya K, Swathi CH, Ratnakar KS, Sriharan V. Quorum-sensing system in *Acinetobacter baumannii*: a potential target for new drug development. *J Appl Microbiol*. 2020;128(1):15-27. doi:10.1111/jam.14330
6. Kallet RH. Ventilator Bundles in Transition: From Prevention of Ventilator-Associated Pneumonia to Prevention of Ventilator-Associated Events. *Respir Care*. 2019;64(8):994-1006. doi:10.4187/respcare.06966
7. Paköz NİE, Kaya E, Orhan Z, Kayış A, Aral M. Comparison of disc diffusion, E-test and automated system methods for the determination of resistance to tigecycline and colistin by multiple resistant *Acinetobacter baumannii* isolates which isolated from different samples. *Türk Hji Deney Biyol Derg*. 2018;75(2):109-116. doi:10.5505/TurkHjiyen.2018.13334
8. Peng J, Chen X, Hou M, et al. The TCM Preparation Feilike Mixture for the Treatment of Pneumonia: Network Analysis, Pharmacological Assessment and Silico Simulation. *Front Pharmacol*. 2022;13:794405. doi:10.3389/fphar.2022.794405
9. Fei QU, Huang X, Cui Y, et al. Effect of Qingfei Huatan Decoction on Mucus Hypersecretion in Rats with Chronic Obstructive Pulmonary Disease and Its Mechanism. *Zhonghua Zhongyiyao Xuekan*. 2019;37(09):2064-2067.
10. Lin H. Efficacy of the Qingfei Huatan decoction on senile pneumonia. *Clinical Journal of Chinese Medicine*. 2018;10(22):72-73.

11. Ren T, Zhu H, Wang R. Research Progress of Combination of Traditional Chinese and Western Medicine in Treatment of Infertility in Older Women. *Clinical nursing research*. 2021;0(004):005. doi:10.26689/jcnrv5i4.2288
12. Zhangyanhui, Cui H, Genglei. Combination of Traditional Chinese and Western Medicine in Sports in Pharmaceutical Health. *Appl Bionics Biomech*. 2021;2021:1840915. doi:10.1155/2021/1840915
13. Qu JM, Shi Y. [Update and understanding: 2018 Chinese guidelines for the diagnosis and treatment of adults with hospital-acquired and ventilator-associated pneumonia]. *Zhonghua Jie He He Hu Xi Za Zhi*. 2018;41(4):244-246. doi:10.3760/cma.j.issn.1001-0939.2018.04.002
14. Shokouhi S, Niyati R, Darazam IA, Gachkar L, Goharani R, Kahkoe S. Resolution of Chest X-Ray Opacities in Patients with Ventilator-associated Pneumonia. *Infect Disord Drug Targets*. 2018;18(1):23-28. doi:10.2174/1871526517666170505122057
15. Karbasy SH, Sabertanha A, Bayati M, Meshkini A, Fatemeh Shaks Emampour B. Study of the effect of added bronchoscopic suction to routine treatment of ventilator-associated pneumonia patients in surgical ICU. *J Pak Med Assoc*. 2021;71(5):1326-1331. doi:10.47391/JPMA.1086
16. Sathitakorn O, Jantarathaneewat K, Weber DJ, et al. The feasibility of procalcitonin and CPIS score to reduce inappropriate antibiotics use among severe-critically ill COVID-19 pneumonia patients: A pilot study. *Am J Infect Control*. 2022;50(5):581-584. doi:10.1016/j.ajic.2022.01.030
17. Gürsoy G, Gürsoy C, Kuşçu Y, Gümüş Demirbilek S. APACHE II or INCNS to predict mortality in traumatic brain injury: A retrospective cohort study. *Ulus Travma Acil Cerrahi Derg*. 2020;26(6):893-898. doi:10.14744/ujtes.2020.22654
18. Tumor N, De Cunto A, Basma Y, Klein JL, Meau-Petit V. Ventilator-associated pneumonia in neonates: the role of point of care lung ultrasound. *Eur J Pediatr*. 2021;180(1):137-146. doi:10.1007/s00431-020-03710-8
19. Ladbroke E, Bouchoucha SL, Hutchinson A. Lessons learned from a rapid implementation of a ventilator-associated pneumonia prevention bundle. *J Infect Prev*. 2019;20(6):274-280. doi:10.1177/1757177419846588
20. Mishra DR, Shah DS, Shah N, Prasad JN, Gupta PP, Agrawal KK. Study of microbiological and antibiotic sensitivity pattern of ventilator-associated pneumonia (VAP) in ICU of a tertiary care hospital in Nepal. *J Family Med Prim Care*. 2020;9(12):6171-6176. doi:10.4103/jfmpc.jfmpc_1430_20
21. Sabour S. Reliability of Surveillance for Ventilator-Associated Events and Pneumonia; Methodological and Statistical Issues. *Infect Control Hosp Epidemiol*. 2017;38(6):755-756. doi:10.1017/ice.2017.46
22. Wu J, Sun B, Hou L, et al. Prospective: Evolution of Chinese Medicine to Treat COVID-19 Patients in China. *Front Pharmacol*. 2021;11:615287. doi:10.3389/fphar.2020.615287
23. Guan Z, Song S, Zhang Y, et al. Phlegm-Heat Obstructing in Lung of Mycoplasma Pneumonia in Children in Children by Stage Non-Sequential Therapy with Sangxia Qingfei Decoction. *J Tradit Chin Med*. 2018;33(6):979-985.
24. Fan C, Zhou W, Zhang Y, et al. Effect of Qingfei Decoction on virulence factors of drug-resistant *Pseudomonas aeruginosa*. *Report on Traditional Chinese medicine*. 2019;16(13):20-23.
25. Liu AJ, Yu J, Ji HY, Zhang HC, Zhang Y, Liu HP. Extraction of a Novel Cold-Water-Soluble Polysaccharide from *Astragalus membranaceus* and Its Antitumor and Immunological Activities. *Molecules*. 2017;23(1):62. doi:10.3390/molecules23010062
26. Wang W, Jie Y, Zhou J. Values of serum PCT, suPAR combined with severity scores for evaluating prognosis of septic shock patients. *Rev Rom Med Lab*. 2021;29(4):395-402. doi:10.2478/rrlm-2021-0034
27. Kung PL, Chou TW, Lindman M, et al. Zika virus-induced TNF- α signaling dysregulates expression of neurologic genes associated with psychiatric disorders. *J Neuroinflammation*. 2022;19(1):100. doi:10.1186/s12974-022-02460-8
28. Holzknecht M, Reinstadler SJ. CRP: a potential target in reperfused STEMI? Reply to the letter: "Targeting CRP in microvascular obstruction after PCI". *Int J Cardiol*. 2022;355:5. doi:10.1016/j.ijcard.2022.02.019
29. Wu HP, Xia PY. [Metabolic Characteristics of WBC-depleted RBC suspension during Different Storage Stage in MAP Based on UPLC-MS/MS]. *Zhongguo Shi Yan Xue Ye Xue Za Zhi*. 2019;27(2):563-568. doi:10.19746/j.cnki.issn.1009-2137.2019.02.041
30. Zhang X, Wang J, Liu B, et al. Potential mechanism of Huatan Qushi decoction on improving phlegm-dampness constitution using microRNA array and RT-qPCR targeting on hsa-miR-1237e3p. *Journal of Traditional Chinese Medical Sciences*. 2021;0(001):008.
31. Hellyer TP, McAuley DF, Walsh TS, et al. Biomarker-guided antibiotic stewardship in suspected ventilator-associated pneumonia (VAPrapid2): a randomised controlled trial and process evaluation. *Lancet Respir Med*. 2020;8(2):182-191. doi:10.1016/S2213-2600(19)30367-4
32. Xue M, Da C. The protective effect of Qingfei Huatan decoction on pulmonary function and its influence on the immunological function in children with severe pneumonia. *Am J Transl Res*. 2021;13(8):9404-9412.