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Original Article

Effects of acetylcysteine combined with bronchoalveolar lavage under fiberoptic bronchoscopy on blood oxygenation and inflammation in elderly severe pneumonia patients

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Abstract: Objective: To determine the effects of acetylcysteine (NAC) plus bronchoalveolar lavage (BAL) under fiberoptic bronchoscopy (FB) on blood oxygenation and inflammation in elderly severe pneumonia patients. Methods: The data of 180 elderly patients with severe pneumonia treated in the Affiliated Hospital 2 of Nantong University between January 2022 and January 2024 were analyzed retrospectively. Eighty-six patients were treated with BAL under FB (BAL group) and 94 patients were treated with NAC based on BAL under FB (BAL + NAC group). Outcomes included pre-/post-treatment blood gas, pulmonary function, inflammatory factors, correlation between inflammatory markers and blood gas parameters, clinical efficacy, symptom resolution time, and adverse reactions. Results: After treatment, both groups exhibited an increase in arterial partial pressure of oxygen (PaO_2), arterial oxygen saturation (SaO_2), forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC) and decreased C-reactive protein (CRP) and interleukin-6 (IL-6), with more significant changes in the BAL + NAC group (all $P < 0.05$). Inflammatory markers (CRP/IL-6) were negatively correlated with oxygenation parameters (PaO_2/SpO_2, all $P < 0.01$). Additionally, the BAL + NAC group had earlier resolution time of chest pain, expectoration, cough, and lung rales, a higher overall response rate, and no significant difference in adverse reaction incidence versus the BAL group. Conclusion: NAC combined with BAL under FB is effective for elderly patients with severe pneumonia. It can strongly improve the blood gas indexes and lung function, relieve inflammatory reactions, and quickly relieve clinical symptoms, without increasing adverse reactions. Thus it is worthy of clinical promotion.

Keywords: Acetylcysteine, bronchoalveolar lavage under fiberoptic bronchoscopy, severe pneumonia in the elderly, blood gas level, efficacy

Introduction

Severe pneumonia is a common disease seen in respiratory medicine. In addition to frequent respiratory symptoms of pneumonia, manifestations of respiratory failure also occur as well as obvious involvement of systems including the circulatory system and nervous system, and these features are predominantly observed in elderly patients [1, 2]. Elderly patients are characterized by physical deterioration, weak constitution and low immunity. Thus, most elderly patients with severe pneumonia present with serious clinical manifestations, rapid progress, and a high likelihood to develop complications, which is a big challenge in clinical practice with unfavorable prognosis [3, 4]. Patients with severe pneumonia often suffer fever, cough, sputum expectoration and dyspnea. Control and relief of pulmonary infection is primary for the management of severe pneumonia, so clinical treatment mainly involves anti-infection plus sputum suction [5].

Acetylcysteine (NAC), a mucus solubilizer, can promote glycoprotein lysis in sputum, effectively reducing sputum viscosity and thus exerts strong effects of mucus and sputum dissolution [6]. Reportedly, NAC also plays a significant part in inhibiting the reproduction of pathogen-

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ic bacteria, reducing the production of reactive oxygen species and alleviating inflammatory reactions [7]. As one of the routine methods for diagnosis and treatment of lung diseases, bronchoalveolar lavage (BAL) under fiberoptic bronchoscopy (FB) can be adopted to explore the interior of bronchi and alveoli to help doctors make a correct diagnosis [8]. In the treatment of severe pneumonia, BAL under FB can help patients recover respiratory function by removing pathogens, alleviating pathological process and improving ventilator-associated pneumonia [9]. Gradually over the past few years, BAL under FB has been extensively adopted as the primary treatment for elderly patients with severe pneumonia [10]. However, its treatment effect is still limited. Hogea et al. [11] pointed out a crucial role of BAL under FB in the evaluation of pulmonary interstitial diseases. If combined with NAC together, more favorable results are observed. However, this has been rarely reported. Therefore, this study analyzed the effects of NAC combined with BAL under FB on blood gas levels in elderly patients with severe pneumonia, with the purpose of providing reliable references for the management of severe pneumonia in the elderly.

Materials and methods

Patient data

The data of 230 elderly patients with severe pneumonia treated in Affiliated Hospital 2 of Nantong University between January 2022 and January 2023 were retrospectively analyzed. Following the application of the inclusion and exclusion criteria, 180 elderly patients were finally enrolled.

Inclusion criteria: 1. Aged ≥ 60 years; 2. Presented with clinical symptoms including cough, expectoration, and pulmonary wet rales; 3. Met the diagnostic criteria for severe pneumonia [12]; 4. Had complete and detailed clinical data.

Exclusion criteria: 1. Received anti-infection therapy, aerosol inhalation therapy, or other relevant treatments within 4 weeks prior to enrollment; 2. Had a history of allergies to the drugs used in this study; 3. Suffered from severe dysfunction of important organs (e.g., heart, liver, kidney); 4. Had severe nervous system abnormalities (e.g., consciousness disturbance, severe cerebrovascular disease); 5. Complicated with severe uncontrollable complications; 6. Had significantly abnormal coagulation function; 7. Comorbid with malignant lung tumors; 8. Comorbid with autoimmune diseases.

Among the enrolled 180 patients, 96 patients treated with BAL under FB were assigned to a BAL group, and the other 84 patients treated with NAC based on BAL under FB were enrolled into a BAL + NAC group. The specific screening and grouping process are presented in **Figure 1**. This study was carried out with approval from the Medical Ethics Committee of the Affiliated Hospital 2 of Nantong University. As the study involved only the analysis of anonymized historical data, the requirement for individual informed consent was waived by the Ethics Committee, in accordance with national guidelines and the Declaration of Helsinki.

Therapeutic regimen

Patients in the both groups received routine treatment, including oxygen inhalation, anti-infection, sputum aspiration, nutritional support, maintenance of water-electrolyte balance etc. They were also given BAL under FB through a BFXP60 electronic fiberoptic bronchoscope (Olympus, Japan). Before operation, the patient was fasted from solids and liquids for 4-6 h. Anesthesia was administered via intravenous injection of propofol (Guangdong Jiabo Pharmaceutical Co., Ltd., State Food and Drug Administration (SFDA) approval number: H201-43369, 50 mL:1 g) at 1-1.5 mg/kg and given nasopharyngeal topical anesthesia through 1% lidocaine (Shandong Hualu Pharmaceutical Co., Ltd., SFDA approval number: H37022072) followed by the insertion of a bronchoscope. After the bronchoscope reached the lesion, BAL was performed with 37°C normal saline (Shandong Qidu Pharmaceutical Co., Ltd., SFDA approval number: H20013043). The lavage was conducted three times, with a volume of 0.5-1 ml/kg each time. The liquid was withdrawn at negative pressure of 100-150 mmHg for bacterial culture. After BAL, the two groups were perfused with different expectorant drugs, and the bronchoscope was withdrawn after lavage. During the operation, the vital signs were monitored.

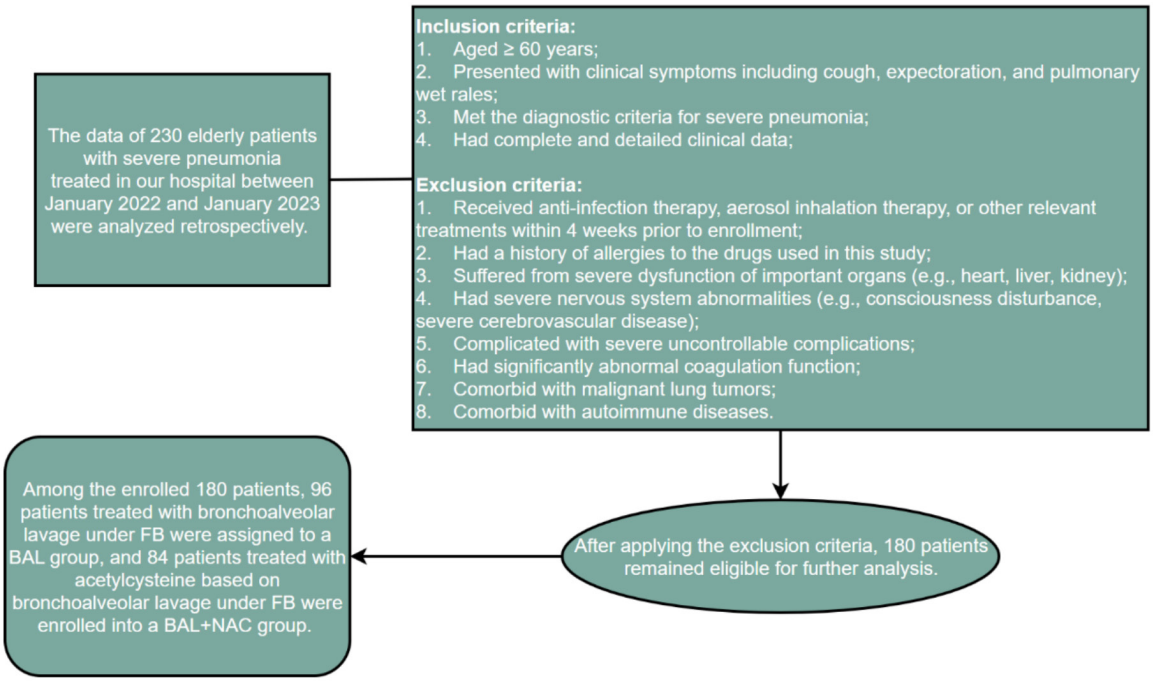

Figure 1. Screening and grouping process. Notes: FB: fiberoptic bronchoscopy.

On the basis of treatment given to the BAL group, the BAL + NAC group was additionally treated with local injection of NAC (Shanxi Guorun Pharmaceutical Co., Ltd., SFDA approval number: H20183359, 20 mL:4 g). In BAL under FB, 3 mL 5% NAC was mixed with 10 mL 0.9% sodium chloride solution (Shandong Hualu Pharmaceutical Co., Ltd., SFDA approval number: H20083433) and then injected into the severely affected area through fiberoptic bronchoscope, and the injection was completed after 2-3 applications, with a volume of 5 mL each time. Both groups were evaluated 7 days after treatment.

Outcome measures

Primary outcome measures: (1) The blood gas indexes including arterial partial pressure of oxygen (PaO_2) and arterial oxygen saturation (SaO_2) were compared between the two groups before and after treatment; (2) The lung function indexes were compared between the two groups before and after treatment. Before treatment and 7 days after treatment, a lung function detector (Sichuan Sikeda Technology Co., Ltd., model S-980A III, approval number: Sichuan Food and Drug Administration (zhun) [Zi No. 2210145]) was adopted for measurement of the forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), and FEV1/FVC was calculated; (3) The clinical efficacy in the two groups was compared. Markedly effective: Symptoms including cough and chest pain disappeared, and lung shadows were completely absorbed; Effective: Symptoms including cough and chest pain were relieved, and lung shadows were partially absorbed; Ineffective: Symptoms including cough and chest pain had no changes and lung shadows were not absorbed. The overall response rate = the number of cases with (markedly effective + effective)/total number of cases × 100%.

Secondary outcome measures: (1) The levels of inflammatory factors before and after treatment were compared between the two groups. Fasting venous blood (5 mL) was acquired from each patient before treatment and 7 days after treatment, followed by 10-min centrifugation (3,000 r/min) to take serum. Then serum C-reactive protein (CRP) and interleukin-6 (IL-6) was determined through enzyme-linked immunosorbent assay (ELISA) with human CRP ELISA Kit (Abbexa, Cat# abx152258) and human IL-6

Table 1. Baseline data of the two groups

Factors	BAL + NAC group (n = 94)	BAL group (n = 86)	X^2 value	*P* value
Age			0.735	0.391
< 70 years old	53 (56.38%)	43 (50.00%)		
≥ 70 years old	41 (43.62%)	43 (50.00%)		
Gender			2.892	0.089
Male	63 (67.02%)	47 (54.65%)		
Female	31 (32.98%)	39 (45.35%		
BMI			0.197	0.658
≥ 23 kg/m^2	32 (34.04%)	32 (37.21%)		
< 23 kg/m^2	62 (65.96%)	54 (62.79%)		
Course of disease			2.372	0.124
2-4 d	30 (31.91%)	37 (43.02%)		
5-8 d	64 (68.09%)	49 (56.98%)		
Smoking history			0.344	0.558
Yes	44 (46.81%)	37 (43.02%)		
No	50 (53.19%)	49 (56.98%)		
Place of residence			0.145	0.704
Rural areas	26 (27.66%)	26 (30.23%)		
Urban areas	68 (72.34%)	60 (69.77%)		

Notes: BMI: body mass index; NAC: acetylcysteine; BAL: bronchoalveolar lavage.

ELISA Kit (Multi Sciences, Cat# EK1060), respectively. (2) The resolution time of symptoms was compared between the two groups, including the resolution time of chest pain, expectoration, cough and lung rale; (3) The occurrence of adverse reactions was compared between the two groups. (4) The correlations between inflammatory markers and gas parameters were analyzed before and after treatment.

Statistical analysis

This study adopted SPSS v22 statistical software (IBM Corp, Armonk, NY, USA) for statistical analyses of all acquired data, and used GraphPad Prism 8 (GraphPad Software Inc., San Diego, CA, USA) for figure illustration. Counting data were presented as rate, and the inter-group comparison was conducted using the chi-square test. Measurement data were normally distributed and expressed as mean ± SD. For within-group comparisons before and after treatment, paired t-test was used. For between-group comparisons, an independent t-test was employed. The correlations between inflammatory markers and oxygenation parameters were analyzed using Pearson's correlation coefficient. $P < 0.05$ indicates a significant difference.

Results

Baseline data of patients

The two groups were similar in baseline data including age, gender, body mass index (BMI), course of disease, smoking history and place of residence (all $P > 0.05$, **Table 1**). Thus, the two groups were comparable.

Comparison of blood gas indexes

Before treatment, the PaO_2 and SaO_2 levels between the two groups had no differences (both $P > 0.05$). After treatment, the PaO_2 and SaO_2 levels in both groups were significantly increased ($P < 0.0001$), with notably higher levels in the BAL + NAC group than those in the BAL group (both $P < 0.0001$, **Figure 2**).

Comparison of related inflammatory factors

Before treatment, CRP and IL-6 levels in the two groups were not greatly different ($P > 0.05$). After treatment, CRP and IL-6 levels in the two groups were decreased greatly ($P < 0.0001$), with notably lower levels in the BAL + NAC group than those in the BAL group (both $P < 0.0001$, **Figure 3**).

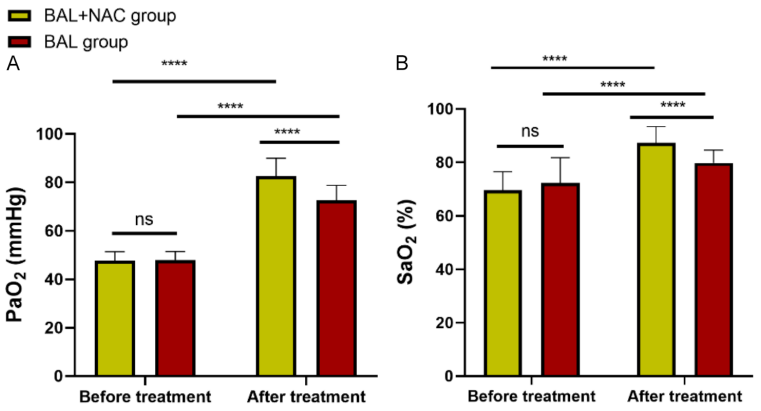

Figure 2. Comparison of blood gas indexes between the two groups before and after treatment. A: Comparison of PaO_2 between the two groups before and after treatment; B: Comparison of SaO_2 between the two groups before and after treatment. Note: ns: Non-significant; ****P < 0.0001. PaO_2: arterial partial pressure of oxygen; SaO_2: arterial oxygen saturation; NAC: acetylcysteine; BAL: bronchoalveolar lavage.

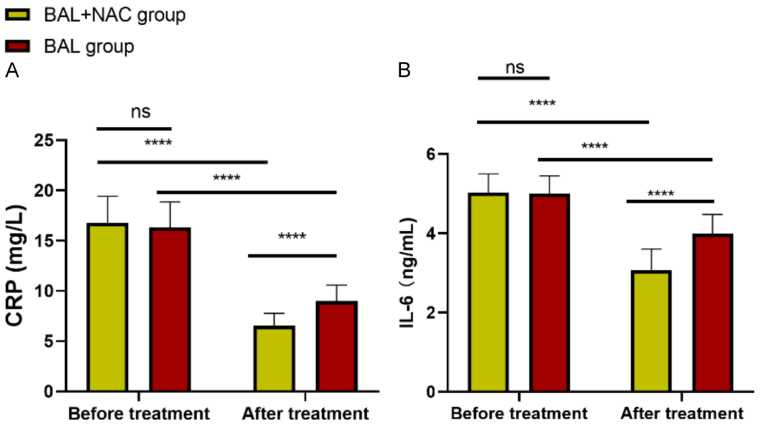

Figure 3. Comparison of inflammatory factors between the two groups before and after treatment. A: Comparison of CRP between the two groups before and after treatment; B: Comparison of IL-6 between the two groups before and after treatment. Notes: ns: Non-significant; ****P < 0.0001. CRP: C-reactive protein; IL-6: interleukin-6; NAC: acetylcysteine; BAL: bronchoalveolar lavage.

Correlation analysis between inflammatory markers and gas parameters

To investigate the relationship between inflammatory response and oxygenation function, we further analyzed the correlations of CRP and IL-6 with PaO_2 and SpO_2 (**Figure 4**). The results showed that before treatment, CRP was weakly negatively correlated with PaO_2 (r = -0.315, P < 0.001) and SpO_2 (r = -0.312, P < 0.001), while IL-6 also exhibited negative correlations with PaO_2 (r = -0.364, P < 0.001) and SpO_2 (r = -0.236, P = 0.002). After treatment, these correlations strengthened further. CRP was more strongly associated with SpO_2 (r = -0.466, *P* < 0.001) and PaO_2 (r = -0.627, *P* < 0.001), and IL-6 maintained a robust relationship with both PaO_2 (r = -0.552, *P* < 0.001) and SpO_2 (r = -0.675, *P* < 0.001).

Comparison of lung function indexes

The lung function indexes of the two groups were analyzed and compared before and after treatment. According to the results, before treatment, the levels of FEV1, FVC and FEV1/FVC were not greatly different between the two groups (*P* > 0.05), while after treatment, their levels increased greatly in both groups (*P* < 0.05), with notably higher levels in the BAL + NAC group than in the BAL group (*P* < 0.05, **Figure 5**).

Comparison of symptom resolution time

The BAL + NAC group experienced notably earlier resolution time of chest pain, expectoration, cough and lung rale than the BAL group (all P < 0.0001, **Figure 6**).

Comparison of efficacy

According to comparison of efficacy on the two groups, the BAL + NAC group showed a notably higher overall response rate than the BAL group (P = 0.006, **Table 2**).

Comparison of adverse reactions

The incidence of adverse reactions in the two groups was statistically analyzed, and no notable difference was found between the BAL + NAC and BAL groups in the incidence of adverse reactions (P = 0.299, **Table 3**).

Discussion

Severe pneumonia, a critical condition common in the elderly, is characterized by rapid pro-

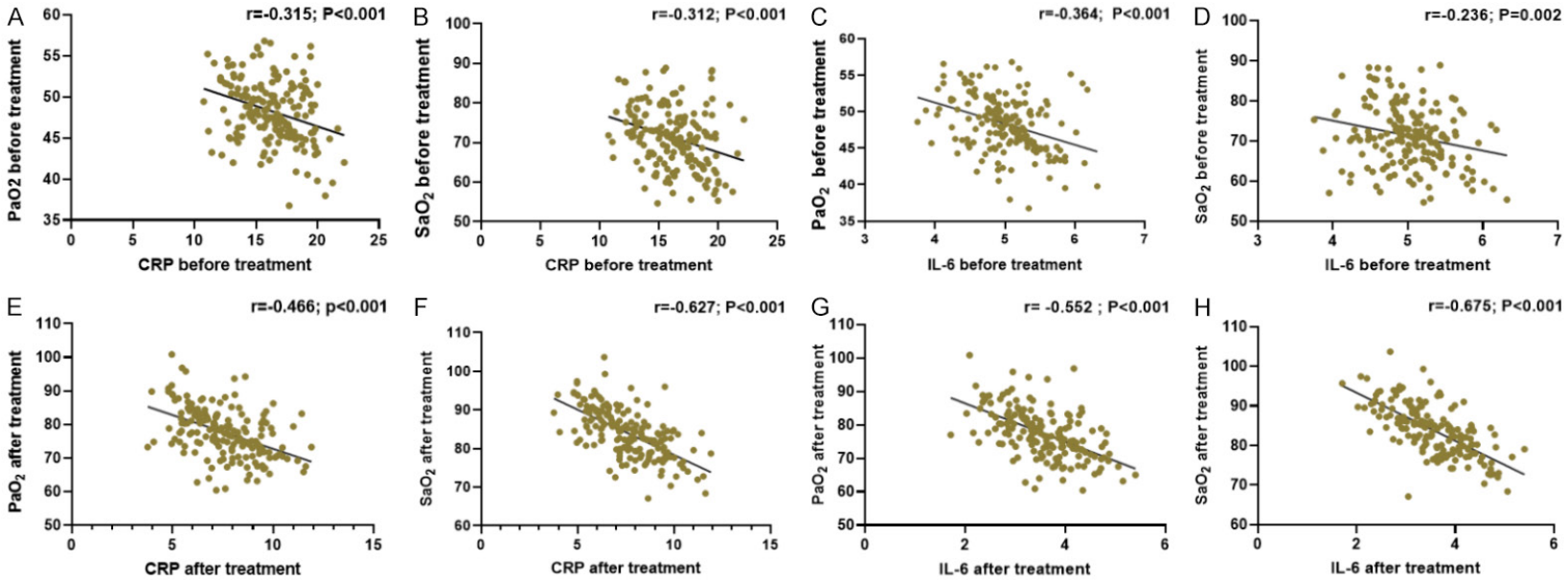

Figure 4. Correlation analysis between inflammatory markers and gas parameters. A: Correlation between CRP and PaO_2 before treatment; B: Correlation between CRP and SpO_2 before treatment; C: Correlation between IL-6 and PaO_2 before treatment; D: Correlation between IL-6 and SpO_2 before treatment; E: Correlation between CRP and PaO_2 after treatment; F: Correlation between CRP and SpO_2 after treatment; G: Correlation between IL-6 and PaO_2 after treatment; H: Correlation between IL-6 and SpO_2 after treatment; Notes: PaO_2: arterial partial pressure of oxygen; SaO_2: arterial oxygen saturation. CRP: C-reactive protein; IL-6: interleukin-6.

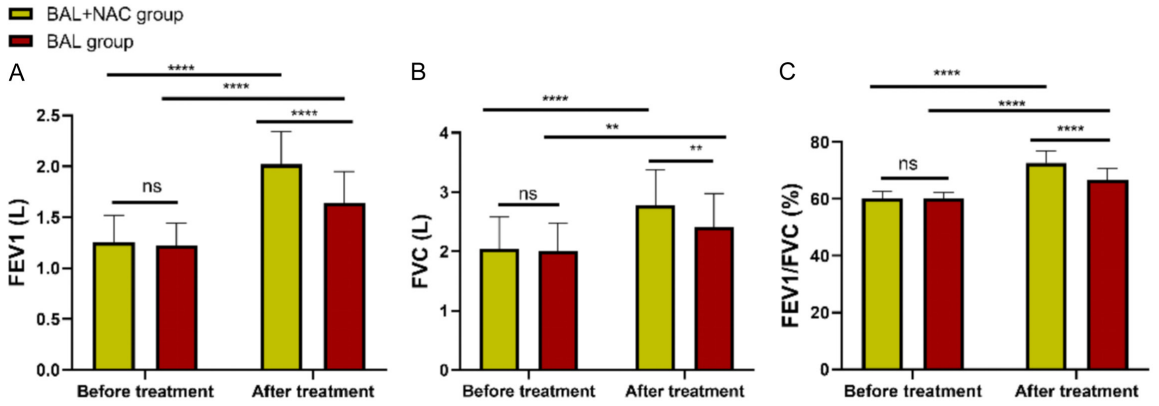

Figure 5. Comparison of lung function indexes between the two groups before and after treatment. A: Comparison of FEV1 between the two groups before and after treatment; B: Comparison of FVC between the two groups before and after treatment; C: Comparison of FEV1/FVC between the two groups before and after treatment. Note: ns: Non-significant; **P < 0.01; ****P < 0.0001. FEV1: Forced expiratory volume in 1 second; FVC: Forced vital capacity; NAC: acetylcysteine; BAL: bronchoalveolar lavage.

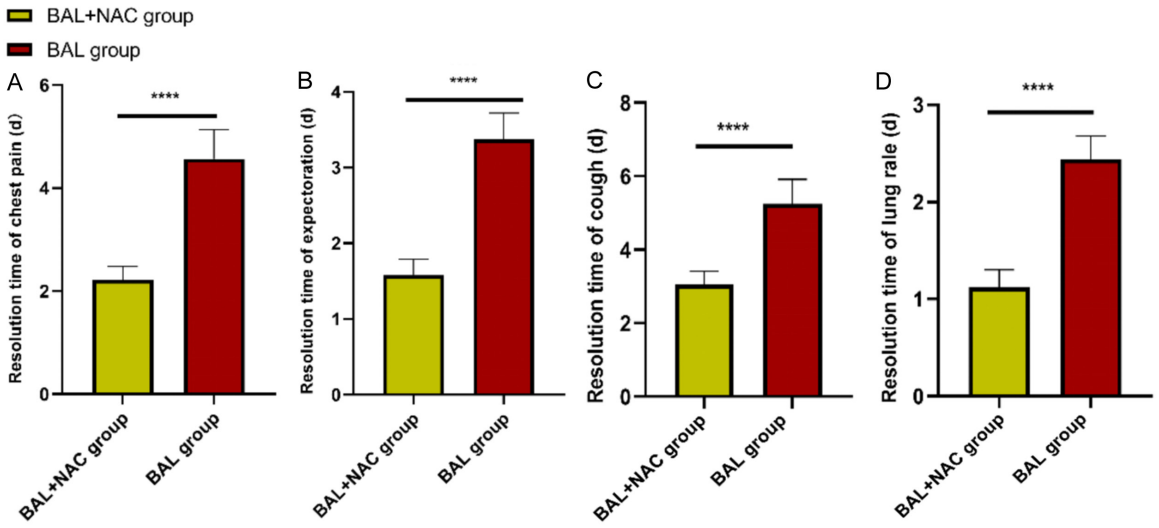

Figure 6. Comparison of symptom resolution time between the two groups. A: Comparison of the resolution time of chest pain between the two groups; B: Comparison of the resolution time of expectoration between the two groups; C: Comparison of the resolution time of cough between the two groups; D: Comparison of the resolution time of lung rales between the two groups. Note: ****P < 0.0001.

gression and high mortality [13]. Age-related immune decline and frequent comorbidities increase susceptibility to severe bacterial, viral, or fungal infections [14-16]. Without prompt intervention, patients may develop respiratory failure, cardiovascular dysfunction, and shock. Effective management requires timely clearance of airway secretions, improved ventilation, and infection control [17-20]. This study evaluates the effect of NAC combined with BAL under FB on blood gas levels in elderly patients with severe pneumonia.

BAL under FB is often considered as the standard diagnostic method for pneumonia in immunocompromised patients [21], but it has limited effect on severe pneumonia. Grigoriu et al. [22] have revealed that alveolar lavage might cause cytological damage to patients with severe pneumonia, suggesting potential limitations of lavage alone. In contrast, our study demonstrated that when combined with NAC, BAL not only improved oxygenation but also reduced inflammatory markers, indicating a synergistic effect. This is consistent with the

Table 2. Efficacy in the two groups [n (%)]

Group	Markedly effective	Effective	Ineffective	Overall response rate (%)
BAL + NAC group (n = 94)	54 (57.45%)	32 (34.04%)	8 (8.51%)	86 (91.49%)
BAL group (n = 86)	43 (50.00%)	23 (26.74%)	20 (23.26%)	66 (76.74%)
X^2 value				7.434
P value				0.006

Notes: NAC: acetylcysteine; BAL: bronchoalveolar lavage.

Table 3. Incidence of adverse reactions in the two groups [n (%)]

Group	Vomiting	Headache	Infection	Adverse reactions
BAL + NAC group (n = 94)	4 (4.26%)	4 (4.26%)	0 (0.00%)	8 (8.51%)
BAL group (n = 86)	2 (2.33%)	2 (2.33%)	0 (0.00%)	4 (4.65%)
X^2 value				1.075
P value				0.299

Notes: NAC: acetylcysteine; BAL: bronchoalveolar lavage.

findings of a recent clinical study by Li [23] on refractory *Mycoplasma pneumoniae* pneumonia in children, which demonstrated that bronchofiberscopic lavage with NAC instillation significantly improved the effective treatment rate and the absorption of lung lesions, and also reduced levels of inflammatory markers such as CRP and IL-6, compared to standard treatment alone. NAC, a non-essential amino acid, playing a great role in antioxidant defense *in vivo*, regulating blood cholesterol and blood sugar, is extensively adopted in treating cardiovascular diseases and preventing liver injury [24, 25]. The pronounced reduction in systemic inflammatory markers (CRP and IL-6) observed in our combination therapy group may be attributed not only to the mechanical clearance of secretions via lavage but also to the potent intrinsic anti-inflammatory and antioxidant properties of NAC itself. This is strongly supported by an experimental animal study of Suleyman Uraz et al. [26], which have demonstrated that NAC can significantly suppress the production of key pro-inflammatory cytokines, including IL-6, IL-1β, and TNF-α, and mitigate oxidative stress in models of severe inflammation.

Blood gas indexes, useful for evaluating and monitoring many diseases and physiological functions, are crucial in clinical practice [27]. Our findings that NAC combined with BAL significantly improved PaO_2 and SaO_2 are also supported by a randomized controlled trial conducted by Zhang et al. [28], which demonstrated that systemic administration of NAC as an adjunct to conventional therapy significantly reduced oxidative stress and the key inflammatory cytokine TNF-α in patients with community-acquired pneumonia. Moreover, the stronger negative correlation between inflammatory markers and oxygenation parameters after treatment in our study underscores the central role of inflammation in driving hypoxemia. This finding resonates with the novel 'Micro-CLOTS' (microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome) hypothesis proposed by Ciceri et al. [29], which provides a mechanistic framework for how severe systemic inflammation can culminate in microvascular thrombosis and profound ventilation-perfusion mismatch, thereby exacerbating hypoxemia in viral pneumonia. Lung function indexes are a set of indexes to evaluate the function of the respiratory system, and they are of great significance for diagnosing and monitoring the progress of pulmonary diseases [30]. This study found notably increased levels of FEV1, FVC and FEV1/FVC after treatment, with notably higher levels in the BAL + NAC group than those in the BAL group. This outcome is in line with the results of a study from Xue et al. [31], which demonstrated that treatment with NAC significantly improved lung function parameters, including FVC, FEV1, and the FEV1/FVC ratio, in patients with pneumonia.

In order to understand the resolution of clinical symptoms in the two groups after treatment, this study analyzed and compared the resolution time of chest pain, expectoration, cough

and lung rale, and found significantly earlier resolution time of the above symptoms in the BAL + NAC group than that in the BAL group. The data imply that the combined use can quickly alleviate the clinical symptoms of elderly patients with severe pneumonia. In addition, in this study, the BAL + NAC group showed a notably higher overall response rate than the BAL group, implying the superior efficacy of combined treatment for the elderly with severe pneumonia. Demedts et al. [32] revealed that NAC plus prednisone and azathioprine have better effects on idiopathic pulmonary fibrosis than standard therapy alone, which is consistent with the results of this study. Finally, this study analyzed the incidence of adverse reactions between the two groups, and found no notable difference in the incidence of adverse reactions between groups, indicating that the additional use of NAC would not increase the adverse reactions of patients.

This study does have several limitations. First of all, the limited sample size collected in this study may result in some deviation in the conclusions. In addition, only the short-term efficacy was evaluated in patients. Thus, how the treatment exerts a long-term effect on patients' outcomes requires further investigation. We hope to carry out a more systematic and comprehensive analysis in subsequent studies to yield robust findings.

To sum up, NAC combined with BAL under FB is effective in treating elderly patients with severe pneumonia, which can strongly improve the blood gas indexes and lung function, relieve inflammatory reaction, and quickly relieve clinical symptoms, without increasing adverse reactions. Thus it is worthy of clinical promotion.

Disclosure of conflict of interest

None.

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References

[1] Li L, Zhang M, Wei Y, Tu X, Lu Z and Cheng Y. Clinical significance of procalcitonin in critically ill patients with pneumonia receiving bronchoalveolar lavage. Sarcoidosis Vasc Diffuse Lung Dis 2022; 39: e2022031.

[2] Mizgerd JP. Pathogenesis of severe pneumonia: advances and knowledge gaps. Curr Opin Pulm Med 2017; 23: 193-197.

[3] Lv SJ, Lai DP, Wei X, Yan Q and Xia JM. The protective effect of Shenfu injection against elderly severe pneumonia. Eur J Trauma Emerg Surg 2017; 43: 711-715.

[4] Gutierrez F and Masia M. Improving outcomes of elderly patients with community-acquired pneumonia. Drugs Aging 2008; 25: 585-610.

[5] El-Solh AA, Sikka P, Ramadan F and Davies J. Etiology of severe pneumonia in the very elderly. Am J Respir Crit Care Med 2001; 163: 645-651.

[6] Han DW, Ji W, Lee JC, Song SY and Choi CM. Efficacy of nebulized acetylcysteine for relieving symptoms and reducing usage of expectorants in patients with radiation pneumonitis. Thorac Cancer 2019; 10: 243-248.

[7] Choi SM, Lee PH, An MH, Yun-Gi L, Park S, Baek AR and Jang AS. N-acetylcysteine decreases lung inflammation and fibrosis by modulating ROS and Nrf2 in mice model exposed to particulate matter. Immunopharmacol Immunotoxicol 2022; 44: 832-837.

[8] Yang M, Yang DH, Yang X, Wang YS, Wu L and Chen ZM. Efficacy of bronchoalveolar lavage and its influence factors in the treatment of Mycoplasma pneumoniae pneumonia with atelectasis. Zhonghua Er Ke Za Zhi 2018; 56: 347-352.

[9] Liu J, Zhao HR, Wei HL, Chen C, Qiu RX, Ren XL, Zhang L and Gao YQ. Efficacy of bronchoalveolar lavage as adjunct therapy in the treatment of neonatal severe pneumonia: a prospective case-control study. J Trop Pediatr 2020; 66: 528-533.

[10] Zhao Y, Dai X, Ji J and Cheng P. Bronchial lavage under fiberoptic bronchoscopy in the treatment of severe pulmonary infection. Pak J Med Sci 2020; 36: 396-401.

[11] Hogea SP, Tudorache E, Pescaru C, Marc M and Oancea C. Bronchoalveolar lavage: role in the evaluation of pulmonary interstitial disease. Expert Rev Respir Med 2020; 14: 1117-1130.

[12] Peng L, Wang Y, Zhao L, Chen T and Huang A. Severe pneumonia in Chinese patients with systemic lupus erythematosus. Lupus 2020; 29: 735-742.

[13] Tang H, Yuan Z, Li J, Wang Q and Fan W. The application of ambroxol hydrochloride combined with fiberoptic bronchoscopy in elderly patients with severe pneumonia: a meta-analysis and systematic review. Medicine (Baltimore) 2022; 101: e28535.

[14] Tang L, Li Q, Bai J, Zhang H, Lu Y and Ma S. Severe pneumonia mortality in elderly patients is associated with downregulation of Toll-like receptors 2 and 4 on monocytes. Am J Med Sci 2014; 347: 34-41.
[15] Baek MS, Park S, Choi JH, Kim CH and Hyun IG. Mortality and prognostic prediction in very elderly patients with severe pneumonia. J Intensive Care Med 2020; 35: 1405-1410.
[16] Liu C, Zhou Y, Zhao J and Geng N. Clinical value of comprehensive nursing intervention in prevention of ventilator-assoc-iated pneumonia. J Mod Nurs Pract Res 2021; 1: 10-53964.
[17] Sikka P, Jaafar WM, Bozkanat E and El-Solh AA. A comparison of severity of illness scoring systems for elderly patients with severe pneumonia. Intensive Care Med 2000; 26: 1803-1810.
[18] Nakamura S, Yanagihara K, Mihara T, Izumikawa K, Seki M, Kakeya H, Yamamoto Y, Soejima Y, Tashiro T and Kohno S. Clinical characteristics of pneumonia in the oldest old patients. Nihon Kokyuki Gakkai Zasshi 2008; 46: 687-692.
[19] Faverio P, Aliberti S, Bellelli G, Suigo G, Lonni S, Pesci A and Restrepo MI. The management of community-acquired pneumonia in the elderly. Eur J Intern Med 2014; 25: 312-319.
[20] Rancic N and Simic VD. Therapeutic drug monitoring: is there anything new? J Mod Pharmacol Pathol 2023; 1: 1.
[21] Zhou W, Zhou C, Liu X, Shi N, Quyang W, Tu D, Xin Y and Ji L. A randomised trial on the therapeutic effectiveness of bronchoalveolar lavage under fiberoptic bronchoscopy in patients with severe lung infection living in the Tibetan plateau area. Ann Palliat Med 2021; 10: 3336-3342.
[22] Grigoriu B, Jacobs F, Beuzen F, El Khoury R, Axler O, Brivet FG and Capron F. Bronchoalveolar lavage cytological alveolar damage in patients with severe pneumonia. Crit Care 2006; 10: R2.
[23] Li PL, Fu HM, Liu K, Li F and Yang JW. Effect of bronchofiberscopic lavage with acetylcysteine instillation on refractory mycoplasma pneumoniae pneumonia in children: a retrospective clinical observation. Ital J Pediatr 2025; 51: 62.
[24] Cazzola M, Calzetta L, Page C, Jardim J, Chuchalin AG, Rogliani P and Matera MG. Influence of N-acetylcysteine on chronic bronchitis or COPD exacerbations: a meta-analysis. Eur Respir Rev 2015; 24: 451-461.
[25] Mokra D, Drgova A, Petras M, Mokry J, Antosova M and Calkovska A. N-acetylcysteine alleviates the meconium-induced acute lung injury. Adv Exp Med Biol 2015; 832: 59-67.
[26] Uraz S, Tahan G, Aytekin H and Tahan V. N-acetylcysteine expresses powerful anti-inflammatory and antioxidant activities resulting in complete improvement of acetic acid-induced colitis in rats. Scand J Clin Lab Invest 2013; 73: 61-66.
[27] Cheng J, Dou X and Zhao N. The effects of sequential ventilation therapy on blood gas indexes, pulmonary function indexes, clinical efficacy, and safety in patients with severe cor pulmonale. Contrast Media Mol Imaging 2022; 2022: 3618592.
[28] Zhang Q, Ju Y, Ma Y and Wang T. N-acetylcysteine improves oxidative stress and inflammatory response in patients with community acquired pneumonia: a randomized controlled trial. Medicine (Baltimore) 2018; 97: e13087.
[29] Ciceri F, Beretta L, Scandroglio AM, Colombo S, Landoni G, Ruggeri A, Peccatori J, D'Angelo A, De Cobelli F, Rovere-Querini P, Tresoldi M, Dagna L and Zangrillo A. Microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome (MicroCLOTS): an atypical acute respiratory distress syndrome working hypothesis. Crit Care Resusc 2020; 22: 95-97.
[30] Xu W, He G, Pan C, Shen D, Zhang N, Jiang P, Liu F and Chen J. A forced cough sound based pulmonary function assessment method by using machine learning. Front Public Health 2022; 10: 1015876.
[31] Xue A, Zhang H, Song S and Yu X. Effects of N-Acetylcysteine combined with Ambroxol Hydrochloride on clinical symptoms, CRP, and PCT in children with pneumonia. Clinics (Sao Paulo) 2024; 79: 100476.
[32] Demedts M, Behr J, Buhl R, Costabel U, Dekhuijzen R, Jansen HM, MacNee W, Thomeer M, Wallaert B, Laurent F, Nicholson AG, Verbeken EK, Verschakelen J, Flower CD, Capron F, Petruzzelli S, De Vuyst P, van den Bosch JM, Rodriguez-Becerra E, Corvasce G, Lankhorst I, Sardina M and Montanari M; IFIGENIA Study Group. High-dose acetylcysteine in idiopathic pulmonary fibrosis. N Engl J Med 2005; 353: 2229-2242.