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Effects of low-dose methylprednisolone sodium succinate on lung function and blood gas function in elderly patients with chronic obstructive pulmonary disease complicated with respiratory failure

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Abstract: **Background**: Elderly patients with chronic obstructive pulmonary disease (COPD) complicated with type II respiratory failure (RF) have high morbidity and poor prognosis. Conventional therapy shows limited efficacy, while high-dose glucocorticoids easily cause adverse reactions, and targeted data on low-dose regimens are insufficient. **Objectives**: To investigate the pharmacological application value of low-dose methylprednisolone sodium succinate (LD-MSS) in elderly patients with COPD complicated with respiratory failure (RF). **Methods**: A total of 96 COPD patients with RF admitted to 3201 Hospital were analyzed by propensity score matching. The patients were divided into experimental group (n=48) and control group (n=48), and received LD-MSS treatment and conventional treatment respectively. The RF correction time and APACHE II score of both groups were recorded, and pre- and post-treatment lung function, blood gas function, and inflammatory factor levels were measured. **Results**: Compared with the control group, the LD-MSS group had a significantly shorter RF correction time and a significantly lower APACHE II score (P<0.05). In addition, the experimental group had better pulmonary and blood gas functions and lower levels of inflammatory factors than the control group (P<0.05). Finally, no marked difference was identified between groups in the incidence of adverse reactions (P>0.05). **Conclusion**: LD-MSS is effective in anti-inflammation and in improving blood gas function, and has a good safety profile.

Keywords: Blood gas function; Chronic obstructive pulmonary disease; Lung function; Methylprednisolone sodium succinate; Respiratory failure

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD), a chronic progressive condition with irreversible airway obstruction, is the fifth leading disease burden in the world at present, with more than 100 million cases in China, of which the elderly over 60 years of age account for more than 60% (Christenson *et al.*, 2022). Clinical research shows that COPD is mostly caused by long-term smoking and its clinical manifestations are repeated cough, expectoration (mainly white mucus sputum), chest tightness and dyspnea (Ritchie & Wedzicha, 2020). As the disease progresses, COPD will gradually develop into cor pulmonale and even respiratory failure (RF), which is also the prime reason for death in COPD patients (MacIntyre, 2023; Zhang, 2025). The Global Burden of Disease Study estimates that COPD complicating RF is the third-leading cause of death worldwide in 2024 (Zhang *et al.*, 2024). Therefore, timely and effective intervention and treatment of COPD are of great significance for ensuring patients' life safety.

In addition to the primary COPD, bronchodilators and glucocorticoids can also be used to alleviate dyspnea in patients currently in clinical treatment (Marti *et al.*, 2020). Among them, methylprednisolone sodium succinate (MSS) is a glucocorticoid with anti-inflammatory, anti-virus and anti-shock actions, which can also be used to treat respiratory diseases (Les *et al.*, 2022; Lu *et al.*, 2020), with its an important role in the treatment of COPD validated (Yu & Zhang, 2022). It is well known that glucocorticoids can interfere with intestinal calcium absorption and renal calcium excretion, leading to increased calcium loss from the body. It also inhibited osteocyte growth and bone formation (Beuschlein *et al.*, 2024). Therefore, in the use of such agents, the preference for low doses (LD) will help to reduce the risk of osteoporosis (Figueroa-Parra, *et al*., 2025). For older people with more severe calcium loss, the choice of LD appears to be more important (Boers *et al*., 2022). However, there is still a lack of clinical data on the pharmacodynamics of low-dose MSS in COPD-RF population, especially on the balance between inflammation inhibition and safety.

Accordingly, this study conducts a comprehensive evaluation of the application effects of LD-MSS, aiming to provide more effective guidance for future clinical treatment of elderly COPD + RF patients and to fill the pharmacological evidence gap for LD-MSS in the elderly population.

MATERIALS AND METHODS

Patient data

Sample size calculation was performed using G*Power 3.1

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software before patient enrollment. Based on a previous study (Zhang *et al*., 2018), the expected difference in respiratory failure correction time between the two groups was set as 1.5 days, with a significance level (α) of 0.05 and a statistical power (1-β) of 80%. The calculated minimum sample size was 42 cases per group. Considering a potential dropout rate of 15%, 48 cases were enrolled per group, for a total of 96. A total of 161 COPD patients with RF admitted to our hospital from February 2021 to May 2023 were selected for retrospective analysis. The matching caliper value was set to 0.05, that is, matching was performed when the difference in propensity scores between the two patients was less than 0.05, and the matching process did not allow repeated matching. After matching, standardized mean difference (SMD) was used to evaluate the balance of baseline characteristics between the two groups, and SMD<0.1 was considered to be good balance between the two groups. After propensity score matching (PSM, 1:1), a total of 96 patients were included. Patients were assigned to either the experimental group (n=48) or the control group (n=48) according to the treatment they received. Ethical approval has been obtained from the Medical Ethics Committee (No.l2021017) and all patients were informed and provided informed consent. The clinical baseline data for the two groups of patients are shown in Table 1, and no statistical inter-group difference was identified (P>0.05).

Eligibility and exclusion criteria

Eligibility criteria: Patients (age: 60-75 years) diagnosed as COPD and type II RF by 3201 Hospital (Kahnert *et al.*, 2023; Chen & Rackley, 2024), with stable vital signs, expected survival time > 3 months (KPS score ≥ 60 was used as the quantitative evaluation standard for expected survival time > 3 months. The KPS score evaluates the patient's ability to take care of themselves and engage in daily activities, with scores ≥ 60 indicating that the patient can take care of most of their daily needs independently and has a low risk of short-term death) and no pneumonia or severe limb dysfunction before enrollment were included.

Exclusion criteria: Patients who had received hormone therapy in the last month, with treatment contraindications, respiratory tract abnormalities, serious systemic infections, blood system diseases, serious heart, liver and kidney dysfunction, mental illness, inability to take care of themselves due to physical disability and drug allergies were excluded.

Treatment methods

Both groups were treated with routine antispasmodics, antiasthmatics, phlegm-resolving therapies and nutritional support, with dosages adjusted based on blood gas analysis results. In addition, non-invasive assisted ventilation was carried out. On this basis, the control group received 375 mg of nikethamide (Tianjin Jinyao Pharmaceutical Co., Ltd., H12020962) and 100 mL of 5% glucose solution via intravenous drip. Nikethamide was selected as the control drug because it is a commonly used respiratory stimulant in clinical practice for the treatment of COPD complicated with respiratory failure (Xu *et al*., 2025), and it is included in the routine treatment plan of 3201 Hospital for this disease. This selection allows a direct comparison of the anti-inflammatory and ventilatory improvement effects of LD-MSS with the respiratory stimulant effect of nikethamide. The experimental group received LD (40 mg) MSS for injection (Liaoning Haisike Pharmaceutical Co., Ltd., H20133234) and 100 mL of 5% glucose solution intravenously once daily for 7 consecutive days. The dosage, frequency and treatment duration were determined based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2023 guidelines and clinical practice consensus for elderly COPD patients (Ribau *et al.*, 2023). This regimen was not adjusted based on body weight, age, renal function, or disease severity, as a fixed low-dose regimen is more effective at reducing metabolic adverse reactions in elderly patients with unstable physiological function. Both groups were treated for 7 days. In addition, both groups of patients received respiratory care for COPD after hospitalization. Specifically, it includes personalized care for the airway, respiratory tract, diet and complications.

Lung function test

Forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), FEV1/FVC and peak expiratory flow (PEF) were measured using a calibrated spirometer (CHEST, Japan) at 1 day before treatment initiation and 24 hours after the end of 7-day treatment. All measurements were performed in strict accordance with the standards of the American Thoracic Society/European Respiratory Society (ATS/ERS), with patients in a sitting position and wearing a nose clip during testing. Each index was measured three times, and the average value was taken.

Blood gas function test

Arterial blood samples were collected from the radial artery in both groups before and after treatment. Blood gas indexes (pH, SaO_2, PaO_2, $PaCO_2$) were measured using an automatic blood gas analyzer (GEM Premier5000, Wofen, USA).

Inflammatory reaction detection

Fasting cubital venous blood was collected into a coagulation tube before and after treatment and the serum was obtained by centrifugation after standing at room temperature for 30 min. Then, C-reactive protein (CRP) and procalcitonin (PCT) were determined by an automatic biochemical analyzer (BS-600M, Mindray, USA).

Assessment of quality of life and satisfaction with care

The quality of life of patients was assessed using the Activities of Daily Living (ADL) scale (Lewis-Hunstiger, 2025) before and after treatment, with higher scores indicating better quality of life. In addition, nursing satisfaction was assessed upon hospital discharge, and the satisfaction rate was calculated.

Table 1: Comparison of clinical baseline information [n(%)].

Group	n	Genders		Age (years old)	Course of COPD (years)	Smoking		Comorbidity with diabetes mellitus		Comorbidity with high blood pressure	
		male	female			yes	no	yes	no	yes	no
Control	48	31 (64.58)	17 (35.45)	62.75±5.64	4.23±0.75	26 (54.17)	22 (45.83)	22 (45.83)	26 (54.17)	18 (37.50)	30 (62.50)
Experimental	48	35 (72.92)	13 (27.08)	61.52±7.11	4.08±0.71	22 (45.83)	26 (54.17)	19 (39.58)	29 (60.42)	20 (41.67)	28 (58.33)
χ^2/t		0.776	0.351	0.978	0.667	0.383	0.174	0.776	0.351	0.978	0.667
P		0.378	0.969	0.331	0.414	0.536	0.676	0.378	0.969	0.331	0.414

Outcome measures

(1) *Symptom improvement*: The RF correction time and pre- and post-treatment APACHE II scores (Ezz Al-Regal *et al*., 2024) were recorded. Respiratory failure correction time was defined as the time from the start of treatment to the achievement of the following two criteria for 24 consecutive hours: (1) Arterial blood gas indexes returned to normal ($PaO_2 \geq 60$ mmHg, $PaCO_2 \leq 45$ mmHg under room air); (2) The patient's clinical symptoms (dyspnea, cyanosis) were significantly relieved and there was no need for non-invasive ventilation support. The time was calculated in days, with the data recorded by the attending nurse every 12 hours (Tang *et al.*, 2022). (2) *Lung function*: FVC, FEV1, FEV1/FVC and RR were recorded. (3) *Blood gas function*: pH, SaO_2, PaO_2, and $PaCO_2$ were measured. (4) *Inflammatory factors*: CRP and PCT were determined. (5) The research team monitored adverse reactions through daily ward rounds during the 7-day treatment period. All AEs were recorded in detail, including the time of occurrence, symptoms, severity, and relationship with the study drugs. AEs were classified according to the Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0, with severity graded as grade 1 (mild) to grade 5 (severe). *Management measures*: Grade 1-2 mild AEs (e.g., mild abdominal distension, nausea) were treated symptomatically without stopping the study drugs; grade 3 or higher severe AEs required immediate discontinuation of the study drugs and referral to a specialist for treatment. No grade 3 or above AEs were observed in either group during the study. (6) Care outcomes: ADL scores and nursing satisfaction.

Blinding of methods

This trial was a non-blinded study due to the differences in administration routes and regimens between the two groups. To minimize potential bias, the following measures were adopted: (1) All lung function, blood gas and inflammatory factor measurements were performed by laboratory technicians who were unaware of the group allocation; (2) The evaluation of APACHE II scores and respiratory failure correction time was standardized using unified criteria and completed independently by two senior clinicians; (3) Data entry and statistical analysis were conducted separately by different researchers to avoid subjective interference.

Statistical analysis

SPSS24.0 software was used for statistical analysis. Chi-square tests were performed to compare patients' sex, adverse reaction rate, and other counting data [n(%)]; independent samples t tests were used for inter-group comparisons of lung function, blood gas analysis results and other measurement data ($\chi \pm s$), and paired t tests were used for intra-group comparisons. The presence of significance was indicated by $P<0.05$.

RESULTS

Symptoms improved faster in the experimental group

As shown in Fig. 1, the RF correction time of the experimental group was (3.19±0.45) d, shorter than that of the control group ($P<0.05$). In addition, a significant reduction in the APACHE II score was observed in both groups after treatment, with a lower score in the experimental group ($P<0.05$).

The experimental group had better lung function after treatment

As shown in Fig. 2, the two groups did not differ in lung function parameters before treatment ($P>0.05$). Both groups showed markedly elevated FVC and FEV1 after treatment, with higher levels in the experimental group compared with the control group ($P<0.05$); FEV1/FVC was also elevated in both groups after treatment compared with before treatment, but there was still no significant difference between the two groups ($P>0.05$); while RR was reduced after treatment, with an even lower level in the experimental group ($P<0.05$).

The blood gas function was better in the experimental group after treatment

As shown in Fig. 3, the pre-treatment blood gas function did not differ significantly between groups ($P>0.05$). After treatment, pH altered littler in both groups, with no notable inter-group difference ($P>0.05$). SaO_2 and PaO_2 increased significantly in both groups after treatment, especially in the experimental group (P<0.05), while PaCO2 decreased and was lower in the experimental group than in the control group ($P<0.05$).

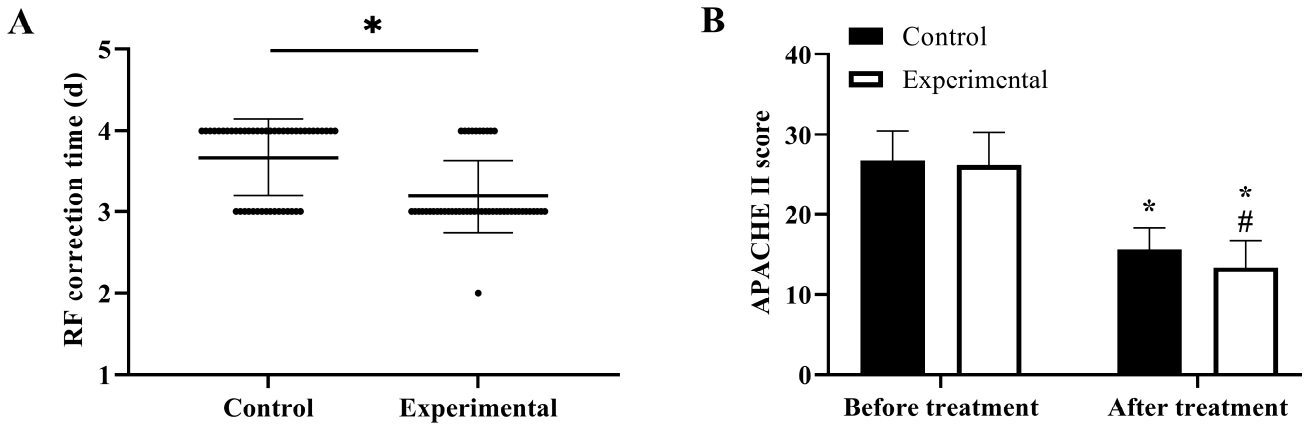

Fig. 1: Comparison of symptom improvement. (A) Comparison of time to RF correction time between the two groups (**P*<0.05); (B) Comparison of APACHE II scores before and after treatment between the two groups (comparison with before treatment $^{*}P$<0.05, comparison with control group $^{\#}P$<0.05).

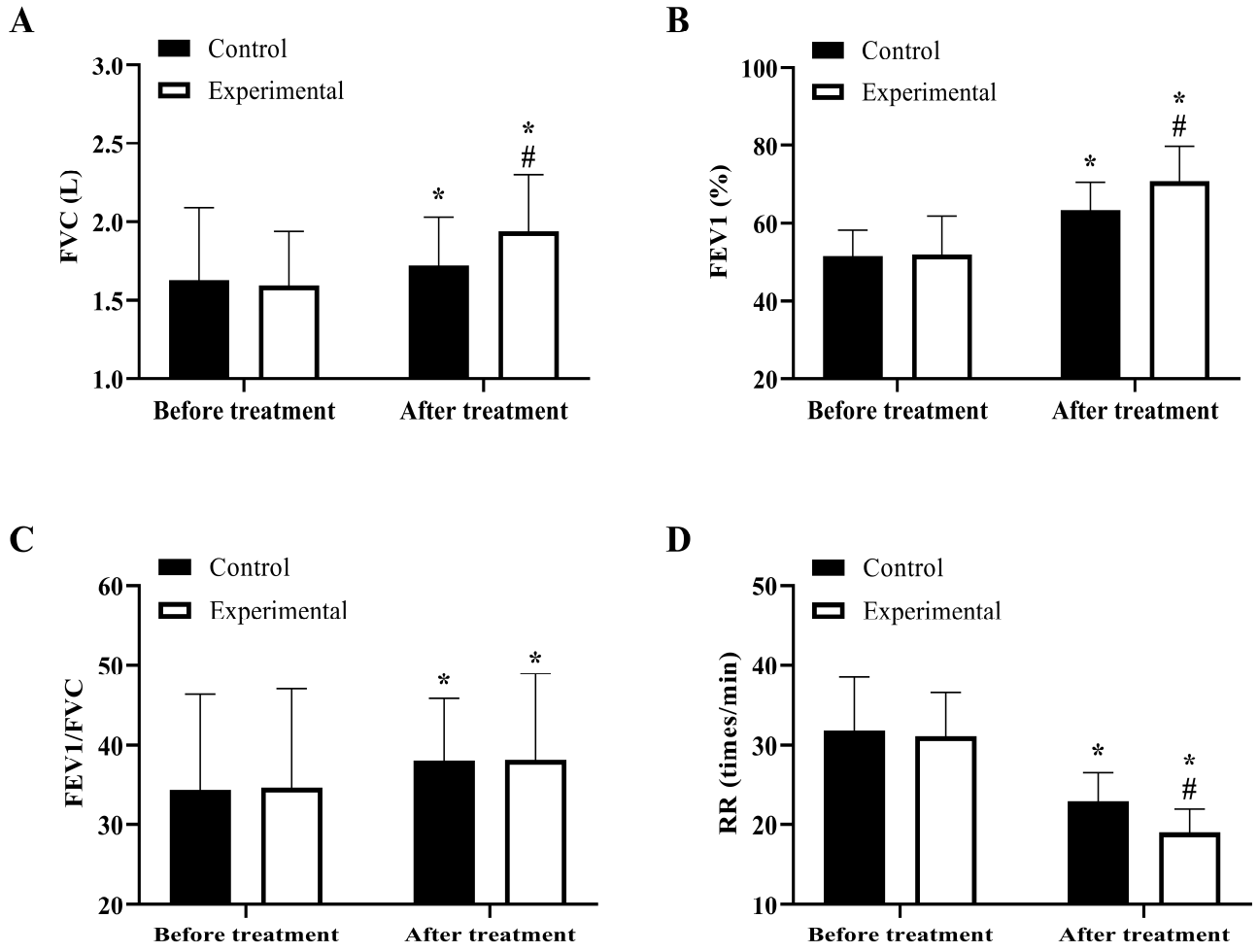

Fig. 2: Comparison of lung function (comparison with before treatment $^{*}P$<0.05, comparison with control group $^{\#}P$<0.05). (A) Comparison of FVC before and after treatment between the two groups; (B) Comparison of FEV1 scores before and after treatment between the two groups; (C) Comparison of FEV1/FVC scores before and after treatment between the two groups; (D) Comparison of RR before and after treatment between the two groups.

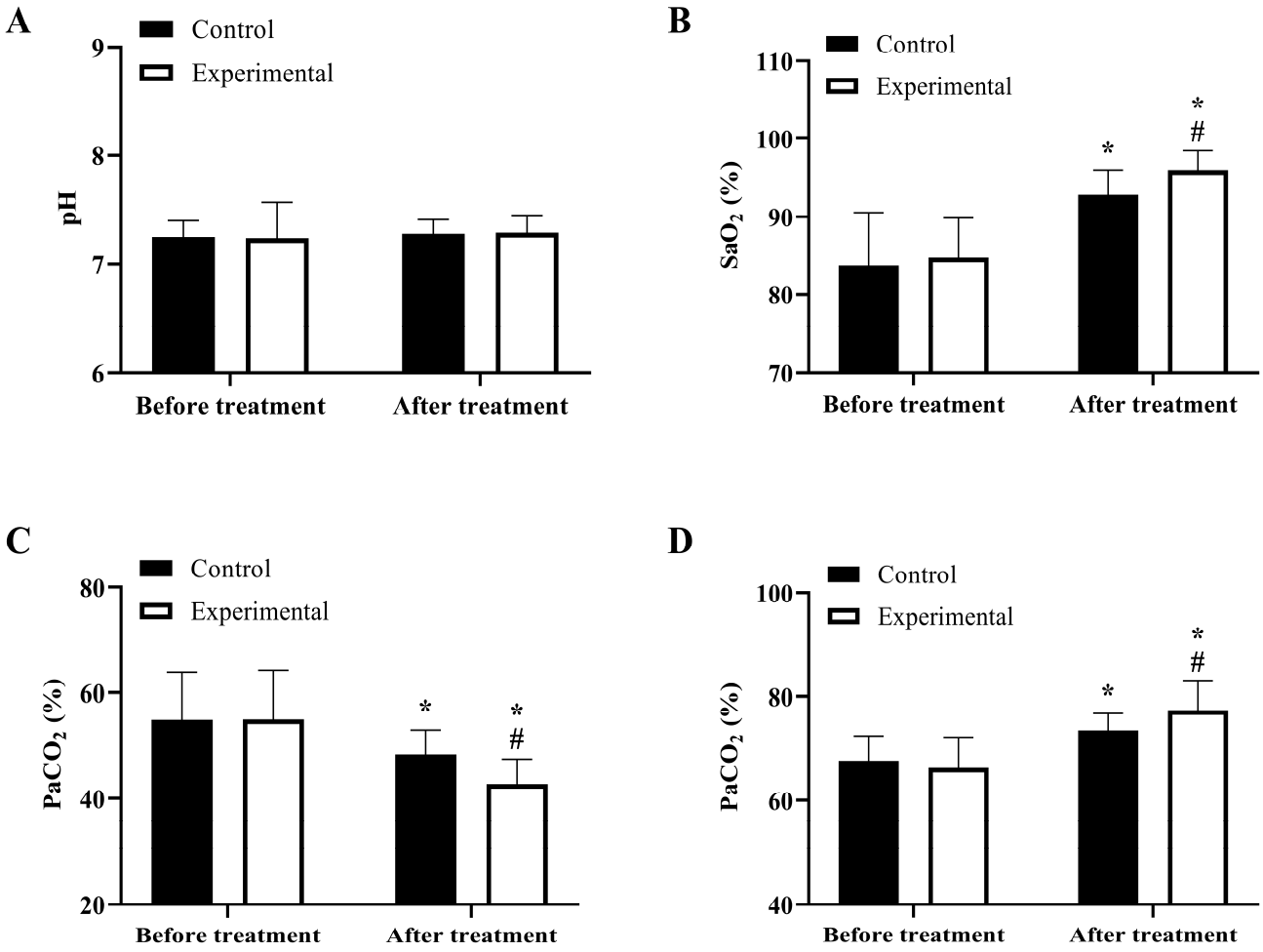

Fig. 3: Comparison of blood gas function (comparison with before treatment $^{*}P<0.05$, comparison with control group $^{\#}P<0.05$). A: Comparison of pH before and after treatment between the two groups. B: Comparison of SaO_2 scores before and after treatment between the two groups. C: Comparison of PaO_2 scores before and after treatment between the two groups. D: Comparison of $PaCO_2$ before and after treatment between the two groups.

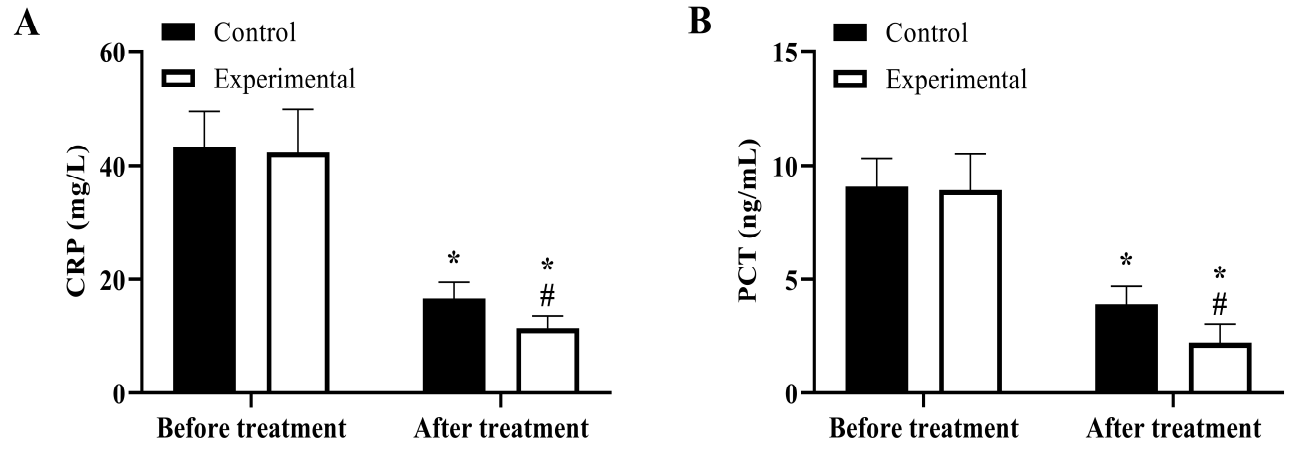

Fig. 4: Comparison of inflammatory reaction (comparison with before treatment $^{*}P<0.05$, comparison with control group $^{\#}P<0.05$). (A) Comparison of CRP before and after treatment between the two groups; (B) Comparison of PCT scores before and after treatment between the two groups.

Table 2: Comparison of adverse reactions [n(%)].

Group	n	Abdominal distension	Expectoration	Nausea and vomiting	Rash	Arrhythmia	Total incidence
Control	48	3 (6.25)	1 (2.08)	2 (4.17)	0 (0.0)	1 (2.08)	14.58
Experimental	48	2 (4.17)	2 (4.17)	3 (6.25)	1 (2.08)	0 (0.0)	16.67
$\chi 2$							0.079
P							0.779

Table 3: Comparison of care outcomes [n(%)].

Group	n	ADL scores		Results of satisfaction survey	
		Before treatment	After treatment	Satisfied	Dissatisfied
Control	48	64.10±6.33	85.92±6.64*	47 (97.92)	1 (2.08)
Experimental	48	65.08±7.63	87.10±5.74*	48 (100.0)	0 (0.0)
χ^2/t		0.685	0.938	1.011	
P		0.495	0.351	0.315	

Note: * indicates a statistically significant difference from before treatment (P<0.05).

The inflammatory reaction was milder in the experimental group after treatment

As shown in Fig. 4, no significant inter-group differences were observed in the levels of inflammatory factors before treatment (P>0.05); however, lower levels of inflammatory factors were observed in the experimental group after treatment (P<0.05). In addition, both groups showed reduced CRP and PCT levels after treatment (P<0.05).

The two groups had no difference in the incidence of adverse reactions

During the course of treatment, patients developed abdominal distension, expectoration, nausea and vomiting and other adverse reactions (Table 2). The incidence of adverse reactions in the experimental group was 16.67%, with no statistically significant difference compared with the control group (P>0.05).

The two groups had no difference in the care outcomes

As shown in Table 3, there was no statistically significant difference in ADL scores between the two groups before treatment (P>0.05). After treatment, the ADL scores of the two groups were higher than those before treatment (P<0.05). In addition, the care satisfaction of the experimental and control groups reached 100.0% and 97.92%, respectively, and there was again no significant difference between the two groups (P>0.05).

DISCUSSION

COPD complicated with type II respiratory failure is a common critical condition in elderly patients, characterized by persistent airway inflammation, ventilation dysfunction and gas exchange disorders (Wang *et al.*, 2020). Systemic glucocorticoids are recommended in clinical guidelines for the treatment of COPD exacerbations with respiratory failure, but the optimal dosage for elderly patients remains controversial due to the risk of adverse reactions. This study explored the efficacy and safety of low-dose methylprednisolone sodium succinate (LD-MSS, 40 mg/day) in elderly COPD-RF patients, with nikethamide as the control (Meduri *et al.*, 2022). Systemic glucocorticoids such as methylprednisolone have been extensively studied and shown to be effective in treating COPD patients with respiratory failure, as reported in previous reviews and studies (Russo *et al.*, 2022). Low-dose strategies in elderly or high-risk patients have also been reported to improve inflammation, lung function and blood gas indexes. However, most of these studies focused on general COPD populations and there is a lack of targeted data for elderly patients aged 60–75 years with stable vital signs (Boers *et al*., 2022). This study fills the gap by providing clinical evidence for the safety and efficacy of LD-MSS in this specific subgroup.

The results showed that the LD-MSS group had a shorter time to correction of respiratory failure and lower APACHE II scores than the control group, indicating that LD-MSS can accelerate the improvement of clinical symptoms. In terms of lung function, LD-MSS significantly increased FVC and FEV1 and reduced respiratory rate, which may be related to its inhibitory effect on airway inflammation and reduction of airway edema. These findings are consistent with previous studies showing that low-dose glucocorticoids can improve lung function in COPD patients without increasing adverse reactions (Guo *et al.,* 2022). In addition, LD-MSS improved blood gas indexes (increased SaO_2 and PaO_2, decreased $PaCO_2$), which are beneficial for correcting hypoxia and carbon dioxide retention. The improvement in blood gas function may be attributed to enhanced airway sensitivity to bronchodilators and to improved alveolar gas exchange following reduced inflammation (Qi *et al*., 2025).

The anti-inflammatory effect of LD-MSS was confirmed by the significant reduction of CRP and PCT levels in the experimental group. CRP and PCT are sensitive markers of

systemic inflammation, and their reductions indicate that LD-MSS can effectively inhibit the inflammatory response in COPD-RF patients. Although this study did not detect IL-6 and TNF-α, previous studies have shown that glucocorticoids can inhibit the release of these pro-inflammatory cytokines by blocking the NF-κB pathway (Wang *et al.*, 2021). However, the specific molecular mechanism of LD-MSS in elderly COPD-RF patients needs to be verified by further studies with molecular marker detection.

In the study of its pathological mechanism, MSS has been shown to improve the sensitivity of trachea by increasing the number of glucocorticoid receptors and prostaglandin H receptors, inhibit the synthesis of acidic mucopolysaccharides in the bronchial glands of patients, promote the contraction of small vessels, increase the tension of endoplasm and reduce inflammatory cell infiltration, thus alleviating the symptoms of tracheal obstruction in patients (Buchheit *et al.*, 2021). Nikethamide is a commonly used respiratory stimulant in clinical practice that can stimulate the patient's respiratory center and reduce carbon dioxide retention while increasing tidal volume and oxygen delivery (Zhong *et al.*, 2022). Therefore, in the treatment of COPD complicated by RF, MSS has a more comprehensive and efficient clinical effect, which explains the better results in terms of time to symptom and condition improvement. The present results are consistent with the report by Zhai X et al. of improved lung function in MSS, but highlight the safety of lower doses in the elderly population (Zhai *et al.*, 2023).

The comparison of blood gas function showed that SaO2 and PaO2 were higher in the experimental group after treatment. At the same time, $PaCO_2$ was lower, indicating that intravenous infusion of MSS helps maintain the body's acid-base balance, reduces fatigue caused by dyspnea, and reduces the work of the respiratory muscles, consistent with the results of previous studie. It is hypothesize that this is because MSS enhances the sensitivity of the trachea to receptor stimulants and to oxygen saturation, and promotes vasoconstriction, thus improving the oxygen-carrying capacity of blood (Jie *et al.*, 2020).

The 40 mg/day dosage of methylprednisolone sodium succinate was classified as a low dose based on the Global Initiative for GOLD 2023 guidelines and clinical practice consensus for elderly COPD patients. In clinical settings, high-dose methylprednisolone for COPD treatment is generally defined as ≥ 80 mg/day. In comparison, doses ≤ 40 mg/day are considered low-dose regimens, which are more suitable for elderly patients to reduce metabolic adverse reactions. The safety of LD-MSS was reflected in similar incidences of adverse reactions between the two groups and in the absence of significant metabolic abnormalities (hyperglycemia, electrolyte disturbances). This is consistent with the clinical consensus that low-dose glucocorticoids have a better safety profile in elderly patients (Sugihara *et al*., 2024), reducing the risk of osteoporosis, hyperglycemia, and other adverse reactions associated with high-dose glucocorticoids (Amano *et al.*, 2021). The 40 mg/day dosage of MSS was defined as low-dose according to the GOLD guidelines and clinical practice, where high-dose MSS is generally ≥ 80 mg/day for COPD treatment.

Previous study have found that patients with COPD combined with RF are generally more resistant to healthcare personnel due to the torture of the disease, the pain of mechanical ventilation and the fear of the psychology, which also results in the low treatment compliance and nursing satisfaction of the patients (Aranburu-Imatz *et al.*, 2022). In this study, respiratory nursing is applied to COPD patients, which can timely intervene to deal with the existing problems and hidden dangers of patients' respiration, on the one hand, greatly improving the safety of treatment, on the one hand, it also brings the relationship between doctors and patients closer and enhances the patients' sense of trust and dependence on health care personnel (Yi *et al.*, 2021). However, these limitations must be addressed. First of all, longer term follow-up of the patients is needed to assess their prognosis. At the same time, it is necessary to compare the therapeutic effect of LD-MSS with that of other treatment regimens. Finally, the study was short, and future pharmacokinetic monitoring is needed to optimize the dosing regimen and provide a more comprehensive reference for clinical practice.

This study has several limitations. First, it is a single-center study with a small sample size and the results need to be verified by multi-center randomized controlled trials. Second, the follow-up period is short, and the long-term efficacy and safety of LD-MSS need to be further evaluated. Third, the study did not detect immunological and molecular markers, so the mechanism of action needs to be further explored. Fourth, metabolic parameters, including blood glucose, electrolytes, and hematologic profiles, were not monitored during the intervention, leading to an incomplete safety assessment of LD-MSS, especially in elderly patients with vulnerable metabolic homeostasis. In addition, the selection of nikethamide as the control was based on its status as a commonly used respiratory stimulant in clinical practice, despite its limited efficacy in COPD-RF, which may highlight the advantages of LD-MSS.

CONCLUSION

LD-MSS (40 mg/day) is effective and safe in the treatment of elderly COPD patients complicated with respiratory failure. It can accelerate the correction of respiratory failure, improve lung function and blood gas indexes and inhibit inflammation, with a good safety profile. This study

provides clinical evidence for the application of low-dose glucocorticoids in elderly COPD-RF patients, complementing the existing literature on low-dose steroid strategies in high-risk populations.

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Authors' contributions
Yuetong Liu: Conceived and designed the project and wrote the paper; Yuetong Liu and Pei Xia: Generated the data; Youwei Wang: Analyzed the data; Yirun Sun: Modified the manuscript.

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Data availability statement
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical approval
The study was approved by the Ethics Committee of Chuzhou Hospital Affiliated to Anhui Medical University (No.l2021017). This study was performed in adherence with the STROBE guidelines. See supplementary file for the STROBE checklist.

Conflicts of interest
The authors report no conflict of interest.

Consent to participate
All authors gave final approval of the version to be published and agree to be accountable for all aspects of the work.

Supplementary data
https://www.pjps.pk/uploads/2026/05/SUP1779448707.pdf

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