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Impact of Sangbaipi decoction and acupuncture combination on acute inflammatory response and stress injury in elderly patients with chronic obstructive pulmonary disease

Jie Xin*
Department of Health Management Center, Baoji High-Tech Hospital, Baoji, Shaanxi, 721000, China.

Abstract: This study aims to explore the impact of Sangbaipi Decoction (SBPD) in combination with acupuncture on chronic obstructive pulmonary disease (COPD) among the elderly, thereby offering valuable insights for clinical applications. A total of 128 COPD patients admitted to our hospital between July 2023 and July 2024 were recruited for this research. Of these, 68 patients undergoing conventional integrated Chinese and Western medicine rehabilitation therapy constituted the control group. The remaining 60 patients, received SBPD therapy based on the control group's regimen, forming the observation group. No significant difference was observed in the overall treatment efficacy between the two groups ($P>0.05$). However, the duration for the disappearance of cough and wheezing was significantly shorter in the observation group compared to the control group ($P<0.05$). Additionally, the observation group demonstrated superior pulmonary function and blood gas parameters after treatment, accompanied by lower levels of airway inflammatory factors and malondialdehyde as compared to the control group ($P<0.05$). These results suggest that SBPD combined with acupuncture can effectively shorten the rehabilitation duration of elderly COPD patients, enhance their lung and blood gas functions, and mitigate the inflammatory response.

Keywords: Chronic obstructive pulmonary disease, Sangbaipi decoction, acupuncture, stress response, inflammatory response

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD), characterized by irreversible and incomplete airflow limitation, generally progresses in a progressive manner. Its pathogenesis is closely linked to respiratory tract infections and inflammatory stimuli, with the elderly being the primary affected group (Labaki & Rosenberg, 2020). A statistical report from *The Lancet* shows that, despite certain achievements in symptomatic treatment and prevention of acute exacerbations of COPD in current clinical practice, there has been little remarkable progress in modifying disease progression. To date, COPD still claims over three million lives each year (Rabe & Watz, 2017). Clinically, COPD is recognized as a global healthcare concern and a socioeconomic burden, imposing a significant negative impact on both patients' health and their families (Akdeniz & Ozkan, 2024). Traditional Western medicine treatments mainly focuses on controlling symptoms combined with anti-infection, cough suppression, and expectoration, and is supplemented by glucocorticoids to achieve rapid symptom amelioration (Kahnert *et al.*, 2023). Nevertheless, long-term use of glucocorticoids not only leads to notable drug resistance but also frequently results in side effects such as immunosuppression and osteoporosis (Axelerad *et al.*, 2021).

In recent years, traditional Chinese medicine (TCM) has increasingly captured the spotlight in clinical applications across a spectrum of diseases due to its remarkable treatment stability and safety (Cao *et al.*, 2023). Acupuncture, a representative TCM therapy, exerts effects such as facilitating blood circulation, dissipating blood stasis, and regulating the functions of meridians and internal organs by stimulating specific acupoints of the human body. As a result, it has become a commonly used approach in the treatment of COPD (F. Shi *et al.*, 2024; Zeng *et al.*, 2024). Nonetheless, relying solely on acupuncture often cannot achieve the optimal therapeutic outcome. To enhance efficacy, adjunctive treatment with Chinese herbal medicine is typically necessary. Sangbaipi Decoction (SBPD) is a time-honored and classic Chinese herbal formula. As recorded in *Yi Lin*, it has the functions of clearing the lung heat, descending qi, resolving phlegm, and relieving cough, and is thus well-suited for the treatment of diverse pulmonary diseases (Wang *et al.*, 2023). In China, SBPD is widely utilized in the management of COPD. However, its use remains uncommon in regions outside of China due to the absence of reliable international reports. A recent network pharmacology analysis conducted by He H et al. has demonstrated that the primary components of SBPD can effectively mitigate the progression of COPD (He *et al.*, 2024), thus establishing a foundation for the promotion of its clinical application.

**Corresponding author:* e-mail: 18992776959@163.com

Nonetheless, further conclusive clinical reports are necessary to substantiate the impact of SBPD on COPD. Consequently, in this study, we aim to investigate the comprehensive effects of acupuncture combined with SBPD on elderly patients with COPD, with the intention of providing novel insights and guidance for the future clinical management of COPD.

MATERIALS AND METHODS

Research subjects

A retrospective analysis was performed on 128 patients with COPD who were admitted to our hospital between July 2023 and July 2024. Among them, 68 patients who received conventional integrated traditional Chinese and Western medicine rehabilitation treatment were regarded as the control group. Another 60 patients who received SBPD treatment on the basis of the control group were regarded as the observation group. The clinical baseline data of the two groups are shown in table 1. This study was conducted in strict adherence to the Declaration of Helsinki and has been approved by the Ethics Committee of our hospital (No. 2023055). fig. 1 shows the main process of this study. The determination of the sample size was based on calculations using G-Power software.

Inclusion and exclusion criteria

Inclusion criteria: Patients with a clear diagnosis of COPD based on clinical manifestations, pulmonary computed tomography (CT) scans, and pulmonary function tests; aged 65 years or older; classified as having the "Phlegm-Turbidity Obstructing the Lungs" syndrome according to TCM differentiation; complete medical records; and no history of drug allergies.

Exclusion criteria: Patients with severe pulmonary infections, extrapulmonary infections, or bronchial asthma; those with concurrent severe cardiac, hepatic, or renal diseases; patients whose condition has progressed to respiratory failure; and patients with a history of thoracic surgery.

Methods

Upon admission to the hospital, all patients were administered conventional anti-infection, oxygen inhalation, and chemotherapy treatments. Specifically, Budesonide (AstraZeneca Pty Ltd, HJ20140474) was given at a dose of 1.0 mg per time, twice daily. Ipratropium Bromide (Laboratoire Unither, H20150158) was used for aerosol inhalation therapy at 0.5 mg per time, also twice daily. Levofloxacin (Yangtze River Pharmaceutical Group Co., Ltd., H20060026) was administered via intravenous drip at 0.4 g per time, once a day. Ambroxol Hydrochloride and Sodium Chloride (Jiangsu Hansoh Pharmaceutical Group Co., Ltd., H20060026) was injected intravenously at 30 mg per time, once a day. In addition, acupoints such as Taiyuan, Fenglong, Taixi, Lieque, Zusanli, Chize, and Zhongwan were selected. After disinfection with alcohol, acupuncture treatment was performed using 0.25 mm × 40 mm filiform needles, with the needles retained for 30 minutes. There was an interval of one day between each acupuncture session, and the treatment lasted for two weeks. The observation group, in addition to the above treatments, received SBPD treatment. The prescription included Cortex Mori at 20 g, Radix Glehniae at 15 g, and each of Fructus Perillae, Rhizoma Coptidis, Radix Glycyrrhizae, Radix Scutellariae, Fructus Gardeniae Praeparatus and Bulbus Fritillariae Thunbergii at 10 g, along with Herba Houttuyniae and Rhizoma Pinelliae Praeparatum at 9 g each, Herba Ephedrae Praeparata at 3 g, and Semen Armeniacae Amarum at 6 g (T. Shi *et al.*, 2024). All medications are provided by Baoji High-Tech Hospital's herbal pharmacy. Soak all the drugs in water for 30 min, add 1000mL of water, cook over high heat until boiling, then change to low heat and cook for another 20 min, filter out all the drug residue, and finally obtain SBPD about 800 mL. SBPD was divided into 2 portions (each portion of about 400mL), and was taken every day in the morning (8:00-9:00) and in the evening (20:00-21:00) for 2 consecutive weeks. for 2 consecutive weeks.

Efficacy evaluation

After the completion of treatment, the clinical efficacy of patients was evaluated with reference to the COPD treatment guidelines (Vogelmeier *et al.*, 2020). A complete disappearance of symptoms was defined as cured, an improvement of symptoms was regarded as effective, and no improvement or an aggravation of symptoms was considered ineffective. The overall effective rate is calculated as (the number of cured patients + the number of effective patients) / the total number of patients × 100%.

Sample collection and testing

Alveolar lavage fluid samples of patients were collected before and after treatment. The levels of interleukin (IL)-17A, IL-1β, tumor necrosis factor-like weak inducer of apoptosis (TWEAK), superoxide dismutase (SOD), and malondialdehyde (MDA) were detected by using the ELISA method. Procalcitonin (PCT) was measured using an automated biochemical analyzer. Arterial blood samples from patients were collected, and partial pressure of arterial oxygen (PaO), arterial oxygen saturation (SaO), and partial pressure of arterial carbon dioxide (PaCO) were tested with a blood gas analyzer. Forced expiratory volume in 1 second (FEV1), forced vital capacity (FCV), peak expiratory flow (PEF), and dynamic lung compliance (C_{dyn}) were determined using a pulmonary function device.

Outcome measurement

(1) Clinical efficacy. (2) Symptom improvement time (including the time to the disappearance of pulmonary rales, cough, and wheezing, as well as the hospital stay). (3) Pulmonary function (FEV1, FVC, PEF, and C_{dyn}). (4) Blood gas function (PaO, SaO, and PaCO). (5)

Inflammatory response and oxidative stress (IL-17A, IL-1β, TWEAK, PCT, SOD and MDA). (6) Safety (adverse reactions during treatment, such as abdominal pain, diarrhea, dizziness and headache).

STATISTICAL ANALYSIS

This study used SPSS25.0 software for statistical analysis. For count data, percentages were calculated, and the chi-square test was applied for comparison. For measurement data, the mean and standard deviation were computed, and paired t-tests and independent samples t-tests were employed for within-group and between-group comparisons, respectively. A P-value less than 0.05 is considered statistically significant.

RESULTS

Clinical efficacy and symptom improvement

As depicted in table 2, when compared with the control group, there was no significant difference in the overall effective rate between the two groups (P<0.05). Additionally, no significant difference was determined in the time to the disappearance of pulmonary rales and the length of hospital stay between the two groups (P>0.05). However, the time to the disappearance of cough and wheezing was shorter in the observation group than in the control group (P<0.05), indicating a faster rate of symptom improvement in the observation group.

Pulmonary function

The pulmonary function test results are presented in fig. 2. After treatment, the FEV1, FVC, PEF, and C_{dyn} of both patient groups increased significantly (P<0.05), suggesting that the pulmonary function of both groups was improved. Further, an inter-group comparison revealed the absence of notable difference in post-treatment PEF and C_{dyn} (P>0.05); however, statistically higher FEV1 and FVC were determined in the observation group compared with the control group after treatment (P<0.05), confirming superior pulmonary function in the observation group.

Blood gas function

In terms of blood gas function (fig. 3), there was likewise no difference in the comparison of pre-treatment detection results between the two groups (P>0.05).

Table 1: Clinical information

Groups		Control (n=68)	Observation (n=60)	Statistical	P
Sex	Male/female	42 (61.76%)/26 (38.24%)	35 (58.33%)/25 (41.67%)	χ^2=0.157	0.692
Age (years)		68.72±2.37	68.35±2.77	t=0.815	0.417
Duration of COPD (years)		5.94±1.15	5.92±1.50	t=0.092	0.927
Time to acute exacerbation (d)		2.43±1.15	2.41±1.19	t=1.005	0.317
Smoking [n(%)]	Yes/no	46 (67.65%)/22 (32.35%)	42 (70.00%)/18 (30.00%)	χ^2=0.082	0.774
Severity [n(%)]	Mild/moderate	33 (48.53%)/35 (51.47%)	26 (43.33%)/34 (56.67%)	χ^2=0.346	0.556

Table 2: Clinical efficacy and recovery time

Groups		Control (n=68)	Observation (n=60)	Statistical	P
Clinical efficacy	Cured [n(%)]	10 (14.71%)	13 (21.67%)	-	-
	Effective [n(%)]	48 (70.59%)	41 (68.33%)	-	-
	Ineffective [n(%)]	10 (14.71%)	6 (10.00%)	-	-
	Overall effective rate (%)	85.29	90.00	χ^2=0.645	0.422
Symptom improvement time (d)	Disappearance of pulmonary rales	6.81±1.96	6.37±1.37	t=1.460	0.147
	Disappearance of pulmonary cough	5.81±1.75	5.07±1.72	t=2.418	0.017
	Disappearance of pulmonary wheezing	4.75±1.23	4.15±1.02	t=2.984	0.003
	Hospital stays	14.44±1.19	14.08±1.05	t=1.797	0.075

Table 3: Adverse reactions

Groups	Control (n=68)	Observation (n=60)	χ^2	P
Abdominal pain/diarrhea [n(%)]	2 (2.94%)	1 (1.67%)		
Dizziness/headache [n(%)]	3 (4.41%)	3 (5.00%)		
Insomnia [n(%)]	1 (1.47%)	2 (3.33%)		
Allergic reaction [n(%)]	1 (1.47%)	2 (3.33%)		
Vomiting [n(%)]	2 (2.94%)	1 (1.67%)		
Total (%)	13.24	15.00	0.082	0.774

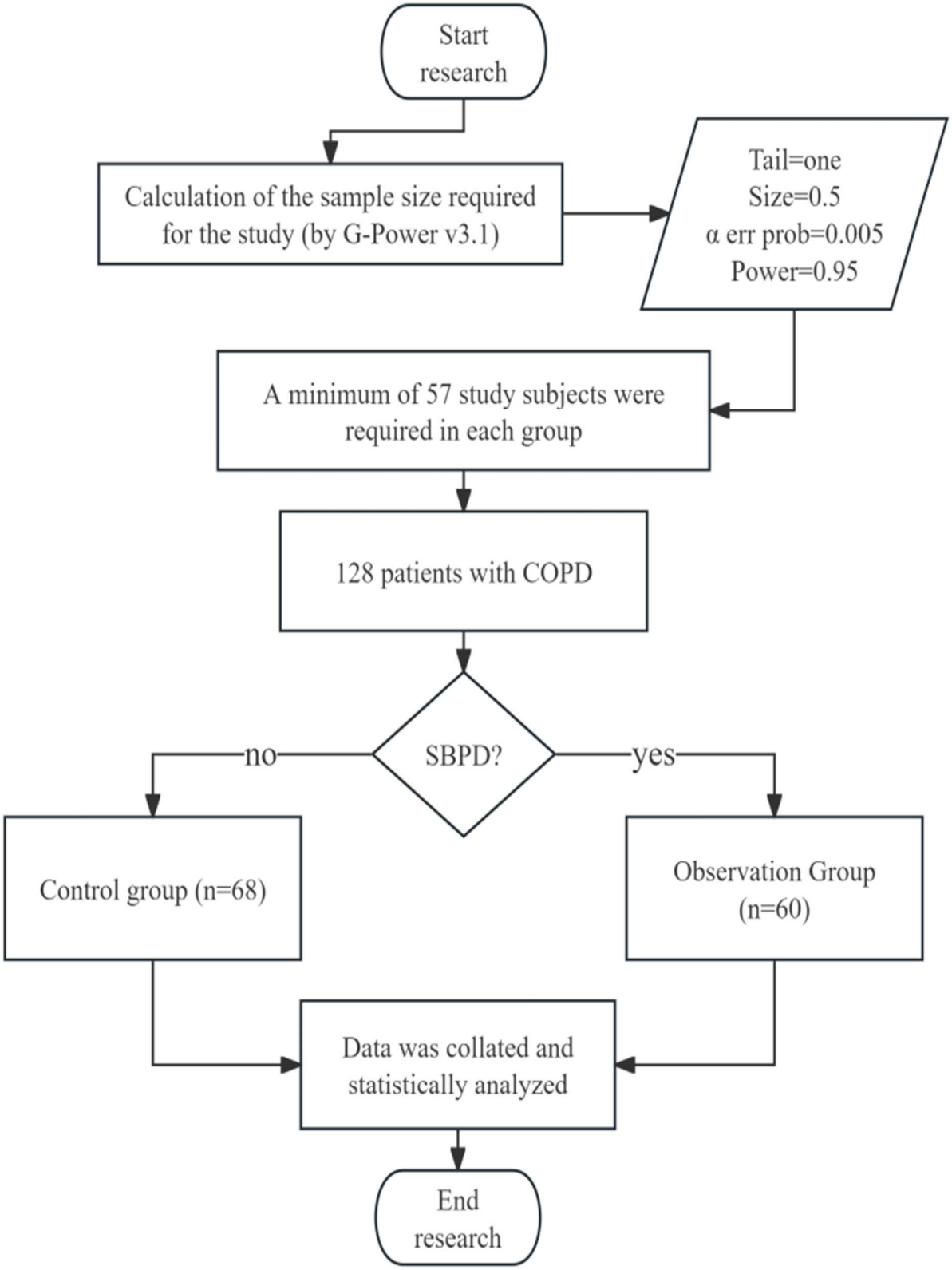

Fig. 1: Shows the main flow of this study.

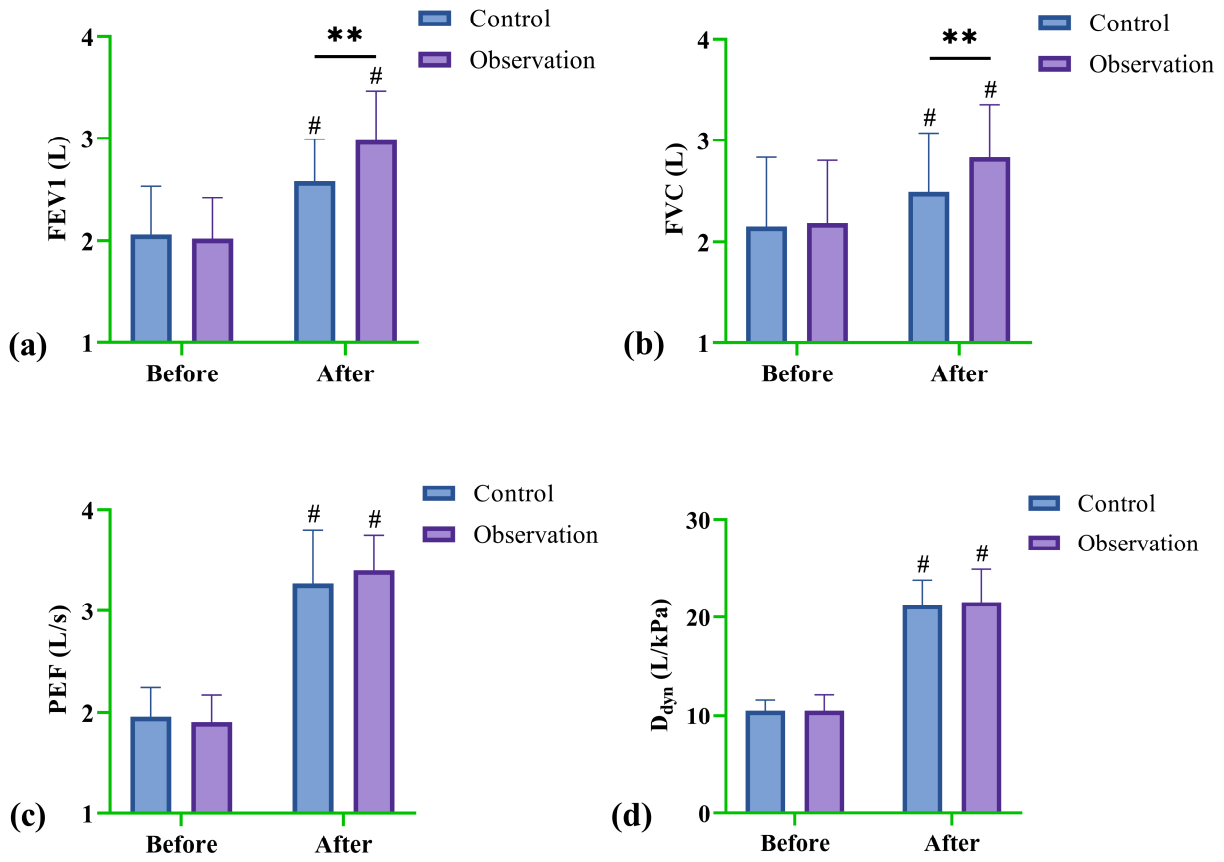

Fig. 2: Pulmonary function. (a-d) show the comparison of FEV1, FVC, PEF, and D_{dyn} before and after treatment, respectively. # indicates P<0.05 compared to before treatment and ** indicates P<0.05 compared to control group.

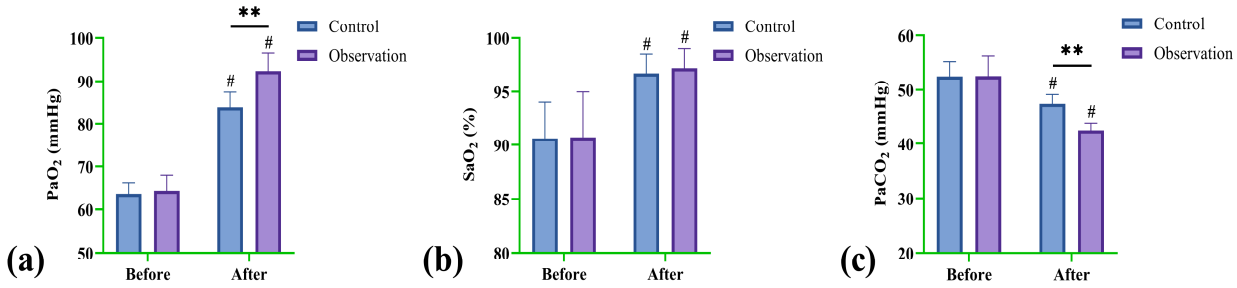

Fig. 3: Blood gas function. (a-c) show the comparison of PaO, SaO, and $PaCO_2$ before and after treatment, respectively. # indicates P<0.05 compared to before treatment and ** indicates P<0.05 compared to control group.

After treatment, both groups exhibited an increase in PaO and SaO, with the PaO_2 in the observation group being significantly higher than that in the control group (P<0.05), while the $PaCO_2$ decreased, being significantly lower in the observation group than in the control group (P<0.05). The above results indicate that the observation group has superior blood gas function.

Inflammatory response and oxidative stress response

As depicted in fig. 4, there was no difference in the comparison of airway inflammation indicators and oxidative stress indicators before treatment between the two groups (P>0.05). After treatment, the airway inflammation indicators of both groups decreased, with the IL-17A, IL-1β, TWEAK and PCT in the observation group being significantly lower than those in the control group (P<0.05). Among the oxidative stress indicators, the MDA of both groups decreased after treatment, with a significantly lower level in the observation group (P<0.05), while the SOD increased, but without a significant inter-group difference (P>0.05). These results suggest that the inflammatory response and oxidative stress in the

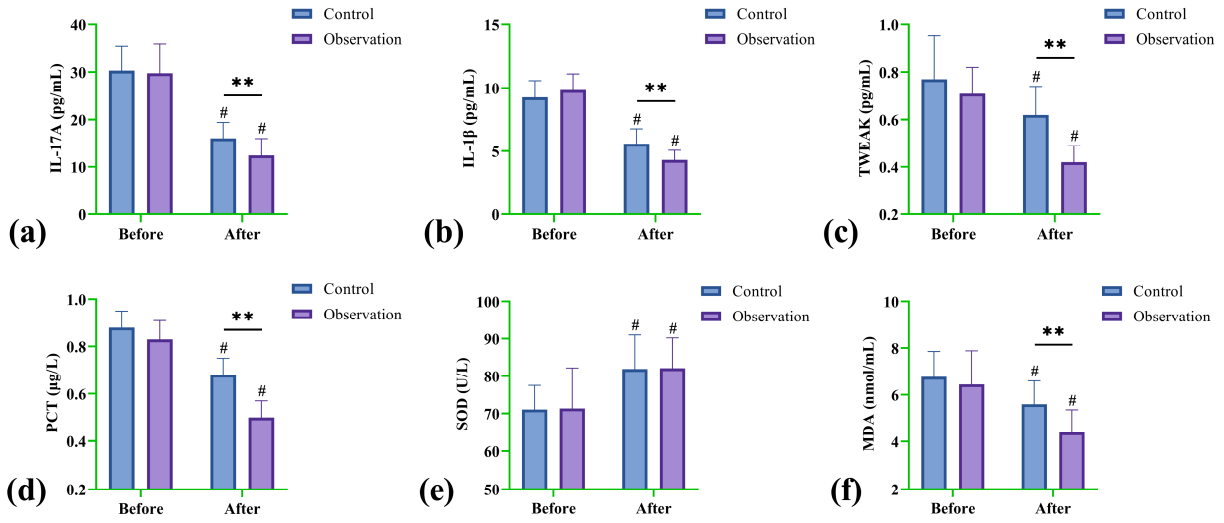

Fig. 4: Inflammatory response and oxidative stress response. (a-f) show the comparison of IL-17A, IL-1β, TWEAK, PCT, SOD, and MDA before and after treatment, respectively. # indicates P<0.05 compared to before treatment and ** observation group are less pronounced after treatment. Indicates P<0.05 compared to control group.

Safety

Finally, the adverse reactions during treatment were recorded, with the results presented in Table 3. There was no statistically significant difference in the comparison of the overall incidence of adverse reactions between the two groups (P>0.05), indicating comparable safety.

DISCUSSION

COPD, as one of the major diseases that endanger middle-aged and elderly individuals at present, exhibits an increasing incidence year by year (Agusti *et al.*, 2020). Therefore, finding more effective and safe treatment protocols is crucial for ensuring the prognosis of patients. In this study, we discovered that the combination of acupuncture and SBPD could lead to more favorable treatment outcomes for COPD patients, confirming the application value of SBPD in the management of COPD.

First of all, regarding clinical efficacy and symptom improvement, there was no difference in the overall treatment effective rate between the two groups. However, the time required for the disappearance of cough and wheezing was shortened in the observation group, suggesting that the use of SBPD can accelerate the rehabilitation process of COPD. Medications such as Budesonide and Ipratropium Bromide are currently recognized conventional treatment regimens for COPD, with their efficacy verified on multiple occasions (Chen *et al.*, 2024; And Alternative Medicine, 2023). Acupuncture, being one of the classic TCM treatment approaches, has also gained recognition in the adjuvant treatment of COPD (Fernandez-Jane *et al.*, 2020). In a randomized controlled trial conducted by Xu G *et al.,* acupuncture was demonstrated to enhance the treatment efficacy and safety of COPD patients (Xu *et al.*, 2024). Consequently, we believe that this is also the reason for the absence of a significant difference in the overall therapeutic efficacy between the two groups. On this basis, the use of SBPD led to more rapid symptom improvement. The underlying reason for this is that various TCM components in SBPD all have a positive influence on improving pulmonary function. For instance, Herba Houttuyniae exhibits diuretic and detumescence effects (Wu *et al.*, 2021); Semen Armeniacae Amarum is capable of relieving cough and asthma (Tomishima *et al.*, 2022); Cortex Mori can suppress upward adverse qi, stop vomiting, and resolve phlegm (Batiha *et al.*, 2023); and Bulbus Fritillariae Thunbergii can clear heat, dissipate nodules, relieve cough, and resolve phlegm (Nile *et al.*, 2021). These favorable impacts are also manifested in the superior pulmonary function and blood gas function of the observation group. The network meta-analysis carried out by Liu S et al. compared the treatment effects of six TCM prescriptions on COPD, demonstrating that SBPD can enhance patients' pulmonary function (Liu *et al.*, 2019), which coincides with our findings.

On the other hand, during COPD progression, the stress response resulting from continuous stimulation by airway inflammatory factors constitutes the main pathogenic mechanism (Brightling & Greening, 2019). Hence, in the treatment of COPD, alleviating airway inflammatory responses is also crucial for enhancing patient prognosis. In this study, the levels of inflammatory factors and MDA in the observation group after treatment exhibited a more pronounced decrease in comparison with the control group, indicating that the utilization of SBPD can significantly ameliorate the airway inflammatory response of COPD

patients. In a pharmacological study on SBPD conducted by Shi T *et al.,* the anti-influenza effect of SBPD both *in vitro* and *in vivo* is associated with its excellent anti-inflammatory effect (T. Shi *et al.,* 2024). The primary component of Cortex Mori is flavonoids, which can effectively inhibit the activity of cyclooxygenase-2 (COX-2) *in vivo*. Additionally, it can reduce NF-κB activity, suppress NO production and iOS expression, downregulate the synthesis of pro-inflammatory factors, reduce the generation of anti-inflammatory factors, and effectively exert an anti-inflammatory effect, thereby alleviating the airway spasm phenomenon in patients (Ren *et al.*, 2020).

Furthermore, the research by Li N *et al.* also noted that Cortex Mori was capable of effectively scavenging cytotoxic peroxides and regulating antiviral capabilities (Li *et al.*, 2024). In an animal experiment, Yan X *et al.* discovered that the extract of Cortex Mori could enhance the proportion of T lymphocyte subsets and suppress ovalbumin-induced asthma responses in mice (Yan *et al.*, 2024). These anti-inflammatory effects are unquestionably of substantial assistance in impeding the progression of COPD. Finally, no notable difference was observed in the comparison of the incidence of adverse reactions between the two groups, which also suggests that SBPD possesses extremely high drug safety and will not lead to the occurrence of other risk events. This result is also in accordance with the viewpoint of Li L *et al.* (Li *et al.*, 2021) and can serve as evidence for our conclusion.

However, due to the limited number of cases, the results of this study may be subject to a certain degree of contingency. In this regard, more cases need to be included for validation and analysis. Additionally, since this study did not carry out long-term follow-up investigations, we are currently unable to assess the impact of SBPD on the prognosis of COPD patients. In subsequent studies, we need to conduct long-term follow-up investigations on the study subjects and supplement the detection of more objective clinical indicators to evaluate the comprehensive impact of SBPD on COPD.

CONCLUSION

SBPD combined with acupuncture can shorten the rehabilitation cycle of elderly COPD patients and improve their lung function and blood gas function. At the same time, SBPD can also inhibit the inflammatory response and oxidative stress of patients, which has a high degree of safety and is recommended for clinical use.

Availability of data and materials

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

Conflicts of Interest

The authors report no conflict of interest.

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