ORIGINAL RESEARCH

Effects of external diaphragm pacing combined with breathing training on pulmonary function of chronic obstructive pulmonary disease patients

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Abstract

Background

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disorder with high global prevalence, yet current therapeutic strategies often fail to fully restore lung function or improve quality of life.

Aim

This study aimed to explore the effects of external diaphragm pacing (EDP) combined with breathing training in improving pulmonary function and quality of life for COPD patients.

Methods

From January 2021 to January 2023, a total of 97 COPD patients admitted to our hospital were selected and randomly divided into the control group (n=48) and the observation group (n=49). The control group received breathing training. The observation group received EDP after 30 minutes of breathing training. The clinical efficacy, lung function, arterial blood gas, oxidative stress, adverse effects that occurred during the treatment process and quality of life between the two both were compared.

Results

Compared with the control group, the observation group had higher total effective rate, higher forced expiratory volume in the first second (FEV1), higher forced vital capacity (FVC), higher FEV1/FVC ratio, lower partial pressure of carbon dioxide in artery (PaCO2), higher partial pressure of oxygen (PaO2), lower malonaldehyde (MDA), higher superoxide dismutase (SOD), higher glutathione (GSH) and higher chronic obstructive pulmonary disease assessment test (CAT) scores.

Conclusion

The combination of EPD and breathing training has a better effect on improving lung function and quality of life in patients with COPD, highlighting its potential as a therapeutic strategy for COPD.

Keywords: chronic obstructive pulmonary disease, external diaphragm pacing, breathing training, pulmonary function

Introduction

Chronic obstructive pulmonary disease (COPD) is a lung disease characterized by persistent airflow limitation[1]. Patients with chronic hypoxia and respiratory muscle weakness due to persistent airflow limitation will experience symptoms such as decreased exercise tolerance and breathing difficulties. This condition is particularly evident in patients with moderate to severe COPD[2]. The incidence and mortality rates of COPD rank first globally, making it a global public health issue[3]. According to a survey, the number of COPD patients in China has reached 100 million, which has imposed a heavy burden on China's economy and society, and has caused great pain to the patients and their families[4].

Studies have shown that pulmonary rehabilitation training for COPD patients can effectively promote the rehabilitation of lung function[5]. Traditional pulmonary rehabilitation training usually involves breathing exercises, where deep and slow breathing is practiced to control the respiratory muscles and enable patients to shift from shallow and rapid breathing to deep and slow breathing[6]. However, due to the cumbersome nature of the breathing muscle exercises and their slow effects, most patients find it difficult to adhere to the training, thus missing the best opportunity for lung function rehabilitation[7]. Therefore, finding other appropriate treatment methods has become the focus of attention.

Studies have shown that significant damage to the diaphragm in COPD patients can lead to a decline in lung function[8]. The diaphragm is composed of muscle fibers and is located between the thoracic and abdominal cavities, responsible for 3/4 of the body's respiratory movements. For patients with COPD, airway obstruction and residual air volume accumulation impair diaphragm contraction, leading to reduced diaphragm function[9]. External diaphragm pacing (EDP) is a method that addresses this by inducing diaphragm nerve potentials through electrical stimulation, promoting rhythmic diaphragm contractions that enhance ventilation and oxygen metabolism[10]. Meanwhile, breathing training focuses on retraining respiratory muscle control, optimizing breathing patterns, and improving exercise tolerance[11].

The combination of EDP and breathing training is hypothesized to produce synergistic effects through complementary mechanisms. EDP provides immediate physiological stimulation to activate dormant diaphragm muscle fibers and restore contractile function, while breathing training reinforces motor learning and strengthens respiratory muscle endurance[12]. This dual approach counteracts two key limitations: EDP alone may increase inspiratory load and risk respiratory muscle fatigue, while breathing training alone lacks direct neuromuscular activation[13].

Therefore, in this study, we aimed to investigate the effect of combining EDP with breathing training on the pulmonary function of patients with COPD.

Methods

Study design

A total of 97 patients with COPD who visited our hospital from January 2021 to January 2023 were selected as the research subjects. Inclusion criteria: (1) Met the relevant diagnostic criteria for COPD as stipulated in the "Guidelines for Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease". (2) Met the indications for EDP. (3) Without malignant tumors or cognitive dysfunction. Exclusion criteria: (1) Had neuromuscular diseases caused by muscle weakness, thoracic deformity or other reasons. (2) Had malignant tumor diseases, malignant pleural effusion or abdominal surgery. (3) Had a history of trauma. (4) Had other respiratory system diseases.

Sample size

Based on the requirements of an α value of 0.05, a β value of 0.2, an efficacy value of 0.8, and a dropout rate of 10%, we determined the sample size to be 100 cases.

Randomization and blinding

Using Stata 17.0 software, a 1:1 random allocation sequence was generated (50 cases in the control group and 50 cases in the observation group), and a block randomization design (block size = 4) was adopted to ensure the balance of baseline characteristics between the two groups. The random sequences were encapsulated in sealed and opaque envelopes (with envelope numbers ranging from ENV-001 to ENV-100), and were managed by statisticians independent of the research implementation. When the patients were enrolled, the research nurse opened the corresponding numbered envelope and carried out the grouping operation according to the sequence instructions. The entire process was conducted in a way that concealed the allocation, avoiding selection bias. A total of 97 cases were successfully completed (48 cases in the control group and 49 cases in the observation group), with 3 cases dropping out (due to the patients' own reasons).

Due to the clear physical characteristics of EDP treatment (such as electrode patch placement, device usage traces, and patient's subjective feelings), evaluators could clearly determine the type of intervention through clinical observation or patient reports, making it impossible to conduct a blinded assessment.

Interventions

Both groups were given basic treatments such as bronchodilators, anti-inflammatory drugs, and expectorants.

The control group received breathing training. During breathing training, patients' blood oxygen saturation and respiratory rate were observed. If cyanosis, dyspnea, severe cough and dyspnea occurred, patients were stop immediately, and received oxygen inhalation and blood oxygen saturation monitoring and other treatment, and breathing training was performed after symptoms subsided or relieved. Specific methods of breathing training:

(1) Abdominal breathing. The patient took a comfortable position and relaxed the whole body, the left hand of patient was put on the chest and the right hand of patient was put on the upper abdomen, and then the patient shut up and took a deep breath slowly through the nose. When inhaling, the abdomen heaved, the right hand of patient was lifted up, and when exhaling, the abdomen collapsed, and the right hand of patient was pressed forward and down to promote the recovery of the diaphragm and exhaled as much as possible. The ratio of inhalation to exhalation was kept 1:2, and the breathing rate was 8 ~ 10 times/min. 10 min each time, 3 ~ 4 times/day.

(2) Lip contraction breathing. The patient relaxed the abdomen, inhaled deeply through the nose, and then shrunk the lips to slowly exhale the gas as "blowing a candle," the ratio of inhalation and exhalation was 1:2, and the breathing rate was 8 ~ 10 times/min, 15 minutes each, 3 ~ 4 times/day.

(3) Holding the breath after deep breathing. The patient took the relaxed position, inhaled slowly and deeply through the nose, and maintained for a few seconds to facilitate the full exchange of gas, so as to promote the re-expansion of the collapsed alveoli, and then slowly exhaled the gas through the mouth or with the contraction of the lips breathing method (blowing out candles). Each training time was 8 ~ 10 min, 3 ~ 4 times/day.

On the basis of breathing training, the observation group was given EPD intervention: alcohol cotton tablet (75%) was used to clean local skin and wait for alcohol volatilizing. During the treatment process, the patient was observed to take a seated/semi-lying position, told to avoid leaning forward, keep the body relaxed, and tilt the head backward. The four electrodes of the pacemaker (EDP-D2, Zhongke Taike (Guangzhou) Electronic Technology Co., Ltd.) were evenly applied with conductive adhesive, and two negative electrodes were affixed to the lower 1/3 position of the left and right edges of the sternocleidomastoid muscle, and two positive electrodes were affixed to the second intercostal space of the midclavicular line to ensure that scars and carotid sinus were avoided. Patients with heart disease are advised to move the large left electrode pad slightly laterally. The pacemaker was fixed with adhesive tape, and the parameters of the pacemaker were adjusted according to the patient's own tolerance and feelings, so as to ensure the stimulation intensity from weak to strong. The pulse frequency was adjusted to 30 ~ 40 Hz according to the patient's own comfort. The pacing frequency was adjusted to 9-12 times/min, 30 minutes/time, and 2 times/day. Diaphragmatic pacing was performed 30 minutes after the end of breathing exercises, and the treatment time was ≥5 days per week for a total of 20 days. If patients experienced adverse reactions such as dizziness, blurred vision, general discomfort, pain in the patch area, and muscle fatigue such as chest tightness and shortness of breath during treatment, the stimulation intensity should be adjusted downward or stopped. Patients were told to rest quietly after treatment.

Primary outcomes

Clinical efficacy: The efficacy was evaluated following the evaluation criteria for the severity of dyspnea in COPD patients in the Guidelines for Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease (2013 Revision). Specifically, the outcomes were categorized as follows: Obvious effect: The severity of dyspnea decreased by 2 or more levels; Effective: The severity of dyspnea decreased

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Table 1 Clinical efficacy in both groups

Groups	Cases	Obvious effect	Effective	Ineffective	Total effective rate (obvious effect rate +effective rate)
Control group	48	25	15	8	40 (83.33%)
Observation group	49	30	17	2	47 (95.92%)
χ^2					5.005
P					0.025

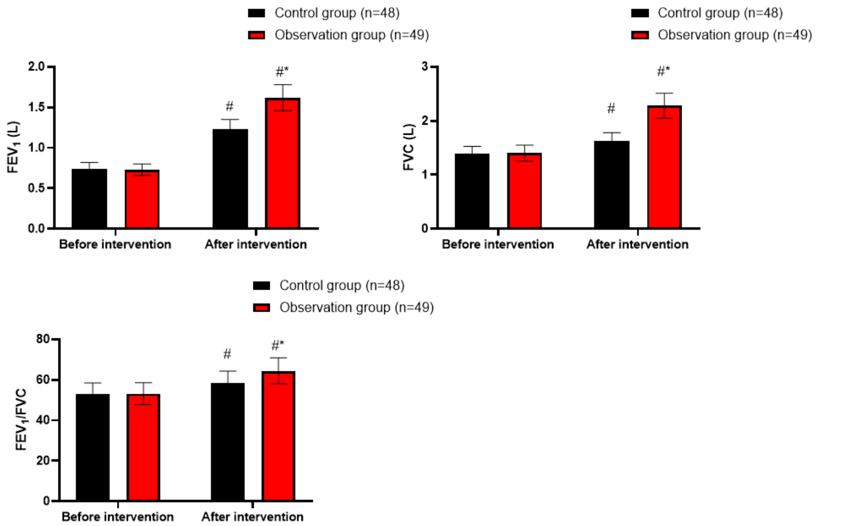

Figure 1 Lung function in both groups. #: Indicates statistically significant difference (P<0.05) compared with baseline (before intervention). *

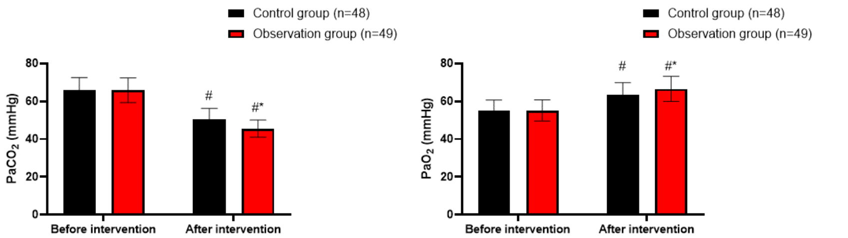

Figure 2 Arterial blood gas index in both groups. #: Indicates statistically significant difference (P<0.05) compared with baseline (before intervention). *:

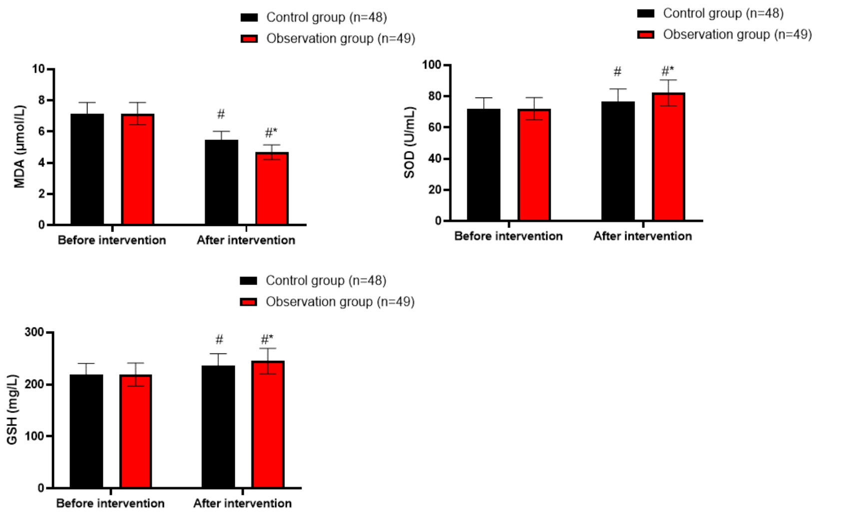

Figure 3 Oxidative stress index in both groups. #: Indicates statistically significant difference (P<0.05) compared with baseline (before intervention). *:

by 1 level; Ineffective: The severity of dyspnea remained unchanged or even worsened. The total effective rate as calculated as the sum of the "obvious effect rate" and the "effective rate".

Lung function: a lung function detector (S-980AI, Sichuan Sikeda Technology Co., Ltd.) was used to assess patient's forced expiratory volume in the first second (FEV1), forced vital capacity (FVC) along with its ratio FEV1/FVC.

Arterial blood gas index: Five mL of the patient's radial artery blood was collected from patients. The partial pressure of carbon dioxide in artery ($PaCO_2$) and partial pressure of oxygen (PaO_2) were measured.

Secondary outcomes

Oxidative stress index: Three mL fasting peripheral venous blood was collected from patients, and the levels of superoxide dismutase (SOD), serum Malonaldehyde (MDA) and Glutathione (GSH) were detected by chemical colorimetry.

The occurrence of adverse reactions during treatment, including dizziness, chest tightness and shortness of breath, and skin redness was recorded and compared between the groups.

(6) The Chronic obstructive pulmonary disease assessment test (CAT) scores of the two groups were compared. CAT included 6 subjective dimensions and 8 daily exercises, and the score ranged from 0 to 40 points. The higher the score, the greater the impact of the disease on the life of the patients, that is, the lower the quality of life.

Statistical analysis

SPSS 20.0 software was adopted for statistical analysis. The Shapiro-Wilk test was employed to assess the normality of all continuous variables. Continuous and categorical variables were presented by mean ± standard deviation and frequencies, respectively. The chi-square tests and t tests were used to test for differences between groups. P<0.05 indicated a statistically significant difference.

Results

General data between the two groups

There were 28 males and 20 females in the control group. The average age was 66.38±6.36 years, ranging from 48 to 78 years. The course of disease ranged from 3 to 14 years, with an average course of 7.29±1.78 years. There were 29 males and 20 females in the observation group. The average age was 66.42±6.43 years, ranging from 50 to 78 years. The course of disease ranged from 3 to 15 years, with an average course of 7.32±1.83 years. No difference was seen in general data between the two groups (P>0.05).

Clinical efficacy in both groups

As shown in Table 1, Compared to the control group, the total effective rate in the observation group was higher (83.33% vs 95.92%) (P=0.025).

Lung function in both groups

As shown in Figure 1, before intervention,

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Table 2 Statistics on adverse reactions

Groups	Cases	dizziness	chest tightness and shortness of breath	skin redness	Total rate
Control group	48	0	2	0	2 (4.17%)
Observation group	49	1	1	2	4 (8.89%)
X^2					0.817
P					0.414

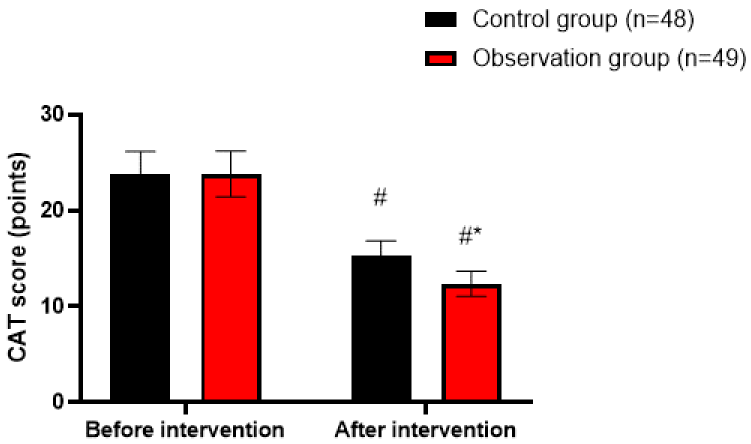

Figure 4 Quality of life in both groups. #: Indicates statistically significant difference (P<0.05) compared with baseline (before intervention). *

there were no significant differences in FEV1, FVC and FEV1/FVC ratio between the two groups (P>0.05). After intervention, FEV1, FVC and FEV1/FVC ratio of both groups were higher than those before intervention (P<0.05). Compared with the control group, FEV1, FVC and FEV1/FVC ratio were higher in the observation group (Cohen's d=2.75, Cohen's d=3.33, Cohen's d=0.97; P<0.05).

Figure 1 Lung function in both groups. #: Indicates statistically significant difference (P<0.05) compared with baseline (before intervention). *: Indicates statistically significant difference (P<0.05) compared with the control group at the same time point.

Arterial blood gas index in both groups

As shown in Figure 2, there were no significant differences in $PaCO_2$ and PaO_2 levels between the two groups before intervention (P>0.05). After intervention, the PaCO2 levels of both groups were lower than those before intervention, while the PaO_2 levels of both groups were higher than those before intervention (P<0.05). Compared with the control group, the observation group had lower $PaCO_2$ level and higher PaO_2 level (Cohen's d=0.96, Cohen's d=0.47; P<0.05).

Figure 2 Arterial blood gas index in both groups. #: Indicates statistically significant difference (P<0.05) compared with baseline (before intervention). *: Indicates statistically significant difference (P<0.05) compared with the control group at the same time point.

Oxidative stress index in both groups

As shown in Figure 3, there were no significant differences in MDA, SOD and GSH levels between the two groups before intervention (P>0.05). After intervention, the MDA levels of both groups were lower than those before intervention, while the SOD and GSH levels of both groups were higher than those before intervention (P<0.05). Compared with the control group, the observation group had lower MDA level and higher SOD and GSH levels (Cohen's d=1.52, Cohen's d=0.66, Cohen's d=0.39; P<0.05).

Figure 3 Oxidative stress index in both groups. #: Indicates statistically significant difference (P<0.05) compared with baseline (before intervention). *: Indicates statistically significant difference (P<0.05) compared with the control group at the same time point.

Adverse reactions in both groups

As shown in Table 2, the total incidence of adverse reactions in the observation group was 8.89% (4/49), and the total incidence of adverse reactions in the control group was 4.17% (2/48). There was no statistical difference in the total incidence of adverse reactions between the two groups (P=0.414).

Quality of life in both groups

As shown in Figure 4, there was no significant difference in CAT score between the two groups before intervention (P>0.05). After intervention, the CAT scores of both groups decreased (P<0.05), and the CAT score of the observation group was lower than that of the control group (Cohen's d=2.05; P<0.05).

Figure 4 Quality of life in both groups. #: Indicates statistically significant difference (P<0.05) compared with baseline (before intervention). *: Indicates statistically significant difference (P<0.05) compared with the control group at the same time point.

Discussion

COPD is a serious chronic respiratory disease characterized by long-term chronic hypoxia[14], which not only affects the lungs but also causes multiple system damage due to prolonged oxygen deprivation[15]. Patients with moderate to severe COPD often face repeated lung infections, declining lung function, poor quality of life, and long hospital stays, imposing significant economic and psychological burdens[16]. Therefore, effectively improving pulmonary function and shortening hospital stays for COPD patients remain key clinical goals.

Breathing training, which involves prolonging expiratory time to increase pressure in the small airway cavity, helps keep airways open, facilitates alveolar air discharge, and improves ventilation and lung function[17]. However, its slow curative effect and difficulty in patient adherence limit its long-term effectiveness. Patients may find it challenging to consistently perform the exercises correctly or may become discouraged by the slow pace of improvement, leading to low compliance rates.

EDP stimulates the phrenic nerve via surface electrodes, promoting regular diaphragmatic contractions[12]. By enhancing diaphragmatic contractility, EDP expands thoracic volume, increases tidal volume, and improves arterial blood gas indices, thereby enhancing pulmonary ventilation[18]. In terms of practical considerations, the cost of the EDP device is an important factor. While the initial investment may be relatively higher compared to some simple breathing

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training aids, the long-term benefits in terms of improved lung function and reduced hospital stays could potentially offset this cost over time. Moreover, as the technology advances and becomes more widespread, the price of EDP devices may decrease, making them more accessible to a larger patient population. Patient compliance is another crucial aspect. EDP offers an advantage in this regard as it is a relatively passive treatment method that does not require patients to actively perform complex exercises. Once the device is properly set up and adjusted, patients can simply receive the electrical stimulation, which may increase their willingness to adhere to the treatment regimen compared to breathing training, which demands consistent self-motivated effort. Ease of use is also a significant consideration. EDP devices are designed to be user-friendly, with clear instructions for operation and adjustment. The surface electrodes are easy to apply and remove, and the overall setup process is straightforward. This simplicity reduces the potential for errors during use and makes it more convenient for patients to incorporate the treatment into their daily routines, whether at home or in a clinical setting.

Our study demonstrated that, compared to the control group, the observation group exhibited significantly higher total effective rates, FEV1, FVC, and FEV1/FVC levels, indicating that EDP combined with breathing training effectively improves lung function in COPD patients. These findings align with previous studies showing that combining aerobic training with EDP significantly enhances physical activity, respiratory function, and diaphragm function in COPD patients[12].

Blood gas analysis, a key indicator of pulmonary ventilation. Our study revealed that after intervention, PaCO2 levels decreased in both groups, with a greater reduction in the observation group. Simultaneously, PaO2 levels increased more in the observation group than in the control group. These results suggest that EDP combined with breathing training improves arterial blood gas in COPD patients, consistent with previous studies[18,19]. This improvement may stem from enhanced respiratory muscle strength and endurance, leading to increased maximum expiratory and inspiratory pressures, deeper breathing, and alleviation of dyspnea[20,21].

Oxidative stress, caused by excessive reactive oxygen species (ROS) production, disrupts the oxidation/antioxidant balance, increases oxidants, and decreases antioxidants[22]. This imbalance leads to lipid peroxidation, reduced antiprotease activity, increased mucus secretion, and damage to airway epithelium and lung tissue, exacerbating COPD[23]. Our study found that after intervention, MDA levels decreased more in the observation group than in the control group, while SOD and GSH levels increased more in the observation group. These results suggest that EDP combined with breathing training better improves oxidative stress in COPD patients compared to breathing training alone. Physiologically, EDP may reduce oxidative stress through several mechanisms. Firstly, by enhancing diaphragmatic contractility and increasing tidal volume, EDP improves alveolar ventilation, reducing areas of atelectasis and ventilation-perfusion mismatch. This optimization of gas exchange helps alleviate local hypoxia within the lung tissue. Hypoxia is a well-known trigger for ROS production, as cells under low oxygen conditions switch to anaerobic metabolism, generating more free radicals[24]. By improving oxygenation, EDP reduces the cellular stress associated with hypoxia, thereby decreasing ROS generation. Secondly, the enhanced respiratory muscle strength and endurance resulting from EDP can lead to more efficient breathing patterns, reducing the work of breathing and minimizing the energy expenditure required for ventilation. This reduction in energy demand may lower the overall metabolic rate of respiratory muscles, subsequently decreasing the production of ROS as a byproduct of cellular metabolism. Finally, improved lung function and ventilation can facilitate the clearance of secretions and pathogens from the airways, reducing the inflammatory response that often accompanies COPD exacerbations. Inflammation is closely linked to oxidative stress, as inflammatory cells release various oxidants as part of their defense mechanisms[25]. By attenuating inflammation, EDP may indirectly reduce the overall oxidative burden in COPD patients. However, further data and experiments are needed to confirm these mechanisms.

Additionally, our study showed that the CAT score decreased more in the observation group than in the control group, indicating that EDP combined with breathing training improves quality of life in COPD patients, consistent with previous studies[26,27]. Similarly, Jiang et al performed a systematic review and meta-analysis to indicate that EDP combined with conventional rehabilitation therapies have better effects on pulmonary function, PaCO2, dyspnea, exercise capacity, and quality of life in COPD patients [13]. This improvement may be attributed to enhanced lung and diaphragm function, which facilitates sputum discharge, improves exercise endurance, prevents acute exacerbations, and ultimately enhances quality of life.

Clinical implications

Our findings highlight the clinical value of combining EDP with breathing training for COPD patients. This approach not only improves lung function and arterial blood gas but also reduces oxidative stress and enhances quality of life. Given its potential benefits, EDP should be integrated into pulmonary rehabilitation programs for COPD patients. Additionally, EDP's adjuvant role in other respiratory conditions suggests broader clinical applications, warranting further exploration.

Limitations

Our experiment still has some shortcomings. Firstly, due to the clear physical characteristics of EDP treatment (such as electrode patch placement, device usage traces, and patient's subjective feelings), evaluators could clearly determine the type of intervention through clinical observation or patient reports, making it impossible to conduct a blinded assessment, which may cause a certain degree of deviation. Secondly, due to the small sample size and the single-center nature of the study, it is recommended to increase the sample size and clarify the sample source in the subsequent stage to further prove the authenticity of the conclusion. Finally, due to the differences in training and treatment methods among different patients and therapists, there is inconsistency in the efficacy, which may affect and interfere with our conclusion. Therefore, larger-scale and multi-center further studies need to be conducted.

Conclusion

EDP combined with breathing training demonstrates superior efficacy in improving lung function and quality of life in COPD patients compared to breathing training alone.

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Ethical statement

This study was approved by the medical committee of the No .215 Hospital of Shaanxi Nuclear Industry, and the approval number was SX2021-0087L.

Acknowledgments

None.

Conflicts of Interest

None.

Author's contributions

Jie Li concepted the study and performed data analysis, Xu Fan and Yafei Liu wrote the initial manuscript and collected data, Yu Guo revised the manuscript and drew figures, Qiang Dong managed data, supervised the study, and was responsible for the conduction of the whole project.

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Availability of data and materials

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

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