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Original Article

Extracorporeal membrane oxygenation (ECMO) for acute exacerbations of chronic obstructive pulmonary disease: care modalities, experience, and precautions

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Abstract: Purpose: The aim of this study was to summarize the care modalities, experiences, and corresponding precautions of ECMO for acute exacerbations of chronic obstructive pulmonary disease (COPD). Methods: Seventy-three patients with acute exacerbations of COPD were enrolled, of whom 38 were treated with ECMO (experimental group) and 35 received conventional low-flow oxygen therapy, management of metabolic acidosis, infection control, bronchodilators for quick relief from severe spasms, and glucocorticoid-mediated suppression of inflammation (control group). The improvement in the patient's pulmonary ventilation and the incidence of complications were recorded. Results: $PaCO_2$ is lower in patients using ECMO, FEV1, FEV1/FVC, and FEV1% are significantly higher in the experimental group than in the control group, and the respiratory rate, heart rate, and CO_2 saturation are significantly lower in patients in the experimental group (i.e., the experimental group) after oxygenation than in the control group, pH and O_2 saturation are significantly higher in experimental group than in the control group, and the incidence of complications in experimental group is significantly higher than in the control group. Conclusion: ECMO significantly improves gas exchange in patients, but also increases the incidence of complications with the extension of usage, so the duration of ECMO support should be monitored and the complications should be prevented.

Keywords: Extracorporeal membrane pulmonary oxygenation, COPD, acute episodes

Introduction

Chronic obstructive pulmonary disease (COPD) is a very common chronic respiratory disease and a global public health concern [1]. Smoking is the leading cause of COPD and is also a trigger for COPD flare-ups. Patients with COPD have to overcome greater resistance to exhalation than inhalation in order to expel the gas, so in the long run the patient's respiratory muscles become fatigued, and the alveoli may also develop into pulmonary bullae which could rupture during severe shock such as coughing, forming a pneumothorax, which is one of the complications of COPD [2]. The clinical symptoms of patients with stable COPD are asthma, dyspnea, and chronic cough, which can lead to acute difficulty in breathing when certain triggers are present, namely, an acute exacerbation [3]. The most common trigger is infection. Currently, COPD is the 4th leading cause of death in the United States [4]. Mortality due to COPD has been projected to rise to 4.5 million deaths in 2020 worldwide. The high mortality rate of COPD is associated with acute exacerbations during which patients' respiratory muscles fail and they have lost the ability to breathe independently and their condition is very critical. Most patients eventually die from asphyxia or systemic infection [5], so noninvasive ventilators or mechanical ventilation are essential for COPD, and ventilators can assist patients to inhale, thus allowing patients' already fatigued respiratory muscles to regain strength and help them recover [6].

ECMO has been increasingly used in clinical practice in recent years, especially during the Covid-19 pandemic. ECMO functions as the respiratory and circulatory systems [7]. When the patient's heart stops beating, ECMO can act as a "pump" to allow blood to flow back into the

Table 1. Comparison of baseline conditions of trial participants at baseline

	Experimental group		Control group	
Total number of patients*	38		35	
Gender*	Male 20	Female 18	Male 18	Female 17
Average age*	78.23 ± 6		76.59 ± 8	
Average duration* (years)	7.56 ± 1.23		7.77 ± 0.12	

Note: *indicates that there is no significant difference between the two groups, $P > 0.05$.

Table 2. Comparison of $PaCO_2$ in the experimental and control groups after treatment

	Total number	$PaCO_2$ ($\bar{x}$ ± SD, mm Hg)	
		Pre-treatment	Post-treatment
Experimental group	38	94.11 ± 10.23	42.35 ± 9.77
Control group	35	95.21 ± 9.85	65.33 ± 10.02
P		> 0.05	< 0.05

body and maintain tissue perfusion pressure, and when the patient is close to respiratory failure, ECMO maintains blood oxygenation and cardiac function [8]. Therefore, it's the equivalent of an artificial heart and lung, leaving a buffer time for clinicians and patients [9]. ECMO also plays an important role in acute exacerbations of COPD, so the purpose of this study was to describe the use of ECMO in relation to COPD episodes.

Materials and methods

General information

Inclusion criteria: (1) Patients diagnosed with COPD. (2) Patients' consent was obtained and they signed the informed consent form. (3) Patients > 65 years old. Exclusion Criteria: (1) Patients with poor treatment compliance. (2) Patients with a history of ACS, acute cerebrovascular events, and mental disorders. (3) Patients who had high fluid intake. A total of 73 patients with acute exacerbations of COPD from February 2019 to the end of July 2020 were enrolled and randomized into two groups, an experimental group and a control group using an Excel function, in which 38 patients were treated with ECMO and 35 patients were treated with low-flow oxygenation therapy, correction of acidosis, antibiotics to control infection, bronchodilators to relieve spasm, and glucocorticoids. These elderly patients were accompanied by a variety of chronic diseases, including diabetes, hypertension, and chronic renal failure. This study has been approved by the Ethics Committee of The First People's Hospital of Wenling.

Methods

As the most common cause of acute exacerbation of COPD is infection, as such routine anti-infection treatment is needed in addition to basic nutritional support, correction of electrolyte disturbance, and anti-deep vein thrombosis, etc. The experimental group was intermittently treated with ECMO on basis of the treatments in the control group. All patients' vital signs were closely monitored and respiratory parameters were adjusted in case of any problems.

Statistical analysis

Statistical data were processed using SPSS and expressed as mean ± standard deviation ($\bar{x}$ ± SD). Microsoft Excel was used to record the data. If the difference within the groups (≥ 3 groups) was compared by the one-factor analysis of variance (ANOVA), while t-test was used for comparison between two groups. Prism Graph software was used to draw the graphs. $P < 0.05$ indicates a significant difference.

Results

Comparison of differences in baseline data between the two groups of patients

Differences in baseline data such as gender, mean age, and mean length of hospital stay between the two groups were not significant ($P > 0.05$) and were comparable (**Table 1**).

$PaCO_2$ is lower in patients using ECMO

There was no significant difference in CO_2 saturation between the two groups before treatment ($P > 0.05$), and after treatment, the blood CO_2 saturation of patients in the experimental group was significantly lower than that of the control group ($P < 0.05$), indicating that ECMO can improve the ventilation of patients with acute exacerbations of COPD and facilitate carbon dioxide excretion (**Table 2**).

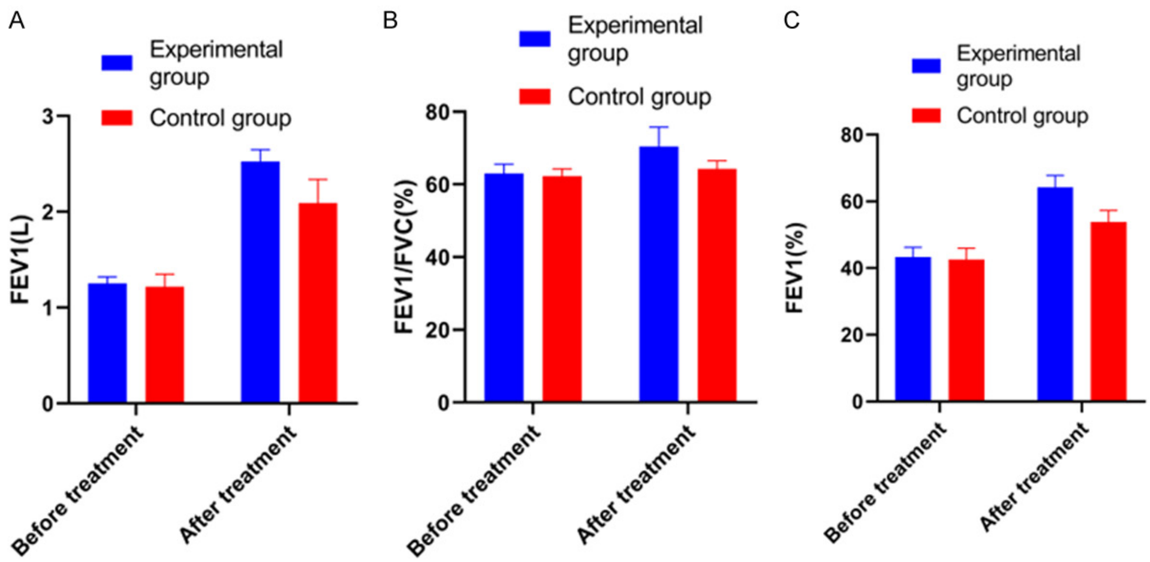

Figure 1. Comparison of FEV1, FEV1/FVC, and FEV1% before and after treatment. After treatment, the FEV1, FEV1/FVC, and FEV1% of patients in the experimental group were significantly higher than those in the control group ($P < 0.05$).

FEV1, FEV1/FVC, and FEV1% were significantly higher in the experimental group than in the control group

There was no significant difference in FEV1, FEV1/FVC, and FEV1% between the two groups before treatment ($P > 0.05$); those indicators were significantly higher in the experimental group than in the control group following treatment ($P < 0.05$) (**Figure 1**).

Comparison of respiratory indexed between the two groups

The respiratory rate, heart rate, and CO_2 saturation were significantly lower while the pH and O_2 saturation were significantly higher in the experimental group than in the control group ($P < 0.05$). After intervention, the condition of patients in both groups improved, as evidenced by a decrease in respiratory rate, heart rate, and CO_2 saturation, and an increase in pH and O_2 saturation. However, the improvement was more pronounced in patients using ECMO ($P < 0.05$) (**Figure 2**).

The odds of complications were higher in the experimental group than in the control group

The experimental group had a higher incidence rate of complications than the control group ($P < 0.05$) (**Figure 3**).

Faster and greater improvement in pulmonary ventilation with ECMO treatment

PEF, TLC, and FEV1 did not differ significantly between the two groups before treatment ($P > 0.05$), and they were higher at 1, 3, 5, 7, 10, and 15 days after treatment in the experimental group than in the control group, indicating that ECMO could improve the ventilation function of the lung. Further observation revealed that the ventilation function improved significantly faster in the experimental group than in the control group ($P < 0.05$), and finally, on day 15 after the intervention, the post-oxygenation PEF, TLC, and FEV1 were all significantly higher in the experimental group than in the control group, respectively ($P < 0.05$) (**Figure 4**).

Discussion

COPD has become one of the most common chronic diseases in the world, affecting a large population. The disease is characterized by shortness of breath, wheezing, cough, fatigue, phlegm production, and chronic respiratory infections during the stable phase, and should be treated systematically [10]. However, in the acute stages, the patient will experience a critical situation in which respiratory rate, heart rate, and CO_2 saturation rise sharply and pH and O_2 saturation fall rapidly. The treatment option at this stage should be rapid and effi-

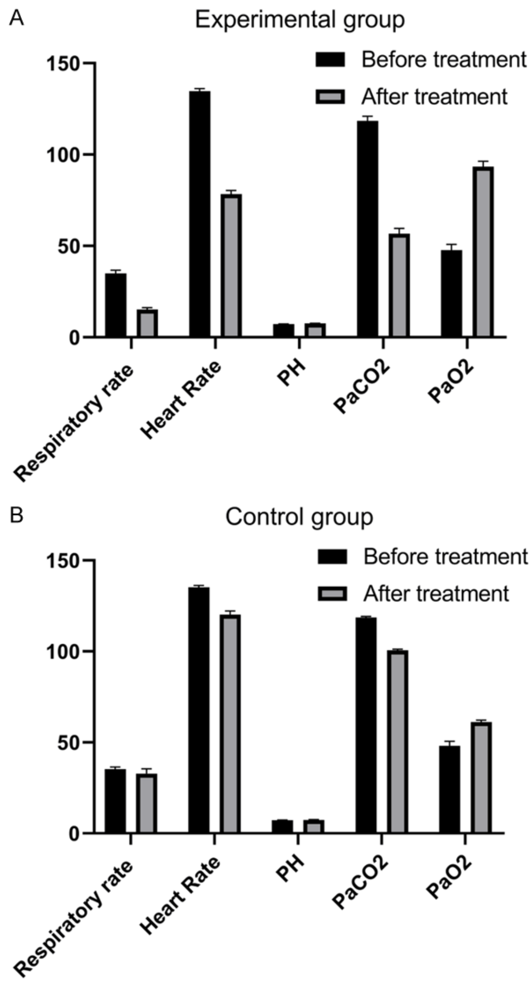

Figure 2. Comparison of values of respiratory rate, heart rate, pH, $PaCO_2$, and PaO_2 between experimental and control groups after intervention.

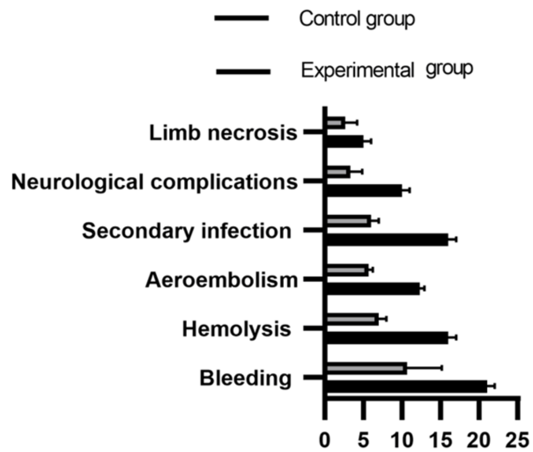

Figure 3. Comparison of the incidence of complications in the experimental and control groups.

cient [11]. When CO_2 saturation and O_2 saturation reach a critical point, it can be defined as respiratory failure, where the respiratory muscles have lost most of their ability to contract and can only be temporarily assisted by an external machine in breathing, thus giving the inspiratory muscles sufficient time to rest [12]. The rapid increase in respiratory rate and heart rate is actually a protective mechanism, increasing inspiratory reserve volume and cardiac ejection, thereby maintaining the perfusion pressure [13]. Moreover, an increase in respiratory rate further aggravates the fatigue of the respiratory muscles and accelerates the pace of respiratory failure and an increased heart rate also consume more myocardial oxygen, promoting hypoxia [14]. The pH indicated acidosis brought on by hypoxia, when aggravated, can make the patient suffer from microcirculatory disorders and in severe cases even confusion and life-threatening events [15].

When this occurs, we immediately give low-flow oxygen, bronchodilators, anti-infection, glucocorticoid, and Ambroxol apart from nutritional support to correct the acid-base balance [16]. However, sometimes many patients fail to recover, at which point a ventilator is necessary to improve ventilation [17]. Ventilators are divided into invasive and non-invasive types, with ECMO belonging to the invasive one, which can greatly improve the patient's ventilatory function, as shown by the faster and greater improvement in lung ventilation parameters in patients treated with ECMO. However, all invasive ventilators, including ECMO, have side effects, such as airway injury, bleeding, hemolysis, secondary infection, neurological complications, limb necrosis , aeroembolism, patient intolerance, and aspiration [18]. This study demonstrated that the incidence of complications associated with ECMO were higher than those of the control group. Thus, ECMO brings rapid improvement in ventilatory function and can also causes injuries, such as nasal bleeding [19]. Secondly, patients who still maintain a rapid respiratory rate while in acute episodes are in a hypoxic brain state, so high-flow oxygenation will result in the removal of the hypoxic stimulation, which will likely result in paralysis of the respiratory center of the brain, respiratory arrest and life-threatening events.

In fact, ECMO is not yet widely used in China, and many hospitals do not have this device due to its expensive price and high incidence of

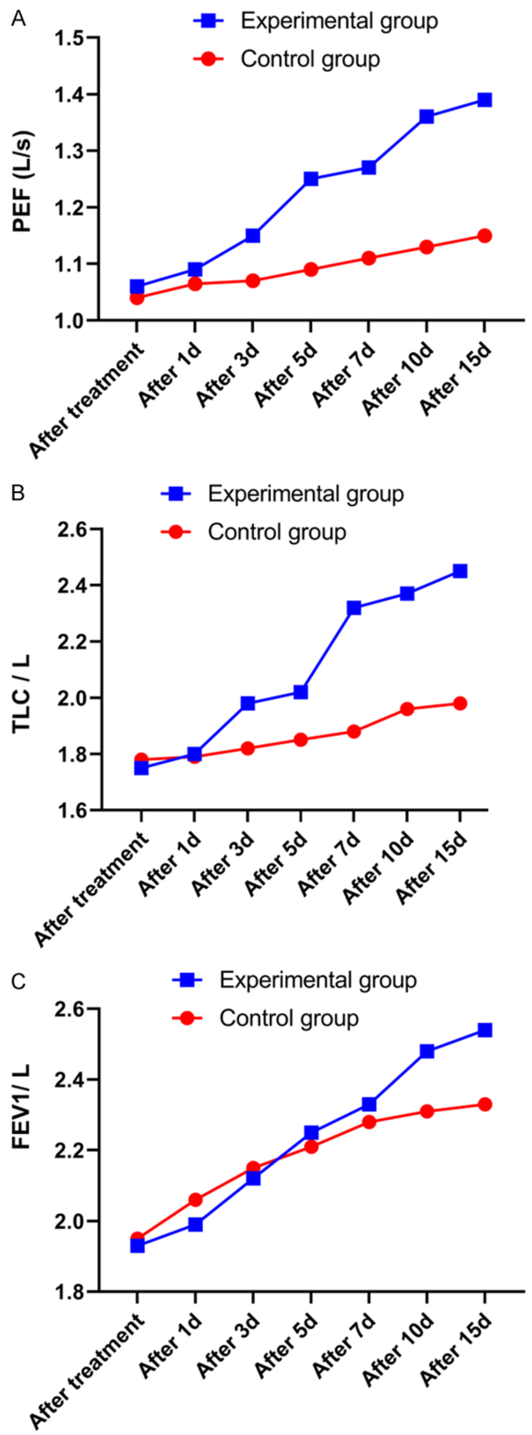

Figure 4. Trends and magnitudes of maximum respiratory flow (PEF), total lung volume (TLC), and maximum volume of first second expiratory volume (FEV1) over time in experimental and control groups after oxygenation.

complications [20]. It is currently used in conditions such as respiratory failure, cardiac surgery, and lung transplantation, and the mortality rate increases dramatically as the duration of use increases [21]. However, ECMO is still the last straw for patients, it has a wide range of applications, and the specific details related to its usage need to be further explored [22].

Disclosure of conflict of interest

None.

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