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Original Article

Comparison of efficacy between sequential ventilation and conventional invasive mechanical ventilation in the treatment of pulmonary hypertension complicated with respiratory failure

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Abstract: Objective: Pulmonary hypertension (PAH) is a serious progressive and fatal pulmonary disease characterized by elevated pulmonary artery pressure. Mechanical sequential ventilation has been gradually applied in the treatment of patients with PAH complicated with RF, which can effectively reduce the incidence of VAP and better promote the recovery of respiratory function. This study is aimed to determine the efficacy of sequential ventilation and conventional invasive mechanical ventilation in the treatment of pulmonary hypertension (PAH) complicated with respiratory failure (RF). Methods: A total of 198 patients with both PAH and RF admitted to our hospital were enrolled. Among them, 102 patients were treated with sequential ventilation as a study group (stu group), and 96 patients were treated with conventional invasive mechanical ventilation as a control group (con group). Then the two groups were compared in efficacy and related indexes before and after treatment. Results: The stu group experienced significantly shorter invasive ventilation time, total mechanical ventilation time, and hospitalization time than the con group (all P<0.05), and showed a significantly lower complication rate than the con group (P<0.05). The reintubation rate, weaning failure rate, and ventilator-associated pneumonia (VAP) rate of the stu group were all significantly lower than those of the con group (all P<0.05), and the stu group showed significantly higher pondus hydrogenii (pH) and arterial partial pressure of oxygen (PaO_2) and significantly lower arterial carbondioxide partial pressure ($PaCO_2$) than the con group after treatment (all P<0.05). Additionally, after treatment, the level of brain natriuretic peptide (BNP) and pulmonary artery pressure in both groups declined significantly (P<0.05), and the decline of them in the stu group was more significant than that in the con group (P<0.05). Moreover, after treatment, endothelin (ET) and angiotensin II (Ang II) in both groups declined significantly, and the decline of them in the stu group was also more significant than that in the con group (P<0.05). Conclusion: Compared with conventional invasive mechanical ventilation, sequential ventilation can effectively minimize the treatment time of patients with PAH complicated with RF, reduce the incidences of adverse events and complications in them, and significantly improve the blood gas analysis indexes and BNP in them, so it is worthy of clinical promotion.

Keywords: Sequential ventilation, conventional invasive mechanical ventilation, pulmonary hypertension, respiratory failure, brain natriuretic peptide

Introduction

Pulmonary hypertension (PAH) is a serious progressive and fatal pulmonary disease characterized by elevated pulmonary artery pressure [1]. It is featured by poor remodeling of small pulmonary artery, which results in increased pulmonary vascular resistance [2]. PAH may be idiopathic (IPAH) or familial, induced by drugs and toxins, and may also be related to many diseases including connective tissue disease (CTD), congenital heart disease (CHD), portal hypertension or schistosomiasis [3, 4]. The most common PAH includes IPAH (82.35%), and CTD-induced PAH (71.31%), and CHD-related PAH (60.26%) [5]. Patients with PAH usually suf-

fer from respiratory failure (RF), fatigue, and syncope meantime. The increase of right ventricular after load will increase the high risk of right ventricular failure and premature death [6]. Patients with PAH have impaired lung ventilation function, which will lead to hypoxia, and then give rise to RF [7].

Currently, PAH complicated with RF is mainly treated by mechanical ventilation, which establish an artificial airway for patients to control their lung infection to the maximum extent and relieve respiratory muscle fatigue, thus effectively improving their respiratory and pulmonary functions [8]. Conventional invasive mechanical ventilation can quickly restore the smooth of respiratory duct in patients with PAH complicated with RF, reduce the retention of CO_2 in the lungs, and thus effectively alleviate clinical symptoms [9]. However, it is traumatic to patients, and it is difficult to tolerate due to long ventilation time, which easily brings about complications such as ventilator-associated pneumonia (VAP) and airway injury, resulting in unsatisfactory clinical efficacy [10]. As science and technology advance, mechanical sequential ventilation has been gradually applied in the treatment of patients with PAH complicated with RF, which can effectively reduce the incidence of VAP and better promote the recovery of respiratory function [11].

This study mainly determined the changes of BNP and pulmonary artery pressure of patients in two groups treated with different mechanical ventilation therapies to determine the efficacy of sequential ventilation and conventional invasive mechanical ventilation in treating PAH complicated with RF, with the goal of providing a theoretical basis for clinical treatment of PAH complicated with RF.

Materials and methods

General data

A total of 198 patients with both PAH and RF admitted to our hospital were enrolled. Among them, 102 patients were treated with sequential ventilation as a study group (stu group), and 96 patients were treated with conventional invasive mechanical ventilation as a control group (con group). The stu group consisted of 68 males and 34 females, with an average age of (52.89±6.43) years, while the con group consisted of 62 males and 34 females, with an average age of (53.02±6.57) years.

The inclusion criteria of the study: Patients accompanied by family members at admission, patients with detailed clinicopathologic data, patients meeting the diagnostic criteria for PAH issued on the World Symposium on Pulmonary Hypertension [12], patients diagnosed as RF according to related examination of blood gas analysis (arterial partial pressure of oxygen (PaO_2≤60 mmHg) and arterial carbondioxide partial pressure ($PaCO_2$≥50 mmHg). The exclusion criteria of the study: Patients with a history of mental disease or a family history of psychosis, patients with a history of autoimmune system deficiency or severe organ diseases, patients with pulmonary infection, patients with a history of drug dependence, and those who were unable to cooperate with examination due to aphasia, dysphoria, unconsciousness, or communication obstacle. This study was approved by the Ethics Committee of our hospital, and all patients and their families provided written informed consent after they we informed of the study.

Methods

Patients in the two groups were given routine treatment including anti-inflammation, phlegm dispelling, water-electrolyte balance adjustment, and acid-base balance adjustment, nutritional support, and infected patients among them were treated with routine antibiotics. Patients in the con group were given conventional invasive mechanical ventilation as follows: After tracheotomy, each patient was connected with a ventilator (Jmmedical Equipment Co., Ltd., Shanghai, China) to assist his/her breathing. The ventilator was adjusted to the synchronized intermittent mandatory ventilation (SIMV) mode, and its parameters were set as follows: Tidal volume of 6-12 mL/kg, oxygen concentration of 30%-100%, and respiratory rate of 12-20 beats/min. The SIMV respiratory rate was adjusted in time according to the patient's specific condition. The ventilator was weaned, and the trachea cannula was withdrawn when the patient was able to breathe spontaneously and his/her symptoms were relieved, with oxygenation index (PaO_2/inspired oxygen (FiO_2)>150 mmHg. Patients in the stu group were given sequential ventilation as fol-

Table 1. Comparison of general clinical data between the two groups ($\bar{x} \pm s$)/[n (%)]

	The study group (n=102)	The control group (n=96)	t/χ^2	*P*-value
Age (Y)	52.89±6.43	53.02±6.57	0.14	0.89
Body mass index (kg/m^2)	22.14±1.34	22.35±1.42	1.07	0.29
Sex			0.10	0.76
Male	68 (66.67)	62 (64.58)		
Female	34 (33.33)	34 (35.42)		
Smoking history			0.35	0.55
Yes	72 (70.59)	64 (66.67)		
No	30 (29.41)	32 (33.33)		
Drinking history			0.11	0.74
Yes	64 (62.75)	58 (60.42)		
No	38 (37.25)	38 (39.58)		
APACHE II score	21.47±2.48	20.89±3.04	1.48	0.14

Note: APACHE II: Acute Physiology and Chronic Health Evaluation II.

lows: Each patient was connected with a ventilator through orotracheal intubation under the guidance of laryngoscope. The ventilator was set as the volume control mode, and its parameters were set as follows: respiratory rate of 12-20 beats/min, and oxygen concentration of 30%-100%, and tidal volume of 6-12 mL/kg. The blood gas indexes of the patient were determined. The mode of the ventilator was adjusted to SIMV and pressure support mode according to the determination results, and the respiratory rate was adjusted according to the specific condition of the patient. In addition, the trachea cannula in the patient was withdrawn when his/her respiratory function improved, and then bi-level positive pressure ventilation with a mask was adopted to treat the patient. The parameters were gradually adjusted according to the patient's specific condition. The ventilator was weaned when the patient was able to breathe spontaneously and his/her PaO_2/FiO_2 was within 200-300 mmHg.

Outcome measures

The treatment time, complications, and adverse events including weaning failure, reintubation and VAP of the two groups were recorded. At 1 day before treatment and 1 day after treatment, arterial and venous blood was sampled from each patient in the two groups, and the arterial blood gas analysis indexes (pondus hydrogenii (pH), PaO_2 and $PaCO_2$), brain natriuretic peptide (BNP), pulmonary artery pressure, endothelin (ET) and angiotensin II (Ang II) of patients in the two groups were determined and compared.

Statistical analyses

All statistical analysis of the experimental results was carried out using SPSS20.0 (IBM Corp, Armonk, NY, USA), and all graphical results were drawn by GraPAHPad Prism 7 (Graphpad Software Co., Ltd., San Diego, CA, USA). Enumeration data were expressed as [n (%)] and compared between groups by the chi-square test. Measurement data were expressed as the ($\bar{x} \pm$ sd), and compared between groups using the t test. P<0.05 suggests a significant difference.

Results

Comparison of general data

General data including age, body mass index, smoking history, and drinking history of the two groups were collected, and summarized in **Table 1**. No notable difference was seen in general data between the two groups (all P>0.05).

Comparison of treatment time between the two groups

Comparison of treatment time between the stu group and the con group showed that the former group experienced significantly shorter invasive ventilation time, total mechanical ventilation time, and hospitalization time than the latter group (all P<0.05) **Figure 1**.

Comparison of complication rate between the two groups

Comparison of complication rate between the stu group and the con group showed that the complication rate of the former group was significantly lower than that of the latter group (17.65% vs. 30.21%, P<0.05), and complications in the stu group were more self-relieving symptoms such as dry nose and mouth and facial pain **Table 2**.

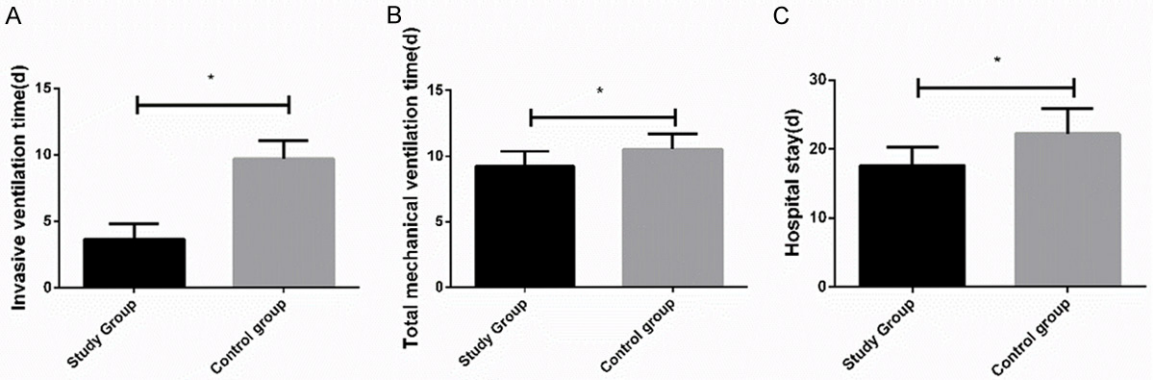

Figure 1. Comparison of treatment time between the two groups. A. The invasive ventilation time consumed by the study group was significantly shorter than that consumed by the control group. B. The total mechanical ventilation time consumed by the study group was significantly shorter than that consumed by the control group. C. The hospitalization time consumed by the study group was significantly shorter than that consumed by the control group. * indicates that in comparison between the two groups, P<0.05.

Table 2. Comparison of complication rate between the two groups [n (%)]

	Dry nose and mouth	Facial pain	Respiratory tract infection	Pneumothorax	Patient-ventilator asynchrony	Incidence of complications (%)
The study group (n=102)	6 (5.88)	8 (7.84)	2 (1.96)	0 (0.00)	2 (1.96)	18 (17.65)
The control group (n=96)	0 (0.00)	0 (0.00)	14 (14.58)	5 (5.21)	10 (10.42)	29 (30.21)
χ^2	-	-	-	-	-	4.31
P	-	-	-	-	-	0.04

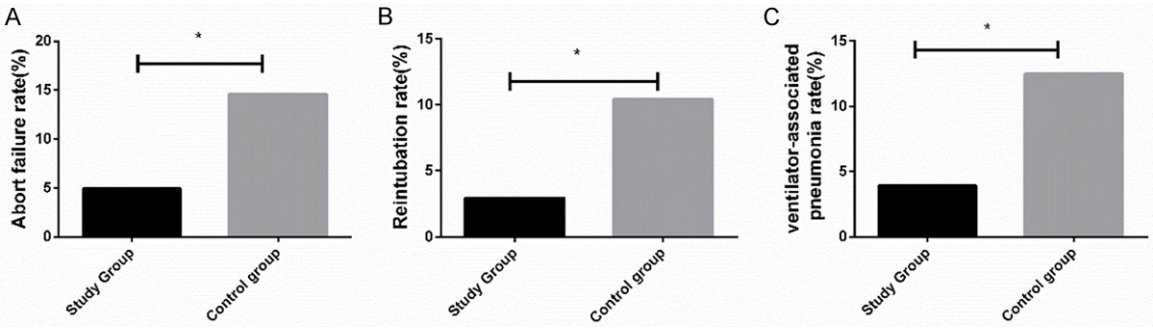

Figure 2. Comparison of the incidence of adverse events between the two groups. A. The weaning failure rate of the study group was significantly lower than that of the control group. B. The reintubation rate of the study group was significantly lower than that of the control group. C. The VAP rate of the study group was significantly lower than that of the control group. * indicates that in comparison of the two groups, P<0.05.

Incidence of adverse events in the two groups

Comparison of the two groups in the incidence of adverse events showed that the weaning failure rate, reintubation rate, and VAP rate of the stu group were all significantly lower than those of the con group (all P<0.05) **Figure 2**.

Comparison of blood gas analysis indexes between the two groups before and after treatment

Comparison of the two groups in terms of blood gas analysis indexes before and after treatment showed that before treatment, there was no significant difference between them in blood gas analysis indexes (all P>0.05), while after treatment, the stu group showed significantly higher pH and PaO_2 and significantly lower $PaCO_2$ than the con group (all P<0.05) **Figure 3**.

Comparison of BNP between the two groups before and after treatment

Comparison of BNP between the two groups before and after treatment showed that before treatment, there was no significant difference

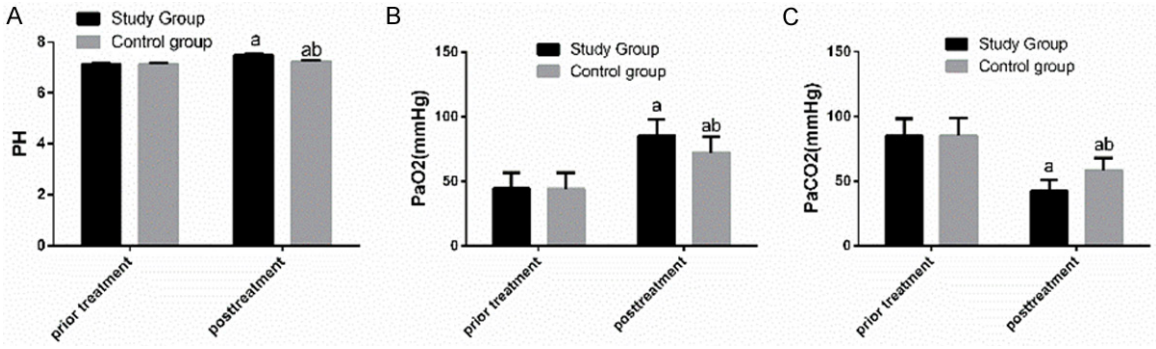

Figure 3. Comparison of blood gas analysis indexes between the two groups before and after treatment. A. Before treatment, there was no notable difference between the two groups in pH, while after treatment, pH of the study group was significantly higher than that of the control group. B. Before treatment, there was no notable difference between the two groups in PaO_2, while after treatment, $PaO_2$of the study group was significantly higher than that of the control group. C. Before treatment, there was no notable difference between the two groups in $PaCO_2$, while after treatment, $PaCO_2$ of the study group was significantly lower than that of the control group. a indicates that in comparison of the same group before and after treatment, $^aP<0.05$. b indicates that in comparison with the study group after treatment, $^bP<0.05$.

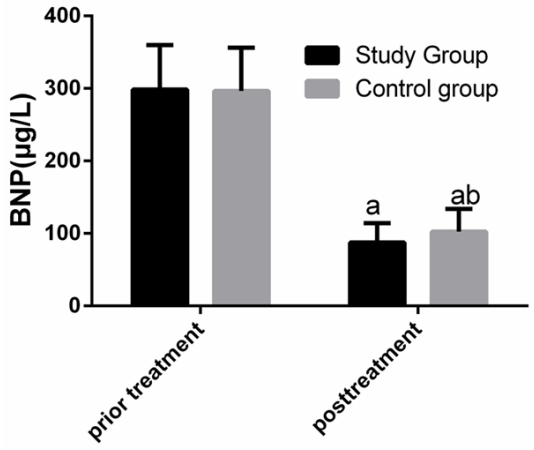

Figure 4. Comparison of BNP between the two groups before and after treatment. Before treatment, there was no significant difference between the two groups in BNP, while after treatment, BNP in both groups decreased significantly, and BNP in the study group was significantly lower than that in the control group. a indicates that in comparison of the same group before and after treatment, $^aP<0.05$. b indicates that in comparison with the study group after treatment, $^bP<0.05$.

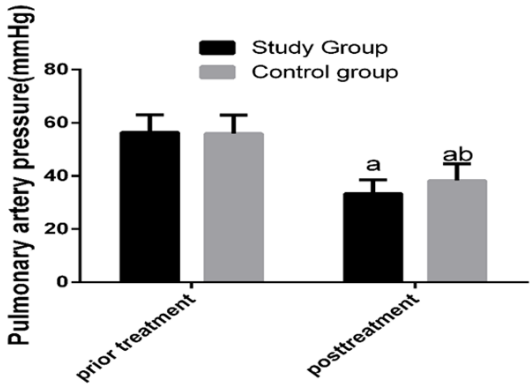

Figure 5. Comparison of pulmonary artery pressure between the two groups before and after treatment. Before treatment, there was no significant difference between the two groups in pulmonary artery pressure, while after treatment, pulmonary artery pressure in both groups decreased significantly, and pulmonary artery pressure in the study group was significantly lower than that in the control group. a indicates that in comparison of the same group before and after treatment, $^aP<0.05$. b indicates that in comparison with the study group after treatment, $^bP<0.05$.

between the two groups in BNP (P>0.05), while after therapy, BNP in both groups decreased significantly (both P<0.05), and the decrease in the stu group was more significant than that in the con group (P<0.05) **Figure 4**.

Comparison of pulmonary artery pressure between the two groups before and after treatment

Comparison of the two groups in pulmonary artery pressure before and after treatment showed that before treatment, there was no significant difference between the two groups in pulmonary artery pressure (P>0.05), while after treatment, pulmonary artery pressure in both groups decreased significantly (both P< 0.05), and the decrease in the stu group was more significant than that in the con group (P<0.05) **Figure 5**.

Comparison of ET and Ang II between the two groups before and after treatment

Comparison of ET and Ang II between the two groups before and after treatment showed that

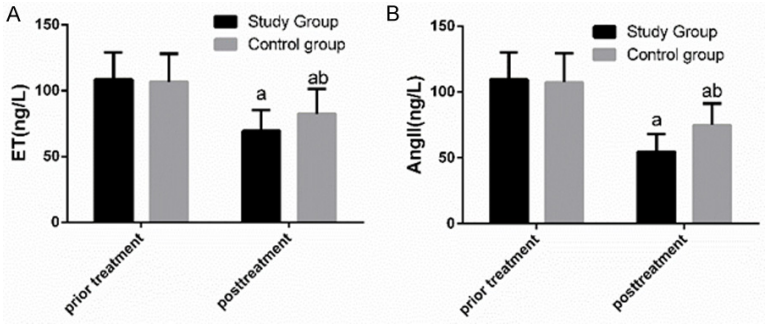

Figure 6. Comparison of ET and Ang II between the two groups before and after treatment. A. Before treatment, there was no notable difference between the two groups in ET, while after treatment, ET of both groups decreased significantly, and ET of the study group was significantly lower than that of the control group. B. Before treatment, there was no notable difference between the two groups in Ang II, while after treatment, Ang II of both groups decreased significantly, and Ang II of the study group was significantly lower than that of the control group. a indicates that in comparison of the same group before and after treatment, $^{a}P<0.05$. b indicates that in comparison with the study group after treatment, $^{b}P<0.05$.

before treatment, there was no significant difference between the two groups in ET and Ang II ($P>0.05$), while after treatment, ET and Ang II in both groups decreased significantly (both $P<0.05$), and the decrease in the stu group was more significant than that in the con group ($P<0.05$) See **Figure 6**.

Discussion

PAH is a disease syndrome featured by elevated pulmonary artery pressure and pulmonary vascular remodeling. It is not a single disease, but a syndrome involving various acute and chronic diseases due to different origins and causes, which have the common feature of average pulmonary artery pressure above 20-25 mmHg [13]. The 3-year survival rate of patients with PAH is less than 60% [14], and women are more likely to suffer from the disease, but the survival rate of women is higher than that of men [15]. According to one study, there were 384 patients hospitalized for PAH in France in 2013, and there were 1271 patients suffering from PAH-related diseases, which implies that although PAH is rare, it accounts for a high economic burden [16]. Clinically, patients with PAH usually suffer from RF [17]. Currently, PAH complicated with RF is usually treated by mechanical ventilation, so this study was designed to determine the efficacy of sequential ventilation and conventional invasive mechanical ventilation in treating PAH complicated with RF.

In this study, the invasive ventilation time, total mechanical ventilation time, and hospitalization time of the stu group were significantly shorter than those of the con group. There is also one study indicating that for ICU patients, rapid examination and relatively short mechanical ventilation time and ventilation time in hospital are all related to the improvement of prognosis [18]. These results imply that compared with conventional invasive mechanical ven-tilation, sequential ventilation can shorten treatment time, relieve the patient's disease more effectively and quickly, and improve their prognosis. In this study, complications of the two groups were detected. It came out that the complication rate of the stu group was significantly lower than that of the con group (17.65% *vs*. 30.21%), and complications in the stu group were more self-relieving symptoms such as dry nose and mouth and facial pain. One study has concluded that VAP is a main complication of mechanical ventilation [19]. In this study, the incidence of VAP in the stu group was significantly lower than that in the con group, and the weaning failure and reintubation rates of the stu group were also significantly lower than those of the con group. Therefore, it can be inferred that compared with conventional invasive mechanical ventilation, sequential ventilation is more effective in reducing the incidences of complications and adverse events in the treatment of PAH complicated with RF, indicating that sequential ventilation causes less stimulation to patients with PAH complicated with RF and contributes to faster recovery of them. We compared the blood gas analysis indexes between the two groups, and found that after treatment, pH and PaO_2 of the stu group were significantly higher than those of the con group, and $PaCO_2$ of the stu group was significantly lower than that of the con group. One study has pointed out that arterial blood gas analysis is an crucial examination method for emergency patients and a means to evaluate human respiratory function and acid-base balance, which can directly reflect lung

ventilation function and acid-base balance [20, 21]. Thus, it can be inferred that sequential ventilation is more effective in improving patients' respiratory function and homoiostasis in the treatment of PAH complicated with RF. As a crucial part in cardiovascular endocrinology, BNP plays a pivotal role in regulating human blood pressure, body fluid balance, and cardiovascular function [22]. It is mainly synthesized and secreted by right ventricular myocyte, and ventricular wall tension and pressure load can stimulate the synthesis and secretion of it [23]. In addition, BNP can be synthesized and secreted instantaneously [24]. Therefore, we adopted pulmonary artery pressure and BNP to judge the efficacy of different mechanical ventilation therapies in treating PAH complicated with RF. In the study, before treatment, there was no notable difference in BNP and pulmonary artery pressure between the two groups, while after treatment, the two indexes of both groups decreased significantly, indicating that both mechanical ventilation therapies can effectively treat patients with PAH complicated with RF. In addition, the decrease of BNP and pulmonary artery pressure in the stu group was more notable than that in the con group after treatment, implying that sequential ventilation can effectively treat patients with the diseases. Moreover, in our study, there was no notable difference between the two groups in ET and Ang II before treatment, while the two indexes in both groups decreased significantly after treatment. Some studies have pointed out that the increase of ET and Ang II can give rise to pulmonary artery vasoconstriction, and thereby lead to continuous increase of pulmonary artery pressure [25, 26]. It can be concluded that both mechanical ventilation therapies can effectively improve ET and Ang II in patients with PAH complicated with RF. The decrease of ET and Ang II in the stu group was more significant than that in the con group, suggesting that sequential ventilation can effectively patients with PAH complicated with RF.

This study mainly determined the changes of blood gas analysis indexes, BNP, and pulmonary artery pressure of patients treated with sequential ventilation and those treated with conventional invasive mechanical ventilation to explore the efficacy of the two ventilation therapies in the treatment of PAH complicated with RF, so as to provide a theoretical basis for clinical treatment of PAH complicated with RF. However, this study has some limitations, because it has not continued to follow up patients. In the future study, the research content will be continuously improved to provide a more scientific reference for clinical treatment, so as to further improve the prognosis of patients.

To sum up, compared with conventional invasive mechanical ventilation, sequential ventilation can effectively shorten the treatment time of patients with PAH complicated with RF, reduce the incidences of adverse events and complications in them, and significantly improve their blood gas analysis indexes and BNP, so it is worthy of clinical promotion.

Disclosure of conflict of interest

None.

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