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Original Article

High-flow nasal cannula oxygen therapy is superior to conventional oxygen therapy in intensive care unit patients after extubation

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Abstract: Background: Optimal oxygen supply is the cornerstone of the management of critically ill patients after extubation. High flow oxygen system is an alternative to standard oxygen therapy. This research explored the efficacy of high-flow nasal cannula (HFNC) oxygen therapy in patients after extubation in the intensive care unit (ICU). Method: We retrospectively analyzed critically ill patients admitted to the ICU and subjected to HFNC or conventional oxygen therapy from January 2018 to June 2022 at the Suzhou Hospital of Integrated Traditional Chinese and Western Medicine. Blood gas analysis, a cough and sputum assessment, and cardiovascular function examinations were performed to evaluate the effect of HFNC oxygen therapy on patients. Also, the 28-d mortality rate, reintubation rate and incidence of respiratory failure were analyzed to evaluate whether HFNC oxygen therapy could improve patients' outcome. Results: In patients who received HFNC oxygen therapy, the partial pressure of oxygen and oxygenation index increased, and the respiratory rate decreased. HFNC oxygen therapy improved the patients' ability to cough up sputum and promoted the expulsion of sputum. In terms of cardiovascular function, patients who received HFNC oxygen therapy had a significant improvement in heart rate, but there was no real effect on patients' arterial pressure. There was no significant difference in the rates of reintubation ($P = 0.202$), 28-d mortality ($P = 0.558$) or respiratory failure ($P = 0.677$) between patients who received different oxygen therapies including HFNC oxygen therapy. Conclusion: HFNC oxygen therapy improves the respiratory function of patients after extubation in their ICU and improves their coughing ability.

Keywords: High-flow nasal cannula oxygen therapy, intensive care unit, respiratory failure, reintubation

Introduction

Approximately 40% of patients in the intensive care unit (ICU) with acute or chronic respiratory failure require mechanical ventilation, and this non-physiologic form of positive pressure ventilation prolongs the patients' stay in the ICU even though it is a "life-sustaining treatment" [1]. These patients often need to continue transitional oxygen therapy after extubation, and some of these patients may become more ill and require reintubation [2].

Oxygen therapy is the first step for the prevention and treatment of hypoxemic respiratory failure and has conventionally been delivered using nasal cannula and regular or Venturi masks [3]. These typically accommodate flow rates of around 15 L/min (although Venturi masks can provide total gas flow > 60 L/min) and therefore have limited ability to meet the inspiratory demands of patients [4]. In addition, the effective inspiratory oxygen concentration depends on the respiratory flow and breathing pattern of individual patient, which makes it difficult to estimate in advance [5]. Conventional high-flow systems, such as Venturi masks, can provide a constant flow of O_2 through precisely sized ports and a more constant fraction of inspired oxygen (FiO_2) via steady entrainment of room air [6]. However, these systems are less well tolerated than a nasal cannula because of the obtrusiveness of the masks and insufficient heating and humidification of the inspired gas.

Also, at high inspiratory flow rates, entrained room air dilutes the oxygen and lowers FiO_2 [7]. Therefore, further technological development is warranted.

High-flow nasal cannula (HFNC) oxygen therapy, using an air/oxygen blender, active humidifier, single heated tube and nasal cannula, is able to deliver heated and humidified gas at flows equal to 60 L/min [8]. Since the first HFNC system, Fisher & Paykel Optiflow system, was put into commercial production in 2006, it has been widely used in the treatment of adult dyspnea and hypoxemia and has achieved good outcomes after the evolution from Pari Hydrate in 2007 to Vapor in 2008 [9]. Recently, its clinical indications have been expanded to post-extubated patients in ICU or following surgery, during bronchoscopy, immunocompromised patients, and patients with "do not intubate" status [10]. Nevertheless, it is unclear whether HFNC oxygen therapy provides significant physiological superiority over conventional oxygen therapy in the setting of ICU after extubation. The purpose of this retrospective analysis is to compare the respiratory function, cardiovascular function, and outcome in ICU patients after extubation who underwent HFNC or conventional oxygen therapy.

Materials and methods

Patients

This is a retrospective analysis of clinical data of 147 ICU patients admitted to Suzhou Hospital of Integrated Traditional Chinese and Western Medicine from January 2018 to June 2022. Among the 147 patients, 75 patients underwent HFNC oxygen therapy (observation group) and 72 patients underwent conventional oxygen therapy (control group). During the treatment, the patients' physiological indicators were closely monitored, and the patients were treated and observed according to normal diagnostic, nursing and treatment procedures.

Inclusion criteria: (1) critically ill patients who were admitted to the ICU at Suzhou Hospital of Integrated Traditional Chinese and Western Medicine, (2) patients with age over 18 years old, (3) patients who passed the Spontaneous Breathing Trial (SBT) and were extubated according to the standard procedures of Suzhou Hospital of Integrated Traditional Chinese and Western Medicine, and (4) patients who were free of lung surgery and lung disease. Exclusion criteria: (1) patients under the age of 18, (2) patients with urgent tracheal intubation such as respiratory and cardiac arrest immediately after extubation, (3) patients with multiple organ failure, tissue damage and other diseases that seriously endangered their lives, (4) patients with preoperative respiratory diseases and failed SBT, (5) patients with contraindications to HFNC or non-invasive positive pressure ventilation, and (6) patients with impaired consciousness, hemodynamic instability (mean arterial pressure < 60 mmHg), or exacerbations.

The Ethics Committee of Suzhou Hospital of Integrated Traditional Chinese and Western Medicine approved the study, and informed consent was waived due to the retrospective nature of the analyses.

Treatment procedures

Patients in the observation group were given HFNC oxygen therapy immediately after extubation, while patients in the control group were given oxygen through a regular nasal cannula, Venturi mask, or non-invasive ventilator, depending on their condition after extubation. The room temperature and the humidity for patients in both groups were controlled at 18-24°C and 60%-70%, respectively. The observation group received HFNC oxygen therapy through a warmed humidified nasal cannula with an initial flow rate of 20-50 L/min, oxygen concentration of 20-50%, and gas temperature of 37°C. The parameters were adjusted according to the patients' symptoms and the changes in physiological indexes during the treatment.

During the treatment, if the level of consciousness decreased, or acute weakening or disappearance of spontaneous respiration was detected, the ventilator or high-flow parameters were adjusted according to the patient's conditions. The patient was immediately intubated if the oxygenation index did not rebound but decreased and the partial pressure of carbon dioxide ($PaCO_2$) increased after the adjustment.

During the treatment after extubation, respiratory failure was defined as when one of the following symptoms presented: respiratory acidosis (PH < 7.35, $PaCO_2$ > 45 mmHg); saturation

Table 1. Baseline data of patients

Variable	Observation group	Control group	*t* value	*p* value
Age (years)	70±14	69±16	0.270	0.788
Sex (female/male)	32/43	34/38	/	0.621
Mechanical ventilation time	10.48±3.23	9.85±3.48	1.138	0.257
Diabetes mellitus	19	24	/	0.365
Brain diseases	17	20	/	0.569
Heart disease	33	29	/	0.739
Chronic kidney disease	10	11	/	0.816
Other diseases	13	8	/	0.349

of peripheral oxygen (SpO_2) less than 90% or partial pressure of oxygen in arterial blood (PaO_2) less than 60 mmHg at a FiO_2 higher than 40%; respiratory rate (RR) more than 30 breaths/min; decreased level of consciousness according to the Glasgow Coma Scale (decrease > 1 point).

Observation indicators

Prior to the treatment, the following clinical characteristics were collected: age, body temperature, comorbidities, reason for hospitalization and duration of mechanical ventilation (**Table 1**). During the treatment, we analyzed the main indicators such as blood gas analysis, difficulty of coughing up sputum, occurrence of respiratory failure and reintubation rate. Secondary indicators such as patient comfort, length of hospital stay, and 28-day mortality were also included.

In detail, blood gas analysis was performed before extubation and after 1, 6, or 24 h of treatment. Oxygenation index (OI), PaO_2, $PaCO_2$, RR, mean arterial pressure (MAP) and heart rate (HR) were recorded for each patient. Meanwhile, during the treatment period, the difficulty of coughing up sputum, sputum consistency, and patient comfort were recorded. The criteria for scoring the difficulty of coughing up sputum were as follows. Sputum was easy to cough up with thin and foamy sputum (1 point); sticky sputum could be coughed up on its own (2 points); sputum was coughed up after forceful or repeated coughing (3 points); sputum could be coughed up only after nebulized inhalation (4 points). Sputum viscosity score: sputum was foamy and dilute (1 point); sputum was thicker in the throat than the front (2 points); viscous yellow phlegm (3 points). Comfort was evaluated based on a Visual Numerical Scale, with score between 1 (extremely uncomfortable) and 5 (very comfortable) [11]. In addition, during the patients' treatment, the length of stay in the ICU, the occurrence of respiratory failure, the reintubation rate, and the 28-d mortality were recorded.

Statistical analysis

GraphPad Prism 9.2 software (GraphPad, San Diego, CA, USA) was applied to draw the statistical charts. Data on age, complications, reintubation rate and 28-d mortality were expressed as counts in both groups (n), and Fisher's exact test was used to compare the differences between the two groups. Measurement data such as blood gas analysis and comfort were expressed as mean ± standard deviation and compared utilizing Student's t-test. Significance was set at a *p* value of < 0.05.

Results

Baseline characteristics

A total of 147 ICU patients who underwent mechanical ventilation and met the criteria for extubation were included, and the subjects were grouped into an observation group with the HFNC oxygen therapy (n = 75) and a control group with conventional oxygen therapy (n = 72) according to the different interventional oxygenation measures after extubation. According to **Table 1**, there was no significant difference in the mean mechanical ventilation time and the primary diseases between the two groups. In addition, blood gas analysis before treatment showed no significant differences in HR, MAP, RR, PaO_2, $PaCO_2$ or OI between the two groups (**Table 2**).

Respiratory parameters

Patients in the observation group were given HFNC oxygen therapy, while the control group was given conventional oxygen therapy, and respiratory-related indexes were evaluated. There was no statistical difference between the two groups in terms of $PaCO_2$ after treatment

Table 2. Variations in blood gas analysis of patients who underwent HFNC and conventional oxygen therapy

Variable	Observation group	Control group	t value	*p* value
Heart rate (beats/min)	104.87±8.38	102.51±11.46	1.429	0.155
MAP (mmHg)	91.74±5.36	90.29±4.82	1.722	0.087
Respiratory rate (beats/min)	25.43±4.75	24.18±3.87	1.745	0.083
Body temperature (°C)	36.7±0.5	36.6±0.6	1.1	0.273
PaO_2 (mmHg)	76.87±9.35	79.14±8.19	1.563	0.120
$PaCO_2$ (mmHg)	38.67±3.27	39.54±4.87	1.276	0.204
OI	205.48±42.36	207.57±53.86	0.2621	0.794

Note: HFNC, High-Flow Nasal Cannula; PaO_2, Partial pressure of Oxygen in arterial blood; $PaCO_2$, Partial pressure of Carbon dioxide; OI, Oxygenation Index; MAP, Mean Arterial Pressure.

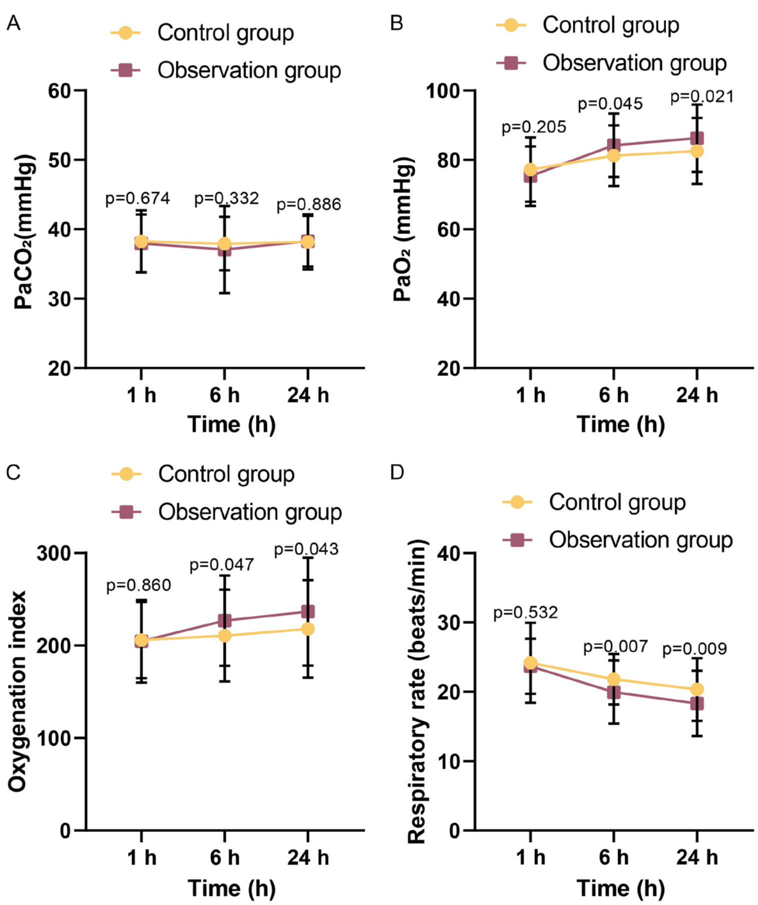

Figure 1. Changes in respiratory indexes in the patients. A. $PaCO_2$ levels after 1 h, 6 h, and 24 h of treatment. B. PaO_2 levels after 1 h, 6 h, and 24 h of treatment. C. Oxygenation index after 1 h, 6 h, and 24 h of treatment. D. Respiratory rate after 1 h, 6 h, and 24 h of treatment. Data are presented as mean ± SD and compared by unpaired *t* test. PaO_2, Partial pressure of Oxygen in arterial blood; $PaCO_2$, Partial pressure of Carbon dioxide.

(**Figure 1A**). It was noted that the patients in the observation group displayed a significant increase in PaO_2 and OI after 6 h and 24 h of HFNC oxygen therapy (**Figure 1B**, **1C**). In addition, we found that the degree of RR reduction in the observation group after 6 h and 24 h of HFNC oxygen therapy was significantly greater than that of the control group (**Figure 1D**). This indicates that HFNC oxygen therapy can alleviate the respiratory disorders of patients to a certain extent.

Difficulty of coughing up sputum, sputum viscosity, and comfort of the patients

The difficulty of coughing up sputum and sputum viscosity were analyzed during the treatment, and there was no significant difference in the difficulty in these measures between the two groups after 1 h of treatment. After 6 h and 24 h of treatment, the observation group had reduced difficulty of coughing up sputum and sputum viscosity (**Figure 2A**, **2B**), showing dilution and expulsion of sputum. In terms of the comfort score, HFNC oxygen therapy did not have an alleviating effect on patients' comfort at 1 h. However, after 6 h and 24 h of treatment, there was a significant improvement in patients' comfort in the observation group (**Figure 2C**).

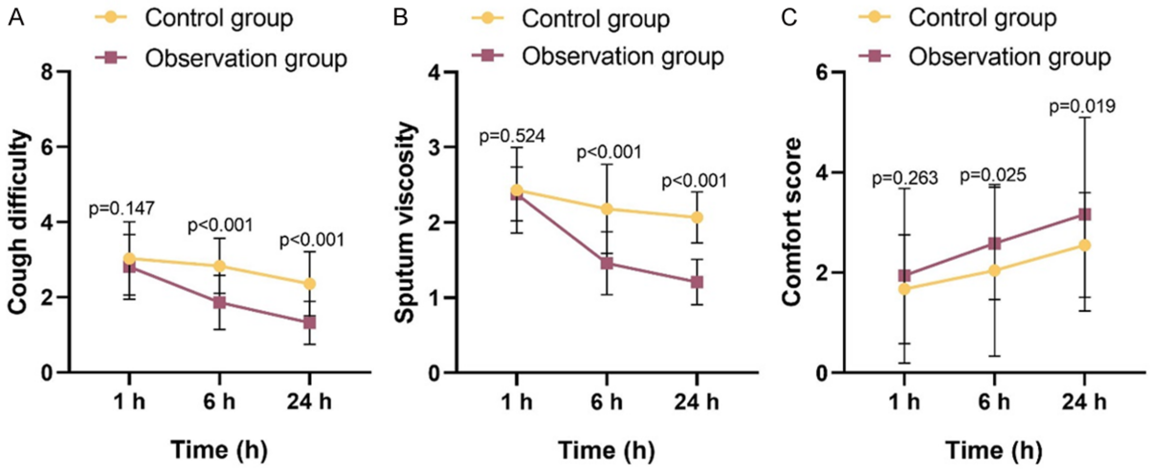

Figure 2. Comparison of coughing difficulty, sputum viscosity, and subjective comfort between the two groups. A. Cough difficulty scores of patients after 1 h, 6 h, and 24 h of treatment. B. Sputum viscosity of patients after 1 h, 6 h, and 24 h of treatment. C. Comfort score of patients after 1 h, 6 h, and 24 h of treatment. Data are presented as mean ± SD and compared by unpaired *t* test.

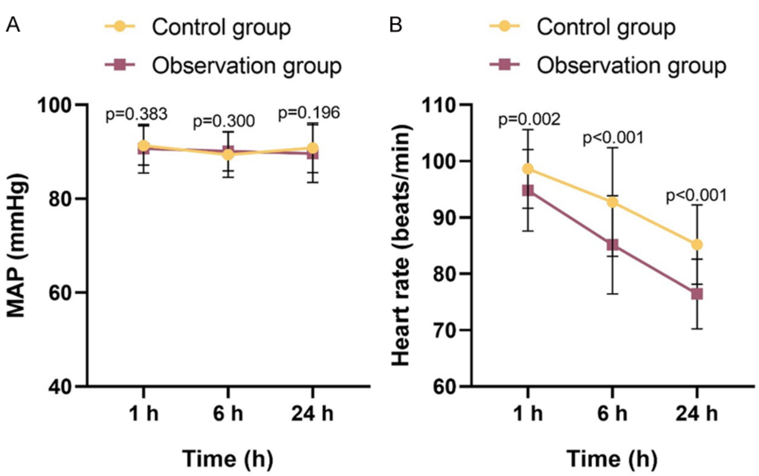

Figure 3. Comparison of cardiovascular function between the two groups. A. The changes in MAP of patients after 1 h, 6 h, and 24 h of treatment. B. The changes of heart rate of patients after 1 h, 6 h, and 24 h of treatment. Data were presented as mean ± SD and compared by unpaired *t* test. MAP, Mean Arterial Pressure.

Table 3. Clinical prognosis of two groups

Variable	Observation group	Control group	t value	*p* value
Respiratory failure	8 (10.67%)	15 (20.83%)	/	0.677
ICU stay	12.84±3.24	13.17±3.45	0.598	0.551
Reintubation rates	6 (8.00%)	11 (15.28%)	/	0.202
28-d mortality	5 (6.67%)	7 (9.72%)	/	0.558

Note: ICU, Intensive Care Unit.

Cardiovascular function

There was no significant difference in MAP between the two groups during the treatment period (**Figure 3A**). Regarding HR, the observation group revealed a significantly greater reduction in the HR than the control group did (**Figure 3B**).

Outcome of patients

In terms of patient clinical prognostic outcomes, we found a significant reduction in the incidence of respiratory failure in the observation group. The reintubation rate in the observation group was lower than that in the control group, although the difference was insignificant. The data also showed that there was no significant difference between the two groups in terms of 28-d morbidity and total ICU stay (**Table 3**).

Discussion

The selection of an appropriate respiratory support device after extubation can improve the clinical outcome of patients [12]. The main findings of our study can be summarized as follows: in post-extubated patients in the ICU, HFNC oxygen therapy was associated with better respiratory function and comfort, and lower reintubation rate relative to the conventional oxygen therapies.

We found that patients in the observation group had a significant higher PaO_2 and OI, and lower RR levels after 6 h and 24 h of HFNC oxygen therapy, indicating alleviated respiratory function in these patients. These results are largely consistent with the results of previously reported clinical trials [13, 14]. The above effects of HFNC oxygen therapy are closely related to its principle of work, which can be summarized in the following three aspects. First, the main physiologic impact of HFNC therapy is a decrease in the work of breathing [15, 16]. Second, prolonged and continuous provision of normal airway pressure can trigger a positive end-expiratory effect [17]. Third, the effectiveness of the wetting effect improves patients' tolerability. Hoffman *et al.* found that the active warming of the gas delivered to the patient not only promoted the frequency of ciliary movement on the mucosal surface of the patient's respiratory tract, but also facilitated the clearance of respiratory secretions and reduced the probability of secondary pulmonary atelectasis [18]. Therefore, we concluded that the improved effects of HFNC oxygen therapy on the respiratory function were associated with this working principle.

Furthermore, we observed that the patients in the observation group showed greater ease in coughing up sputum and reduced sputum viscosity. Similarly, HFNC oxygen therapy had lower sputum viscosity at 48 h after extubation than non-invasive positive pressure ventilation [19]. Since the ciliary motility is reduced when the temperature of inhaled gas is below 34°C [11], the warmed gas in HFNC oxygen therapy can facilitate the dilution and discharge of sputum. In addition, after 6 h and 24 h of HFNC oxygen therapy, the comfort score of the patients was markedly elevated compared to that of patients with the conventional therapy. Tiruvoipati *et al.* reported that for patients after a stabilization period of 30 min after extubation, the tolerance of HFNC oxygen therapy was significantly better than that of high-flow face mask [20]. According to a meta-analysis and a review, HFNC oxygen therapy has better comfort and tolerance than noninvasive positive pressure ventilation and conventional oxygen therapies [21, 22]. These findings indicate that HFNC oxygen therapy can provide better comfort to patients compared to the conventional oxygen therapies.

This study also showed that compared to the control group (15.28%), the observation group had a lower rate of re-intubation (8.00%). There is also evidence showing that compared to the conventional oxygen therapy, HFNC oxygen therapy reduced the rate of intubation, mechanical ventilation, and further respiratory support [23]. However, the use of HFNC oxygen therapy in the transition after extubation of preterm infants has been reported to show different conclusions. In a review by Wilkinson *et al.*, they summarized that HFNC oxygen therapy was not effective in reducing reintubation rates in preterm infants compared to non-invasive respiratory support, and that the reintubation rates were even higher after HFNC oxygen therapy [24]. The effectiveness of HFNC oxygen therapy in reducing secondary intubation is, therefore, debatable, and more studies with large samples are needed. Moreover, reintubation after failed extubation is associated with ICU patient mortality (up to 50%), incidence of hospital-acquired pneumonia (approximately 30%), delayed ICU stay, and mechanical ventilation [25]. These patients are more difficult to care for and often require a longer recovery time. Even though published data presented an association of HFNC oxygen therapy with shorter length of stay in ICU and total length of hospitalization in patients with severe COVID-19 [26], our study did not find a significant difference in 28-d mortality and ICU stay between the two groups. This paradoxical finding might be caused by the relatively small number of our cohort, which represents a limitation of our study.

HFNC oxygen therapy is a more effective and superior alternative to conventional oxygen therapy as further post-extubation oxygen therapy. HFNC oxygen therapy can effectively improve patients' OI and comfort. However, the effectiveness of HFNC oxygen therapy in preventing reintubation and reducing ICU stay in extubated patients still needs to be further elucidated.

Disclosure of conflict of interest

None.

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