Prospective Clinical Research Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
2023, Vol. 51(6) 1–8

DOI: 10.1177/03000605231182558
journals.sagepub.com/home/imr
Sage

Effects of high-flow nasal cannula oxygen therapy for patients with acute exacerbation of chronic obstructive pulmonary disease in combination with type II respiratory failure

Aiming Liu, Yaqing Zhou and Zunguo Pu

Abstract

Objective: To evaluate the therapeutic effects of high-flow nasal cannula (HFNC) oxygen therapy in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and type II respiratory failure.

Methods: Seventy-two patients with AECOPD and type II respiratory failure were randomly allocated to an HFNC oxygen therapy trial group or a non-invasive positive-pressure ventilator therapy (NIPPV) control group. Their arterial blood gas parameters and comfort, evaluated using a questionnaire, were compared before and after the therapeutic interventions.

Results: The $PaCO_2$ and blood HCO_3^- concentration of both groups were significantly reduced by the treatments, whereas the pH, PaO_2 and PaO_2/FiO_2 were increased. The $PaCO_2$ of the experimental group was significantly lower than that of the control group following treatment. The PaO_2 of the experimental group was significantly higher than that of the control group. The tracheal intubation rates of the two groups did not significantly differ. After treatment, all the indices of comfort were rated higher in the HFNC group than in the NIPPV group.

Conclusions: HFNC has a good therapeutic effect in patients with AECOPD and type II respiratory failure. It improves patient comfort and has clinical value.

Department of Critical Care Medicine, Affiliated Hai'an Hospital of Nantong University, Hai'an County, Nantong City, Jiangsu Province, 226600, China

Corresponding author:
Yaqing Zhou, Department of Critical Care Medicine, Affiliated Hai'an Hospital of Nantong University, No. 17, Zhongba Middle Road, Hai'an County, Nantong City, Jiangsu Province 226600, China.
Email: sysxzs@163.com

Keywords
Acute exacerbation, chronic obstructive pulmonary disease, high-flow nasal cannula oxygen therapy, patient comfort, therapeutic effect, type II respiratory failure

Date received: 13 February 2023; accepted: 30 May 2023

Introduction

Chronic obstructive pulmonary disease (COPD) is currently the most common chronic respiratory disease and has become a significant public health issue because of its high prevalence and the associated disability, morbidity, and mortality. It is characterized by airflow limitation with persistent and progressive dyspnea and is often accompanied by chronic coughing and chest tightness.[1–2] Acute exacerbations of COPD (AECOPD) are more common in middle-aged and older patients, often occur in combination with type II respiratory failure, and are characterized by weak coughing, concomitant infection, and poor lung function, which have negative effects on patient health, and increase the risks of hospitalization, readmission and disease progression. As AECOPD worsens, CO_2 retention and hypercapnic respiratory failure may occur.[3–4] Therefore, the treatment of AECOPD in combination with type II respiratory failure requires treatment by mechanical ventilation and rational oxygen therapy, according to the physiological and pathological characteristics of the patient.

Patients with AECOPD in combination with type II respiratory failure are often treated using non-invasive positive-pressure ventilation (NIPPV), which is relatively non-invasive and significantly improves oxygenation.[5–6] However, NIPPV can cause respiratory discomfort, owing to compressive skin damage and gas-related drying associated with the mask. In addition, a large amount of mask leakage may occur in some patients because of poor fit associated with certain facial shapes, necessitating an escalation of respiratory support if patients have unrelieved symptoms of hypoxia and CO_2 retention.

High-flow nasal cannula (HFNC) oxygen therapy is a novel non-invasive respiratory support technique that provides patients with warm, humidified oxygen at a high flow rate through a thick nasal catheter. This method is associated with high levels of comfort and tolerance, and this mode of respiratory support has been widely used globally in recent years.[7–8] However, the advantages of HFNC therapy for patients with AECOPD have not been fully elucidated. Therefore, in the present study, we evaluated the clinical efficacy and patient comfort levels associated with the use of HFNC therapy in patients with AECOPD in combination with type II respiratory failure, to provide a theoretical basis for the clinical use of this therapy.

Patients and Methods

General information

Patients with AECOPD and type II respiratory failure who were admitted to the intensive care unit of Hai'an People's Hospital between January 2018 and May 2021 were selected for the study. Using a random number table, they were allocated to experimental and control groups. The experimental group was treated with HFNC oxygen therapy, while the control group was treated with NIPPV.

We included patients who met the diagnostic criteria for AECOPD (updated 2017),[9]

had Global Initiative for Chronic Obstructive Lung Disease stage I–III, were >45 years old, had an arterial partial pressure of oxygen (PaO_2) <60 mmHg (or oxygenation index <300 mmHg under oxygenation) and had an arterial partial pressure of carbon dioxide ($PaCO_2$) >50 mmHg.

We excluded patients with the following conditions: cardiac or respiratory arrest requiring emergency tracheal intubation with invasive mechanical ventilation; coma; ventilatory dysfunction; very severe type I respiratory failure (oxygenation index <60); hemodynamic instability; altered mental status or inability to cooperate; predisposition toward aspiration of foreign material; dense, voluminous secretions; craniofacial trauma or burns; fixed nasal foreign body; and recent facial or gastro-esophageal surgery.

Treatments

The control group was treated with NIPPV using a bilevel positive airway pressure ventilation model. The initial inspiratory positive airway pressure was 8 to 10 cmH_2O and that of expiratory positive airway pressure was 4 to 6 cmH_2O. The inhaled oxygen concentration was maintained at 30%–50%. Continuous oxygen inhalation for >16 h was administered daily. These parameters were adjusted according to the participants' vital signs and blood gas data, which were closely monitored, and if their condition worsened, more invasive positive-pressure ventilation was performed.

The experimental group was treated by transnasal high-flow humidified oxygen therapy using an Optiflow transnasal high-flow humidified oxygen therapy system (Fisher-Paykel, Auckland, New Zealand), with parameters of 30% to 50% inhaled oxygen concentration, a flow rate of 40 to 60 L/min, a temperature of 37°C and a relative humidity of 100%. The parameters were also adjusted according to the participants' blood gas analysis data and vital signs, and more invasive positive-pressure ventilation treatment was performed in those who deteriorated.

Measurements made

Arterial blood was collected from participants on an empty stomach before and after treatment to measure pH, $PaCO_2$, PaO_2, oxygenation index (PaO_2/FiO_2) and HCO_3^- concentration using a GEM3500 Automatic Blood Gas Analyzer (Werfen, Bedford, MA, USA). Finally, the number of intubated participants was recorded.

Evaluation of patient comfort

Patient comfort was assessed using the Pulmonary Function Status and Dyspnea Questionnaire (PFSDQ),[10] which was completed once before treatment and once 3 months following treatment. The questionnaire included three domains: change in daily activity (CA), dyspnea (DA), and experience (EA), with scores of 0 to 10 for each domain. The participants awarded the scores, with 0 being the least severe, with little change in daily activities and no shortness of breath, fatigue, or discomfort, and 10 being the most severe, with particularly severe breathing problems, shortness of breath, fatigue during daily activities, and extreme discomfort during treatment.

Ethics

The study was approved by the Medical Ethics Committee of Hai'an People's Hospital on June 1, 2018 (approval number: HKL201839). The patients or their guardians provided their written informed consent. The reporting of this study conforms to the CONSORT guidelines.[11]

Statistical methods

SPSS v. 19.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis.

Student's *t*-test and the rank-sum test were used to analyze continuous data, and the chi-square test was used to analyze categorical data. Statistical significance was set at $P < 0.05$. We did not perform a sample size calculation.

Results

Participant characteristics

Seventy-two patients were studied, with n = 36 per group. The general characteristics of the participants in both groups are shown in Table 1. The two groups did not differ significantly in terms of sex, age, duration of disease, or the prevalences of underlying conditions ($P > 0.05$).

Table 1. Comparison of the general characteristics of the two groups.

	HFNC Group	NIPPV group
Number of participants	36	36
Sex (male/female)	20/16	22/14
Age (years)	69.4 (65–74)	69.8 (63–73)
Duration of disease (years)	10.7 ± 2.4	10.8 ± 2.7

Data are mean ± SD or median (interquartile range).
HFNC, high-flow nasal cannula; non-invasive positive-pressure ventilator.

Comparisons of the blood gas data and intubation rates before and after treatment

The blood gas indices before and after treatment of the two groups are shown in Table 2. The blood gas analysis showed no statistically significant differences in the pH, $PaCO_2$, PaO_2, PaO_2/FiO_2, or HCO_3^- concentration of the two groups before treatment. After treatment, the blood pH increased significantly in both groups ($P < 0.05$), but the post-treatment values did not differ significantly between the groups. The $PaCO_2$ decreased significantly in both groups during treatment ($P < 0.01$), but the reduction in $PaCO_2$ was significantly larger in the HNFC group than in the NIPPV group ($P < 0.05$). The PaO_2 increased more in the HFNC group than in the NIPPV group ($P < 0.05$). The PaO_2/FiO_2 ratio increased significantly in both groups ($P < 0.01$); however, it did not differ significantly between the groups

Table 2. Comparison of the specified blood parameters between the two groups before and after treatment.

	Treatment	HFNC Group	NIPPV group
pH	Before	7.21 ± 0.03	7.23 ± 0.03
	After	7.38 ± 0.04[a]	7.34 ± 0.03[a]
$PaCO_2$	Before	63.97 ± 4.79	63.68 ± 4.81
	After	51.63 ± 3.32[b,c]	55.61 ± 3.47[b]
PaO_2	Before	54.15 ± 2.74	54.22 ± 2.69
	After	77.94 ± 3.51[b,c]	68.24 ± 2.67[b]
PaO_2/FiO_2	Before	158.21 ± 20.89	158.38 ± 21.46
	After	254.97 ± 18.45[b]	249.98 ± 17.14[b]
HCO_3^-	Before	33.06 ± 5.17	30.88 ± 4.87
	After	26.81 ± 4.35[a,c]	26.49 ± 4.24[a]
Intubation rate (%)		2.78	2.78

Data are mean ± SD. n = 36. Comparison with before treatment: [a]$P < 0.05$; [b]$P < 0.01$ (paired *t*-test); comparison with the control group: [c]$P < 0.05$; [d]$P < 0.01$ (unpaired *t*-test).
HFNC, high-flow nasal cannula; non-invasive positive-pressure ventilator.

following treatment. After 2 days of treatment, the blood HCO_3^- concentration had decreased significantly in both groups ($P < 0.05$), but it decreased more in the HFNC group than in the NIPPV group ($P < 0.05$) (Table 2). Intubation was required on one occasion in each group (2.8%).

Comparison of the comfort level before and after treatment

The data collected using the questionnaire before and after treatment for the two groups are shown in Table 3. There were no significant differences in CA, DA or EA between the groups before treatment, but all of these were significantly lower following treatment ($P < 0.05$ or 0.01), and the CA and EA showed larger decreases in the HNFC group than in the NIPPV group ($P < 0.05$).

Discussion

The progression of COPD is often accelerated by respiratory infections, and AECOPD ultimately leads to respiratory failure and severe ventilatory dysfunction, which represents the final stage of the disease. In such patients, mechanical ventilation and rational oxygen therapy are typically used as treatments.[12] HFNC has been shown to have beneficial effects in patients with stable COPD, in whom the external positive end-expiratory pressure (PEEP) effect can offset the endogenous PEEP. The flushing effect of HFNC on nasopharyngeal dead space optimizes ventilatory efficiency and promotes CO_2 expulsion. In addition, a sufficient level of warm air-flow reduces inspiratory resistance, prevents dry air-induced bronchoconstriction and improves pulmonary mucosal ciliary clearance. Therefore, HFNC can be highly beneficial in the management of AECOPD, mainly because of the significantly higher comfort, compared with NIPPV.[12–14] Therefore, in the present study, we evaluated the blood gas data, intubation rate, and comfort of patients before and after HFNC therapy for AECOPD in combination with type II respiratory failure, to provide a basis for its clinical use.

Table 3. Comparison of the comfort levels of the two groups before and after treatment.

	Treatment	HFNC Group	NIPPV group
CA	Before	21.13 ± 7.96	21.33 ± 6.56
	After	$13.15 \pm 5.10^{b,c}$	16.53 ± 5.79^{a}
DA	Before	21.41 ± 7.31	22.01 ± 7.69
	After	$15.21 \pm 5.58^{a,c}$	16.50 ± 5.49^{a}
EA	Before	21.91 ± 8.19	21.75 ± 8.45
	After	$12.73 \pm 4.85^{b,c}$	15.83 ± 5.39^{b}

Data are mean ± SD. n = 36. Comparison with before treatment: $^{a}P < 0.05$; $^{b}P < 0.01$ (paired *t*-test); comparison with the control group: $^{c}P < 0.05$; $^{d}P < 0.01$ (unpaired *t*-test).
HFNC, high-flow nasal cannula; non-invasive positive-pressure ventilator; CA, daily activity; DA, dyspnea; EA, experience.

Wenyun *et al.*[15] showed that respiration and the circulation are stimulated when the PaO_2 decreases and the $PaCO_2$ increases. Specifically, the heart and respiratory rates increase, the cardiac blood displacement and cardiac load also increase, and blood pressure shows an abnormal increase, owing to early respiratory acidosis. When the PaO_2 decreases and the $PaCO_2$ increases to within a certain range, respiration and the circulation are impaired, involving reductions in the heart and respiratory rates, lower blood pressure, and complications such as pulmonary encephalopathy, pulmonary heart disease, and cardiac arrest in severe cases.[15–16] We found that the pH, PaO_2, and PaO_2/FiO_2 of patients with AECOPD in combination with type II respiratory failure were higher after treatment with nasal high-flow humidified oxygen therapy. In addition, their HCO_3^- concentration and $PaCO_2$ decreased during this therapy. These results indicate that HFNC has a useful therapeutic effect

in patients with AECOPD and type II respiratory failure. It is worth noting that both the NIPPV and HFNC groups showed higher PO_2 and lower $PaCO_2$, resulting in an improvement in P/F and a normalization of pH in both groups. This indicates that both NIPPV and HFNC can be used to treat AECOPD, and not that HFNC is superior to NIPPV. This may have been, at least in part, because of the small sample size. However, NIPPV can be associated with poor sputum removal, whereas sufficient humidification of the HFNC airway improves this, which should lead to superior $PaCO_2$ and HCO_3^-. The increases in pH, PaO_2, and PaO_2/FiO_2 ameliorated the hypoxemia and low $PaCO_2$ and HCO_3^- concentration of the participants, which greatly reduced CO_2 retention and ameliorated the hypercapnic respiratory failure. This indicates that both HFNC and NIPPV have therapeutic effects in patients with AECOPD.

In the present study, only one participant in each group required intubation, and most were able to largely recover in terms of their respiratory and circulatory function by the end of the treatment period. Patients undergoing HFNC therapy were more comfortable and had a better experience than those undergoing NIPPV. This may be because the HFNC nasal cannula is soft, fits well, and does not require sealing or specific parameter-setting by the operator. Therefore, adverse effects such as claustrophobia and abdominal distension do not occur.[17] In addition, compared with NIPPV, HFNC can improve the comfort of patients by making it easier for them to drink, eat, remove sputum, and communicate; and it is also not associated with pain around the nose, which is caused by tight masks and fixed headbands.[18–19] We evaluated the comfort of the participants before and after treatment by assessing their pulmonary function and dyspnoea, using a questionnaire regarding CA, DA and EA. After treatment, the CA and EA scores of the HFNC group had decreased significantly and to a greater extent than those of the control NIPPV group. The DA scores of the HFNC group were also somewhat better than those of the NIPV group, indicating that HFNC treatment significantly improves the comfort of patients.

In conclusion, transnasal high-flow humidified oxygen therapy improves the blood gas parameters and comfort of patients with AECOPD and type II respiratory failure. The findings of the present study provide a theoretical basis for the clinical use of this treatment. However, the sample studied was relatively small; therefore, further studies of larger samples are needed to corroborate our conclusions. In addition, we did not assess conditions other than AECOPD, such as pneumonia, pulmonary edema, heart failure, and pulmonary hypertension, which may also have led to some bias. Furthermore, we did not follow the participants for a long period of time following the treatment, and therefore future studies should involve longer-term follow-up, to more fully determine its effects on the clinical outcomes of patients. Finally, we only assessed certain clinical parameters and the subjective experiences of the participants. Therefore, research regarding the mechanisms involved and the pathophysiology may be needed.

Author Contributions

AL: Conceptualization, Methodology, Formal analysis, Data curation, Writing–original draft preparation. YZ: Investigation, Writing–Review & Editing, Project administration, Funding acquisition. ZP: Validation, Investigation, Visualization.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Funding

The research was supported by the Fund of Science and Technology Bureau of Nantong City, Jiangsu Province (JCZ2022122).

ORCID iD

Yaqing Zhou https://orcid.org/0000-0003-1887-872X

References

1. Liu CHY, Qiao ZF, Li FL, et al. Effects of transnasal high-flow humidified oxygen therapy on pulmonary artery pressure, ET-1 and NLR in elderly patients with AECOPD combined with type II respiratory failure. *Chin J Gerontol* 2019; 39: 5501–5505.
2. Yang PL, Yu JQ and Chen HB. High-flow nasal cannula for acute exacerbation of chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Heart Lung* 2021; 50: 252–261.
3. Ni YN, Luo J, Yu H, et al. Can high-flow nasal cannula reduce the rate of endotracheal intubation in adult patients with acute respiratory failure compared with conventional oxygen therapy and noninvasive positive pressure ventilation?: a systematic review and meta-analysis. *Chest* 2017; 151: 764–775.
4. Li XY, Tang X, Wang R, et al. High-flow nasal cannula for chronic obstructive pulmonary disease with acute compensated hypercapnic respiratory failure: a randomized, controlled trial. *Int J Chron Obstruc Pulm Dis* 2020; 15: 3051–3061.
5. Lee MK, Choi J, Park B, et al. High flow nasal cannulae oxygen therapy in acute-moderate hypercapnic respiratory failure. *Clin Respir J* 2018; 12: 2046–2056.
6. Yang SQ, Liu Z, Meng SQ, et al. The value of non-invasive ventilation combined with transnasal high-flow oxygen therapy in the sequential treatment of mechanically ventilated patients with chronic obstructive pulmonary disease after withdrawal. *Chin Med J* 2020; 100: 2116–2120.
7. Wang JJ, Jiang HY and Li SF. A randomized controlled study of transnasal high-flow humidified oxygen therapy versus noninvasive positive pressure ventilation in the treatment of acute exacerbation of chronic obstructive pulmonary disease with type II respiratory failure. *Chin J Crit Care Med* 2019; 39: 945–948.
8. Alhazzani W, Moller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). *Intensive Care Med* 2020; 46: 854–887.
9. Chinese Expert Group on Respiratory Medicine. Chinese expert consensus on the management of acute exacerbations of chronic obstructive pulmonary disease (AECOPD) by the Expert Group on the Management of Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD) (2017 update). *Int J Respir Med* 2017; 37: 1041–1057.
10. Guo AM, Han JN, Wang P, et al. Reliability and validity of the pulmonary function status and dyspnea questionnaire for patients with chronic obstructive pulmonary disease. *Chin J Tuberc Respir Dis* 2010; 33: 251–255.
11. Schulz KF, Altman DG and Moher D. CONSORT Group; CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010; 340: 332.
12. Yiqi L, Dongqiong L, Mingju C, et al. Study on the efficacy of transnasal high-flow humidified oxygen therapy and noninvasive positive pressure ventilation in patients with acute exacerbation of chronic obstructive pulmonary disease combined with type II respiratory failure. *J Southwest Med Univ* 2020; 43: 349–353.
13. Pisani L and Vega ML. Use of nasal high flow in stable COPD: rationale and physiology. *COPD*; 2017: 14: 346–350.
14. Liang J and Zhang Y. Effectiveness of ipratropium bromide assisted transnasal high-flow nasal catheter wetting oxygen therapy for acute exacerbation of chronic obstructive pulmonary disease combined with type II respiratory failure in the elderly. *Clin Res Pract* 2021; 6: 38–40.
15. Liu F, Jia WJ, Chen YM, et al. Study on the application of transnasal high-flow humidified oxygen therapy in the treatment of patients with acute exacerbation of chronic obstructive pulmonary disease. *Int J Resp Med* 2018; 38: 1216–1219.

16. Gan WY, Li HM, Wang Y, et al. Effect of non-invasive positive pressure ventilation on plasma brain sodium concentration in patients with acute exacerbation of chronic obstructive pulmonary disease combined with type II respiratory failure. *China Pract Med* 2014; 9: 125–126.
17. Chen HM and Liu L. The effect of transnasal high-flow humidified oxygen therapy on blood gas analysis, reintubation rate and comfort in patients with AECOPD. *J Kunming Med Univ* 2019; 40: 116–119.
18. Yu ZH, Zhang R, Huang H, et al. Efficacy and safety of transnasal high-flow humidified oxygen therapy applied after extubation of tracheal intubation in patients with chronic obstructive pulmonary disease combined with type 2 respiratory failure: a randomized controlled study. *J Second Military Med Univ* 2019; 40: 989–994.
19. Kim DK, Lee J, Park JH, et al. What can we apply to manage acute exacerbation of chronic obstructive pulmonary disease with acute respiratory failure? *Tuberc Respir Dis (Seoul)* 2018; 81: 99–105.