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HIGH-FLOW NASAL CANNULA WARMING AND HUMIDIFICATION OXYGEN TREATMENT FOR SEVERE REFRACTORY PNEUMONIA

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Abstract

This study aimed to compare the efficacy of high-flow nasal cannula (HFNC) with active warming/humidification versus conventional oxygen therapy in improving respiratory outcomes among patients developing severe refractory pneumonia (SRP) following paclitaxel chemotherapy. Clinical data from SRP patients undergoing paclitaxel treatment was randomly split into two groups. The control group got breathing mask oxygen, whereas the intervention group received nasal catheter high-flow heating and humidifying oxygen. Both groups' PaO_2, $PaCO_2$, RR, and oxygenation index (PaO_2/FiO_2) were examined before and after oxygen therapy. The Borg and SGRQ respiratory distress and quality ratings were similar in both groups. The PaO_2/FiO_2 ratio improved considerably in the HFNC group compared to the control group ($p < 0.01$). Borg dyspnea ratings dropped 1.32 points in HFNC ($p = 0.003$). These scores showed a greater impact in the HFNC group. Post-therapy arterial blood gases, including PaO_2, $PaCO_2$, RR, and the PaO_2/FiO_2 ratio, showed substantial changes in both cohorts, with the HFNC group doing better. HFNC patients also had a shorter ICU stay and longer independent breathing than control group patients. HFNC has significant clinical significance as an adjunctive treatment in patients with SRP undergoing paclitaxel chemotherapy.

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Key words: cancer medicine, paclitaxel, refractory pneumonia, oxygen therapy, humidification, high-flow nasal cannula heating

Introduction. Severe refractory pneumonia (SRP), characterized by persistent hypoxemia and resistance to standard antimicrobial therapy, is a life-threatening complication in patients receiving paclitaxel chemotherapy. Paclitaxel-induced immunosuppression and pulmonary toxicity predispose these patients to infections by opportunistic pathogens (*Pneumocystis jirovecii,* drug-resistant bacteria), leading to acute respiratory failure [1]. Patients are prone to developing acute respiratory failure and have a high clinical mortality rate. Oxygen therapy is essential for patients with SRP, as it can improve blood oxygen levels and promote systemic metabolism [2]. However, patients with SRP may still require supplemental oxygen support after extubation, even if they meet standard weaning criteria. Conventional oxygen therapy via masks is often delivered at a low temperature and lacks humidification, which can lead to airway dryness, mucosal irritation, and reduced tolerance, particularly in patients with impaired consciousness or tracheostomy [3].

Recent evidence suggests that high-flow nasal cannula (HFNC) with active warming and humidification offers significant advantages over conventional oxygen masks in post-extubation care. HFNC provides precise FiO_2 delivery, generates low-level positive airway pressure, and maintains optimal airway humidity, thereby enhancing patient comfort and oxygenation efficiency [4]. It can generate a subtle positive pressure within the airway, optimizing the enhancement of blood oxygen levels and improving patient comfort [5]. To validate the clinical effectiveness of HFNC heating and humidification oxygen therapy in individuals with SRP, this research observed patients undergoing chemotherapy who also had SRP. The study involved a comparison of their blood gas analysis, cough difficulty, oxygen tolerance, comfort levels, and reintubation rates.

Materials and methods. ***Study area and participants.*** This study selected 83 critically ill patients from the Department of Intensive Care, Hangzhou First People's Hospital, who received treatment from December 2010 to December 2022. All patients underwent invasive mechanical ventilation prior to enrollment due to acute respiratory failure. After meeting extubation criteria (stable hemodynamics, improved oxygenation), patients were randomly assigned to two groups. The control group received oxygen through a respiratory mask, while the treatment group received HFNC therapy. The control group comprised ($n = 51$), and the HFNC group comprised ($n = 32$). The duration of invasive mechanical ventilation before extubation was 7.04 ± 2.19 days in the HFNC group and 7.83 ± 2.46 days in the control group (Mode: Pressure Support Ventilation (PSV) with a backup rate of 12 breaths/min; Inspiratory Pressure: 10–15 cm H_2O; Positive End-Expiratory Pressure (PEEP): 5–8 cm H_2O; FiO_2: Titrated to maintain $SpO_2 \geq 92\%$.)

Inclusion criteria. (1) Paclitaxel-treated patients meeting severe refractory infectious pneumonia criteria; (2) Microbiologically confirmed or clinically suspected bacterial/fungal pneumonia; (3) Exclusion of paclitaxel-induced pneumonitis via above diagnostic workflow; (4) Arterial oxygen partial pressure < 60 mm Hg, persistent hypoxemia, successful extubation from invasive mechanical ventilation, and subsequent enrollment in the study; (5) Participants, along with their family members, who willingly agreed to engage in the research and finalized the process of informed consent through the signing of necessary documentation.

Exclusion criteria. (1) Hemodynamic stability (MAP ≥ 65 mmHg without vasopressors); (2) Adequate cough reflex (assessed via suctioning); (3) Rapid Shallow Breathing Index (RSBI) < 105 breaths/min/L. (4) $PaO_2/FiO_2 \sim$ ratio ≥ 150 mm Hg.

Treatment methods. Mechanical ventilation parameters prior to extubation. All patients received volume-controlled ventilation with a tidal volume of 6–8 mL/kg predicted body weight, positive end-expiratory pressure (PEEP) of 5–10 cm H_2O, and FiO_2 titrated to maintain $SpO_2 \geq 92\%$. Extubation was performed when patients met standard criteria (e.g., adequate cough reflex, $PaO_2/FiO_2 > 150$ mm Hg).

Both groups of patients received appropriate antibacterial, antispasmodic, bronchodilator, and nutritional support treatment based on changes in their condition. Post-extubation, the control group ($n = 51$) received oxygen therapy through a respiratory mask, while the treatment group ($n = 32$) received HFNC therapy. Both groups of patients received appropriate antibacterial, antispasmodic, bronchodilator, and nutritional support treatment based on changes in their condition. In the control group, patients received conventional oxygen therapy via a non-rebreather mask with FiO_2 adjusted similarly. In the HFNC group, patients received heated (31–37 °C) and humidified (100%) oxygen via HFNC at 40–60 L/min, with FiO_2 titrated to maintain $SpO_2 \geq 92\%$.

Evaluation of treatment efficacy.

- Ineffective: No improvement or worsening of respiratory function and clinical symptoms after treatment.
- Improvement: Partial recovery of respiratory function and effective relief of clinical symptoms after treatment.
- Significant improvement: Near-normal or complete recovery of respiratory function and disappearance or significant alleviation of clinical symptoms after treatment.

Statistical analysis. Data analysis was done using SPSS 22.0. Descriptive statistics for continuous variables were reported as mean ± standard deviation. The t-test was used to compare continuous variables among the two groups, while the chi-square test was utilized for categorical variables. A p-value > 0.05 indicated statistical significance. Both patient groups were assessed for dyspnea utilizing the Borg scale. On this 0–10 scale, higher scores indicated more trou-

ble. QOL was assessed using the St. George's Respiratory Questionnaire. A questionnaire assessed the patient's respiratory status, illness impact on everyday living, and physical activity. It had 50 items and a 100-point limit. Lower scores indicated better patient quality of life.

Results. Table 1 provides the basic features of the two patient groups. There were 25 male and 26 female patients aged 22–75 in the control group. HFNC patients ranged in age from 20 to 74, with 15 men and 17 women. Additionally, the HFNC group used ventilators for an average of 7.04 ± 2.19 days. Importantly, the two groups had similar smoking histories. Comorbidities were likewise balanced across groups. Both the HFNC and control groups improved their respiratory index scores after oxygen assistance. The mean SGRQ score in the HFNC group dropped from 56.26 to 38.09 before oxygen treatment, while the Borg score dropped from 4.44 to 3.12. Figure 1 shows that after therapy, HFNC patients had lower Borg and SGRQ scores than controls. The HFNC and control groups showed improvements in PaO_2, $PaCO_2$, RR, and PaO_2/FiO_2 ratio one week after starting oxygen therapy. Figure 2 shows that the HFNC group outperformed the control group in PaO_2, $PaCO_2$, RR, and PaO_2/FiO_2 ratio. The HFNC and control groups showed improvements in PaO_2, $PaCO_2$, RR, and PaO_2/FiO_2 ratio one week after starting oxygen therapy. Figure 2 shows that the HFNC group outperformed the control group in PaO_2, $PaCO_2$, RR, and PaO_2/FiO_2 ratio. Invasive mechanical ventilation before extubation averaged 7.04 ± 2.19 days in the HFNC group and 7.83 ± 2.46 days in the control group. HFNC had a 6.25% reintubation rate after extubation, compared to 17.76% in the control group (Fig. 3). HFNC patients spent less time in the ICU and breathed unaided. However, hospital stays were not significantly different across groups.

Discussion. Our findings demonstrate that HFNC significantly improves

T a b l e 1

Fundamental characteristics of the two groups of patients

Characteristics	HFNC group ($n = 32$)	Control group ($n = 51$)	p-value
Age, range	20–74	22–75	0.211
Male sex, %	15 (46.87)	25 (49.01)	0.459
Smoking history, %	17 (53.13)	24 (47.05)	0.312
Comorbidities, %	21 (65.63)	32 (62.74)	0.842
Diabetes	18 (56.25)	27 (52.94)	0.187
Hypertension	15 (46.87)	22 (43.13)	0.156
Heart diseases	12 (37.50)	22 (43.13)	0.247
Days of ventilator use	7.04 ± 2.19	7.83 ± 2.46	0.102

Abbreviation: HFNC – nasal catheter high-flow heating and humidifying oxygen therapy

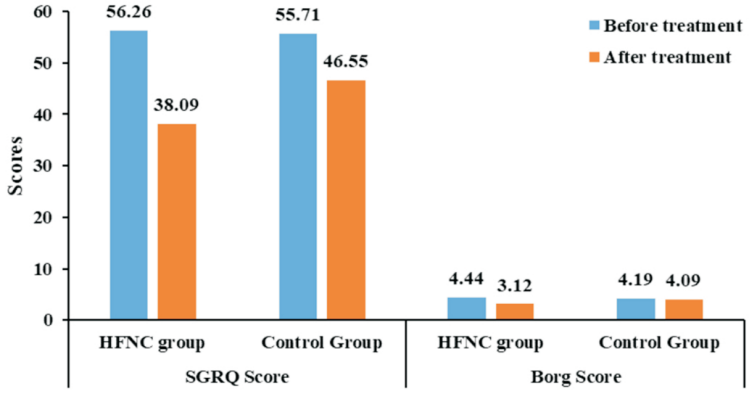

Fig. 1. Comparison of respiratory-related scores SGRQ Score and Borg Score between the two groups of patients
Abbreviation: HFNC – nasal catheter high-flow heating and humidifying oxygen therapy

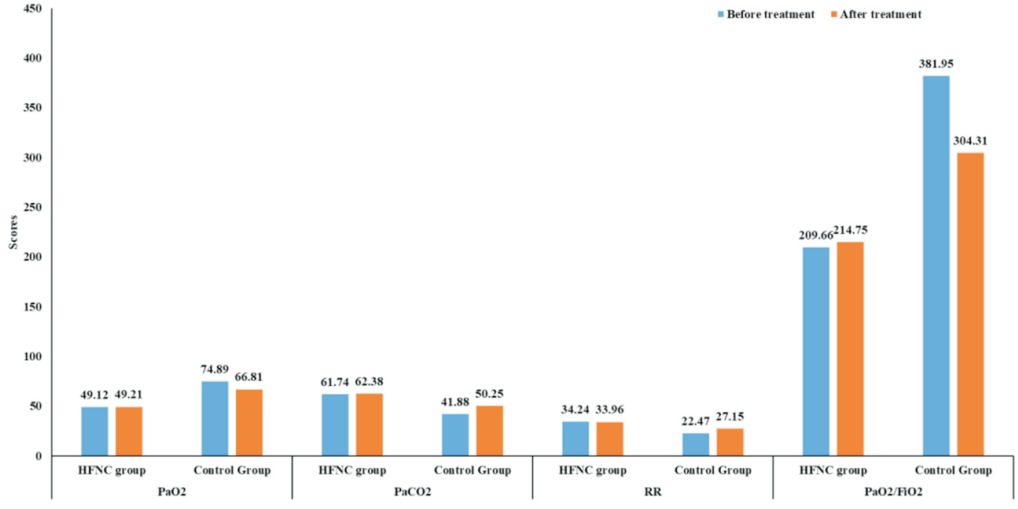

Fig. 2. Comparison of blood gas analysis changes between the two groups of patients
Abbreviations: HFNC – nasal catheter high-flow heating and humidifying oxygen therapy; PaO_2 – partial pressure of oxygen; $PaCO_2$ – partial pressure of carbon dioxide; RR – respiratory rate; PaO_2/FiO_2 – oxygenation index

outcomes in paclitaxel-treated patients with severe refractory infectious pneumonia. It is important to tell this group of people apart from those who have paclitaxel-induced pneumonitis because they need different treatments. These symptoms can be severe in most cases. Clinical treatment often includes antimicrobial therapy, oxygen therapy via mask or nasal cannula, respiratory secretions, and nutritional support [6]. However, critically ill patients may undergo rapid

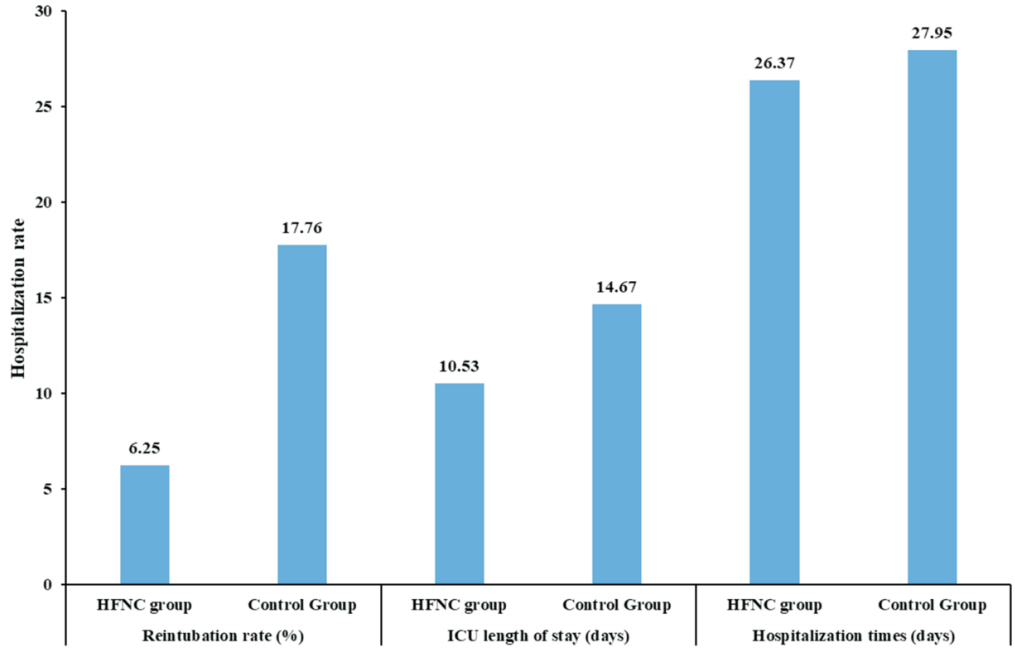

Fig. 3. Comparison of hospitalization conditions between the two groups of patients
Abbreviation: HFNC – nasal catheter high-flow heating and humidifying oxygen therapy

changes in their state, unstable vital signs, and respiratory failure during therapy, causing multi-organ dysfunction [7]. Such instances may need invasive mechanical ventilation to enhance therapy results. However, extubation and reintubation increase ventilator-associated pneumonia risk. Keeping oxygen intake steady is crucial for a successful therapy [8]. After ventilator removal, severe pneumonia patients are more likely to be reintubated. Effective post-extubation transitional procedures reduce this risk [9]. HFNC warming and humidification oxygen therapy represents an advanced respiratory support approach that has gained prominence in recent years [10]. It combines an oxygen-air blending device, a humidification system, a respiratory circuit, and HFNC. This makes clinical procedures much easier, protects the body from harm, and lowers the risk of infection.

Warming and humidification enhance patient comfort, respiratory mucosa tolerance, and self-cleaning. Respiratory failure and comorbidities may increase airway secretions, making it harder to clear, particularly with thick sputum. This may increase respiratory effort and tiredness [11]. Cold gas may also produce airway spasm and aggravate the patient's condition. Therefore, HFNC treatment improves airway dryness by regulating inhaled gas temperature and humidity. This is particularly critical for patients with SRP who need long-term oxygen treatment because dry gas may harm respiratory epithelial cells, change sputum properties, and slow sputum clearance. HFNC therapy normalizes mucous membrane func-

tion, mucus production, and mucociliary system clearance while maintaining gas exchange and airway defense [12].

This research demonstrated that oxygen support improved respiratory index scores in both groups. After treatment, the observation group's Borg and SGRQ scores declined considerably compared to the control group, showing that HFNC therapy may improve extubated patients' airway secretions, respiratory status, disease impact on daily life, and physical activity. Also, breathing efficiency is a key sign of oxygen support treatment success. HFNC improves gas exchange by providing continuous high-flow positive pressure to physiological dead spaces in the nasopharynx and other areas, increasing gas exchange rates, oxygen concentration in the alveoli, oxygen and carbon dioxide exchange, hypercapnia, and spontaneous breathing [13]. Research shows that HFNC treatment increases tidal volume, ventilation, end-expiratory lung capacity, blood oxygen saturation, and cardiothoracic surgery patients' cardiopulmonary load. In the observation group, HFNC therapy, which provided a constant oxygen concentration via air and oxygen, improved breathing and corrected hypoxia. HFNC decreases carbon dioxide and enhances oxygenation compared to mask-based oxygen treatment. It helps remove carbon dioxide, minimizes reintubation risk, and significantly reduces the reintubation rate. Reintubation rates for HFNC patients were substantially lower than the control group by 6.25%. The HFNC group outperformed the control group in ICU stay and unassisted breathing. HFNC may reduce hypoxia-related damage, inflammation, disease duration, and treatment outcomes.

Conclusion. Our research shows that HFNC therapy after extubation improves clinical outcomes in SRP patients receiving paclitaxel chemotherapy. In particular, HFNC improves oxygenation, decreases respiratory distress, and lowers reintubation rates. Additionally, it shortens ICU stays by 7.04 ± 2.19 days and extends independent breathing. Its advantages stem from consistent high FiO_2, airway humidification, and less mucosal damage. HFNC revolutionized post-extubation respiratory assistance for high-risk patients.

Ethical approval. This study protocol was approved by the Ethics Committee of Hangzhou First People's Hospital (Reg no. 2010/O2/34764/342).

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