International Journal of Chronic Obstructive Pulmonary Disease Dovepress

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REVIEW

Noninvasive Positive Pressure Ventilation versus High-Flow Nasal Cannula for Chronic Obstructive Pulmonary Disease: An Updated Narrative Review

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Abstract: Chronic obstructive pulmonary disease (COPD) is one of the most common clinical respiratory illnesses, defined by permanent pathological deterioration that leads to respiratory failure. Regarding COPD treatment, oxygen therapy is very important. Non-invasive positive pressure ventilation (NPPV) is a technique for non-invasive mechanical ventilation that enables patients to get positive pressure support without the need of an artificial airway. Instead, it merely employs the mask by covering the mouth and nose, or simply the nose of patients. NPPV has been shown to be beneficial for COPD patients experiencing respiratory failure. High-flow nasal cannula (HFNC) oxygen therapy shows some advantages, including the reduction of anatomical dead space, the prompt correction of low oxygen levels as well as the improvement of patients' tolerance. Owing to its continuous progress, ventilation technology strongly improves COPD treatment. In this study, the authors analyze the application of NPPV and HFNC in COPD so as to provide recommendations for mechanical ventilation treatment.

Keywords: chronic obstructive pulmonary disease, high flow nasal cannula, non-invasive positive pressure ventilation, respiratory failure

Chronic obstructive pulmonary disease (COPD) is a common respiratory condition with high morbidity and mortality rates, and has become a major cause of death worldwide.[1] Moreover, it is associated with significant economic and societal burdens. Persistent airflow limitation and changes in the respiratory tract caused by COPD lead to symptoms including dyspnea and cough. Acute exacerbation of COPD (AECOPD) describes the sudden worsening of symptoms, such as dyspnea, cough, or phlegm, within a short period, for which a basic medication regimen is required; nevertheless, prognosis may be poor. Respiratory failure is a common and serious complication of AECOPD that impairs effective gas exchange. Patients with type II respiratory failure and hypercapnia have a higher risk for mortality. Currently, drug therapy and respiratory support options, such as conventional oxygen therapy, high-flow nasal cannula (HFNC), noninvasive positive pressure ventilation (NPPV), and invasive positive pressure ventilation,[2] are commonly used to treat patients with AECOPD.

With the assistance of accessories, such as nasal masks, mouth and nose masks, or full-face masks that connect the patient to the ventilator, NPPV can provide positive pressure-assisted ventilation without invasive procedures.[3,4] For patients with AECOPD and acute respiratory failure, NPPV provides good respiratory support because it is not only beneficial for enhancing oxygenation and correcting acute respiratory acidosis, but also helpful in regulating pH and reducing the partial pressure of carbon dioxide ($PaCO_2$) to control respiratory failure. In addition, it reduces the workload of the respiratory muscles, alleviates dyspnea, and provides assistance in COPD treatment. According to some studies,

Received: 23 July 2024
Accepted: 1 November 2024
Published: 9 November 2024

NPPV treatment has some advantages, such as decreased risks for tracheal intubation in patients with COPD, decreased rate of ventilator-associated pneumonia, and shorter hospital stays.[5] However, improper setting of NPPV parameters may negatively affect its therapeutic effect. Moreover, side-effects of NPPV, such as nasal congestion, dryness in the nasal area, facial compression, and gastric emphysema, may reduce tolerance, thereby resulting in treatment failure.

HFNC continuously provides patients with regulated and relatively constant oxygen concentrations (ranging from 21% to 100%), temperature (31–37 °C), and humidity at a high flow rate (8–80 L/min) through a nasal cannula. HFNC offers good patient comfort because the high flow effectively clears nasopharyngeal dead space, increases mean airway pressure, enhances ventilation and, theoretically, improves hypoxia and hypercapnia.[6] In recent years, HFNC has gained widespread acceptance in clinical practice as a new respiratory support technology, playing a pivotal role in saving patients' lives.[7] We herein present a review of the applications of NPPV and HFNC in patients with COPD.

Applications of NPPV in COPD

NPPV provides positive pressure assistance without the need for invasive endotracheal intubation or tracheotomy and connects the patient to a ventilator for positive pressure-assisted ventilation using a nasal mask, orofacial mask, full-face mask, or hood. Bi-level positive airway pressure (BiPAP) and continuous positive airway pressure (CPAP) are two common NPPV modalities.[8] Throughout the breathing cycle, positive airway pressure is continuously maintained using CPAP. In contrast, BiPAP offers more positive end-expiratory and inspiratory positive airway pressures. BiPAP is widely used in the treatment of patients with COPD and respiratory failure.[9] NPPV alleviates respiratory failure by partially reopening the collapsed airways through positive pressure ventilation, enhancing lung ventilation volume, and optimizing ventilation/perfusion ratios to improve oxygenation and reduce CO_2 retention. In contrast to low-flow continuous oxygen administration, NPPV applies positive airway pressure at the end of expiration, further enhancing the oxygen uptake and effective tidal volume, and facilitating airway dilation and patient ventilation. Improved lung ventilation leads to an effective exchange of CO_2, evident in the decreased $PaCO_2$ and increased partial pressure of oxygen (PaO_2) levels post-treatment, significantly ameliorating clinical symptoms in patients with COPD. NPPV has become an effective treatment for reducing morbidity and mortality rates in hospitalized patients with AECOPD. Elshof et al[10] demonstrated that NPPV can significantly alleviate clinical symptoms, control disease progression, improve ventilation function, minimize invasive mechanical ventilation requirements, and enhance survival rates. Additionally, some studies have indicated that NPPV reduces the incidence of ventilator-associated pneumonia compared with invasive ventilation, while protecting the patient's voluntary respiration and enhancing airway defense and swallowing function. As such, NPPV has become a preferred treatment modality for patients who do not fulfill the criteria for invasive mechanical ventilation.[11,12]

In patients with stable COPD and obstructive sleep apnea, CPAP significantly reduces the risk for AECOPD, COPD-related hospitalization, and mortality.[13] A multicenter study focusing on patients with AECOPD and persistent hypercapnia 2–4 weeks after hospital discharge compared the effect of home noninvasive ventilation combined with oxygen therapy versus oxygen therapy alone on the time to rehospitalization and mortality. The results revealed that in patients with persistent hypercapnia in AECOPD, the combination of home noninvasive ventilation and oxygen therapy significantly prolonged the time to rehospitalization and mortality over a 12-month period.[14] The efficacy of NPPV in patients with COPD and prolonged hypercapnia following acute respiratory failure remains uncertain. One study demonstrated improved transcutaneous partial $PaCO_2$ with NPPV compared with conventional home oxygen therapy; however, there was no significant difference in the number of exacerbations, lung function, emotional state, level of daily activity, or dyspnea among patients with COPD.[15] Casanova et al[16] demonstrated that NPPV had no significant effect or only a marginal benefit on the natural course of COPD up to 1 year in patients with stable disease. In contrast, a meta-analysis suggested that home NPPV significantly reduced all-cause hospitalization, risk for intubation, and mortality compared with non-NPPV-treated patients with COPD and hypercapnia, albeit without a significant difference in quality of life.[17] Because the optimal implementation of NPPV requires the selection of appropriate patients and improvement of treatment compliance, healthcare professionals also need to customize respiratory parameters to ensure effective ventilation because inappropriate NPPV treatment settings potentially compromise patient outcomes and survival.[18] Therefore, enhancing healthcare professionals' and patients' awareness of NPPV usage in clinical settings could further improve patient prognosis.

Applications of HFNC in COPD

HFNC is a novel oxygen therapy that directly delivers a specific concentration of air-oxygen at a high flow rate through a specially designed nasal cannula. It uses an air-oxygen mixer connected to a flow meter, turbine, or ventilator with a heated humidifier for gas compression, delivering a continuous stream of heated and humidified gas with oxygen concentrations up to 100% through a nasal interface.[19] HFNC provides heated and humidified airflow to the patient that maintains airway function, facilitates clearance of airway secretions and pathogens, improves oxygenation, generates positive end-expiratory pressure, and increases functional residual capacity.[20] Compared with standard oxygen therapy, HFNC reduces patient inspiratory effort, and respiratory work and rate, resulting in improved comfort and oxygenation.

HFNC exerts multiple physiological effects on the respiratory system. The mucosal cilia transport system acts as a mechanical defense system by transporting pollutants out of the airways, extending from the fine bronchioles to the nasopharynx. Respiratory epithelial cilia are highly sensitive to changes in respiratory temperature and pressure, and function best at core body temperature and 100% relative humidity. In the traditional oxygen delivery method, cool and dry gases cause bronchoconstriction by altering the viscosity of secretions in the respiratory tract, which reduces the frequency of ciliary peristalsis and decreases the rate of mucus clearance by the cilia. Impaired mucus ciliary clearance reduces lung compliance and increases airway resistance and breathing. It also increases the risks for mucus plugging, alveolar shedding, and infection. HFNC optimizes respiratory epithelial function and improves ciliary mucus clearance by warming and humidifying the air-oxygen mixture.[21] Patients with respiratory failure often exhibit an increased respiratory rate, and the gas flow rate of conventional oxygen therapy is insufficient to meet their needs. The air stream delivered by HFNC effectively flushes exhaled gases from the upper airway, maintains stable oxygen concentrations, reduces rebreathing of CO_2, and enhances pulmonary ventilation. A crossover study found that in patients with COPD undergoing long-term oxygen therapy, HFNC improved respiratory rate and respiratory work within a specific period, increased tidal volume and end-expiratory volume, improved lung ventilation, and reduced CO_2 levels and respiratory muscle work.[22]

Positive end-expiratory pressure resulting from high-flow gas has the potential to offset intrinsic positive end-expiratory pressure. In addition, HFNC can enhance ventilatory efficiency and CO_2 elimination by causing a washout effect in the nasopharyngeal dead space.[23,24] Airway pressure can be affected by changes in the expansion and contraction of the nasopharynx. One study found that patients treated with HFNC at a rate of 60 L/min reached a nasopharyngeal pressure of 6.8 cmH_2O with the mouth closed and 0.8 cmH_2O with the mouth open. Mouth closure results in a positive nasopharyngeal pressure proportional to the flow rate and an increase in expiratory resistance, which is significantly reduced with open-mouth breathing.[25]

Compared with NPPV, HFNC offers a more comfortable alternative without facial compression, minimizing adverse effects such as facial pressure sores. In addition, humidified gas delivery through HFNC reduces mucosal dryness and airway mucosal damage associated with traditional oxygen therapy. It effectively promotes sputum discharge, reduces airway resistance, and improves ventilation and oxygenation. Accordingly, HFNC has recently been recommended as the primary respiratory support for patients with acute respiratory distress and hypoxemia to yield significant improvements in dyspnea and oxygenation indices and reduce the risk for endotracheal intubation compared with conventional oxygen therapy.[26]

The long-term efficacy of HFNC in treating COPD-induced chronic hypercapnic respiratory failure remains unclear. Studies have compared the efficacy of long-term HFNC oxygen therapy with that of oxygen therapy alone in patients with hypercapnic COPD. HFNC significantly reduced the incidence of moderate-to-severe AECOPD and prolonged the duration of non-acute exacerbations. Health-related quality of life, peripheral oxygen saturation, and lung function of patients in the HFNC group significantly improved.[27] However, limitations of HFNC have been noted. In severe cases of COPD, the positive airway pressure provided by HFNC cannot meet patient needs and the respiratory rate cannot be improved. The patient then opens the mouth to breathe, resulting in increased leakage and a decrease in airway pressure. This condition undermines the effectiveness of ventilation by reducing the pressure necessary for an effective respiratory effort. A study demonstrated that HFNC is not appropriate in patients with a respiratory rate of >35 breaths/min.[28] Furthermore, the elasticity of lung tissues decreases in some patients who experience repeated COPD because the lungs are in a state of hyperinflation, leading to ventilation dysfunction, resulting in CO_2 retention and, ultimately, chronic hypercapnia. Owing to the increased tolerance to CO_2 retention and elevated airway resistance, HFNC therapy may not offer sufficient respiratory support to effectively eliminate CO_2 from the body. Consequently, this inadequacy can result in poor clinical outcomes. Lu et al[29] found that while HFNC may be beneficial for specific patients with AECOPD, the presence of B-type natriuretic peptide levels ≥ 280 ng/L and arterial blood pH ≤ 7.30 before treatment initiation often indicates that a single HFNC session may be ineffective. In such cases, close monitoring is recommended and prompt consideration should be given to transitioning to NPPV or invasive mechanical ventilation if necessary.[29]

Differences Between NPPV and HFNC in Applications for COPD

Patients with AECOPD often experience acute respiratory symptoms and hypercapnia, and some require admission to the intensive care unit (ICU). Conventional drug therapies may not achieve the desired outcomes in these patients. NPPV improves respiratory symptoms, enhances alveolar ventilation, corrects hypercapnia, reduces the length of ICU stay, and lowers mortality rates. Therefore, NPPV is recommended as a routine treatment for AECOPD accompanied by hypercapnia. However, the effectiveness of NPPV is closely linked to factors including parameter settings, patient comfort, and the level of collaboration between the patient and the device.

HFNC therapy delivers heated and humidified constant airflow to generate positive pressure ventilation, which helps increase end-expiratory lung volume, promotes the clearance of tracheobronchial secretions, and reduces respiratory effort, thereby improving respiratory function. Cortegiani et al[30] demonstrated that HFNC therapy is effective in treating patients with COPD and mild-to-moderate hypercapnia and respiratory failure. This treatment was found to significantly decrease blood CO_2 levels, with efficacy comparable with NPPV, while offering high comfort levels and person–device cooperation. In contrast, in patients with COPD complicated by moderate to severe hypercapnic respiratory failure, there is no significant difference in treatment failure rates between HFNC and NPPV. However, HFNC is associated with fewer complications, reduced need for airway care interventions, and lower risk for breakdown of the facial skin.[31] Further research has shown that in patients having mild-to-moderate AECOPD with similar treatment failure rates between HFNC and NPPV, there is comparable effectiveness in avoiding tracheal intubation.[32] Additionally, the HFNC group exhibited a lower incidence of complications and a reduced risk for barotrauma compared with the NPPV group.[33] During the stable phase and recovery period of AECOPD, HFNC demonstrates effectiveness in reducing respiratory work, lowering respiratory rate, and maintaining adequate gas exchange, and also facilitates superior compliance and adaptability compared with NPPV.[34]

If patients do not achieve satisfactory therapeutic outcomes after NPPV, timely invasive ventilatory support may be necessary. However, invasive ventilation may lead to complications such as ventilator-associated pneumonia. Therefore, in recent years, invasive-noninvasive sequential treatment has been proposed in the clinic. More specifically, endotracheal extubation is performed before meeting the extubation criteria, followed by continued oxygen therapy using noninvasive methods.[35–37] Nevertheless, owing to poor tolerance and contraindications, some patients may require reintubation. Studies have reported HFNC therapy to demonstrate favorable clinical efficacy in preventing reintubation in patients with respiratory failure after extubation.[24,38,39] Jing et al[40] compared the outcomes of invasive-HFNC sequential therapy and invasive-NPPV sequential therapy in patients with COPD and severe respiratory failure, finding that they were equally effective in improving pulmonary oxygenation function; however, invasive-HFNC sequential therapy demonstrated superior tolerance.

Summary

Due to factors such as the aging population in China, the incidence of COPD, especially respiratory failure, is gradually increasing, which significantly affects patient health and quality of life. Owing to its simplicity of operation, NPPV has become an important treatment option. NPPV treatment not only enhances therapeutic effects and reduces the risks associated with tracheal intubation and incision, but also helps to improve lung function. However, it is essential to tailor ventilation modes and parameters according to individual patient conditions to ensure treatment effectiveness and safety. HFNC can actively improve oxygenation and clinical outcomes in patients with respiratory failure, and can be used as a frontline treatment for acute hypoxemic respiratory failure. Nevertheless, while studies have indicated that HFNC can enhance oxygenation and ventilation, reduce hypercapnia, prolong the time until the next moderate acute exacerbation, and improve health-related quality of life scores in patients with AECOPD, acute hypercapnic respiratory failure, and stable hypercapnic

COPD receiving long-term oxygen therapy, the overall assessment of the utility of HFNC in this patient population is currently limited by factors such as small sample sizes, heterogeneity of patient groups, and short follow-up durations. As such, further research and clinical analyses are warranted to better evaluate the value of HFNC in such patients.

Funding

The study was supported by a grant (JDY2022015) from medical education collaborative innovation funding of Jiangsu University.

Disclosure

Yuting Wang and Yan Liu are co-first authors for this study. The authors report no conflicts of interest in this work.

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