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Original Research Article

Comparative Evaluation of High-Flow Nasal Cannula Oxygen Therapy and Non-Invasive Ventilation in COPD Patients with Acute Hypercapnic Respiratory Failure

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Abstract

Background: Acute hypercapnic respiratory failure is a common complication of acute exacerbations of chronic obstructive pulmonary disease (COPD). Non-invasive ventilation (NIV) is the recommended first-line therapy; however, high-flow nasal cannula (HFNC) oxygen therapy has emerged as a potential alternative with improved patient tolerance. This study aimed to compare the clinical effectiveness, physiological outcomes, and patient tolerance of HFNC and NIV in COPD patients with acute hypercapnic respiratory failure.

Methods: This prospective comparative study included 203 patients with COPD presenting with acute hypercapnic respiratory failure. Patients received either HFNC (n = 101) or NIV (n = 102) as respiratory support. Baseline demographic characteristics, physiological parameters, and arterial blood gas values were recorded. Changes in arterial blood gas parameters at 24 hours, clinical outcomes, device-related complications, and predictors of treatment failure were analyzed.

Results: Both HFNC and NIV significantly improved arterial blood gas parameters after treatment. NIV demonstrated a greater improvement in arterial pH and a larger reduction in $PaCO_2$ at 24 hours compared with HFNC ($p < 0.01$). The need for endotracheal intubation was significantly higher in the HFNC group (17.8%) than in the NIV group (9.8%) ($p = 0.009$). Patient comfort scores were significantly higher with HFNC (7.8 ± 1.3 vs 6.2 ± 1.7; $p < 0.001$), and device-related complications such as skin breakdown and gastric distension were more common with NIV. Multivariate analysis identified baseline pH <7.25, $PaCO_2$ >70 mmHg, and respiratory rate >32/min as independent predictors of treatment failure.

Conclusion: Both HFNC and NIV improve gas exchange in COPD patients with acute hypercapnic respiratory failure. NIV provides greater reduction in hypercapnia and lowers the risk of intubation, whereas HFNC offers better patient comfort and tolerance. NIV should remain the preferred first-line therapy, while HFNC may be considered in selected patients, particularly those unable to tolerate NIV.

Keywords: Chronic obstructive pulmonary disease; High-flow nasal cannula; Non-invasive ventilation; Acute hypercapnic respiratory failure; Mechanical ventilation; COPD exacerbation.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a major global health burden and is currently one of the leading causes of morbidity and mortality worldwide. According to the World Health Organization, COPD is the third leading cause of death globally, accounting for approximately 3.2 million deaths annually [1]. Acute exacerbations of COPD frequently lead to hospitalization and are commonly associated with acute hypercapnic respiratory failure (AHRF), characterized by elevated arterial carbon dioxide tension ($PaCO_2$ >45 mmHg) and respiratory acidosis [2]. These episodes significantly worsen prognosis, increase healthcare utilization, and are associated with higher short-term and long-term mortality rates [3].

Non-invasive ventilation (NIV) has been widely established as the first-line ventilatory support modality for COPD patients presenting with acute hypercapnic respiratory failure. NIV improves alveolar ventilation, reduces work of breathing, enhances gas exchange, and decreases the need for endotracheal intubation and mortality in

appropriately selected patients [4,5]. Clinical trials and meta-analyses have demonstrated that NIV reduces intubation rates by nearly 50–60% and mortality by approximately 40% in patients with COPD exacerbations complicated by hypercapnia [6]. Despite its proven effectiveness, NIV is sometimes poorly tolerated due to issues such as mask discomfort, skin breakdown, claustrophobia, gastric distension, and patient–ventilator asynchrony, leading to treatment failure in 15–25% of patients [7].

High-flow nasal cannula (HFNC) oxygen therapy has emerged as a promising alternative respiratory support modality in recent years. HFNC delivers heated and humidified oxygen at high flow rates (up to 60 L/min), allowing precise control of the fraction of inspired oxygen (FiO_2) while generating a small amount of positive airway pressure [8]. The high flow rates also help wash out nasopharyngeal dead space, improve mucociliary clearance, and reduce inspiratory resistance, thereby decreasing the work of breathing [9]. These physiological benefits make HFNC particularly attractive in patients with respiratory failure who may not tolerate conventional non-invasive ventilation interfaces.

Recent studies have suggested that HFNC may improve patient comfort, facilitate secretion clearance, and maintain stable oxygenation while also contributing to modest reductions in $PaCO_2$ levels in hypercapnic respiratory failure [10]. Several clinical trials have compared HFNC with conventional oxygen therapy and NIV in COPD exacerbations, reporting comparable improvements in gas exchange parameters and respiratory rate in selected patient populations [11,12]. However, the evidence remains heterogeneous, and there is ongoing debate regarding whether HFNC can provide outcomes similar to NIV in the management of acute hypercapnic respiratory failure in COPD patients.

Given the increasing adoption of HFNC in emergency and intensive care settings, it is important to evaluate its effectiveness relative to the established standard of care, particularly in terms of gas exchange improvement, patient tolerance, need for escalation of ventilatory support, and clinical outcomes. Therefore, this study aimed to compare the effectiveness of high-flow nasal cannula oxygen therapy with non-invasive ventilation in patients with COPD presenting with acute hypercapnic respiratory failure.

Materials and Methods

Study Design and Setting: This prospective comparative study was conducted in the Department of Pulmonary Medicine and Intensive Care Unit of a tertiary care teaching hospital over a period of 18 months from January 2023 to June 2024. The study aimed to compare the clinical effectiveness of high-flow nasal cannula (HFNC) oxygen therapy and non-invasive ventilation (NIV) in patients with chronic obstructive pulmonary disease (COPD) presenting with acute hypercapnic respiratory failure. The study protocol was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants or their legally authorized representatives prior to enrollment.

Sample Size: The sample size was calculated to compare treatment success between HFNC and NIV in COPD patients with acute hypercapnic respiratory failure. Previous studies have reported treatment success rates of approximately 80% with NIV and 65% with HFNC, suggesting a clinically meaningful difference of about 15%. Using the formula for comparison of two independent proportions with 95% confidence level ($Z\alpha/2 = 1.96$) and 80% power ($Z\beta = 0.84$), the required sample size was estimated to be approximately 101 patients per group (202 total). Allowing for minimal data loss or incomplete records, the final sample size was 203 patients, who were consecutively enrolled during the study period and allocated to HFNC or NIV groups in an approximately 1:1 ratio.

Study Population: The study included adult patients diagnosed with COPD who were admitted with acute exacerbation complicated by hypercapnic respiratory failure. Diagnosis of COPD was established based on clinical history, examination findings, and previously documented spirometry showing persistent airflow limitation according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. Acute hypercapnic respiratory failure was defined as arterial partial pressure of carbon dioxide ($PaCO_2$) greater than 45 mmHg with arterial pH less than 7.35 on arterial blood gas analysis, along with clinical signs of respiratory distress.

Inclusion and Exclusion Criteria: Patients aged 40 years or older with confirmed COPD presenting with acute exacerbation and hypercapnic respiratory failure who required ventilatory support were included in the study.

Patients requiring immediate endotracheal intubation due to severe respiratory failure, hemodynamic instability, cardiac arrest, or inability to protect the airway were excluded.

Additional exclusion criteria included facial trauma preventing NIV mask application, severe encephalopathy, do-not-intubate orders, and respiratory failure due to causes other than COPD exacerbation such as pulmonary embolism, neuromuscular disease, or acute cardiogenic pulmonary edema.

Intervention: Patients were managed with either high-flow nasal cannula (HFNC) oxygen therapy or non-invasive ventilation (NIV) depending on the respiratory support initiated by the treating physician. In the HFNC group, heated and humidified oxygen was delivered through a high-flow nasal cannula system with initial flow rates typically set between 30 and 50 L/min, and the fraction of inspired oxygen (FiO_2) adjusted to maintain peripheral oxygen saturation (SpO_2 88–92%). In the NIV group, ventilatory support was provided using bilevel positive airway pressure delivered through an oronasal or full-face mask. Initial inspiratory positive airway pressure (IPAP) was generally set between 10–14 cm H_2O and expiratory positive airway pressure (EPAP) between 4–6 cm H_2O, with subsequent adjustments based on clinical response and arterial blood gas findings. All patients received standard medical therapy for COPD exacerbation, including bronchodilators, systemic corticosteroids, antibiotics when indicated, and supportive care.

Arterial Blood Gas Measurement and Monitoring: Arterial blood gas (ABG) analysis was performed at baseline prior to initiation of respiratory support and subsequently repeated at 1 hour, 6 hours, and 24 hours after initiation of therapy, and thereafter as clinically indicated. The parameters recorded included arterial pH, $PaCO_2$, PaO_2, bicarbonate concentration, and oxygen saturation. Patients were continuously monitored for respiratory rate, heart rate, blood pressure, oxygen saturation, and clinical signs of respiratory distress throughout the treatment period.

Outcome Measures: The primary outcome measure was improvement in arterial blood gas parameters, particularly reduction in $PaCO_2$ levels and correction of respiratory acidosis following initiation of respiratory support. Secondary outcomes included changes in respiratory rate, improvement in oxygenation parameters, patient tolerance to the respiratory support modality, need for escalation to invasive mechanical ventilation, duration of respiratory support, length of hospital stay, and in-hospital mortality.

Definition of Treatment Failure: Treatment failure for both HFNC and NIV was defined as the need for escalation of respiratory support due to inadequate clinical or physiological improvement. Criteria for failure included persistent or worsening respiratory acidosis with arterial pH <7.25, rising $PaCO_2$ levels, respiratory rate greater than 35 breaths per minute, worsening hypoxemia despite optimized therapy, or signs of severe respiratory distress. Additional indicators included hemodynamic instability, inability to tolerate the device interface, impaired airway protection, or deterioration requiring endotracheal intubation and invasive mechanical ventilation.

Statistical Analysis: Data were entered into a standardized data sheet and analyzed using the Statistical Package for the Social Sciences (SPSS) version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Comparisons between the HFNC and NIV groups for continuous variables were performed using the independent sample t-test, whereas categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Changes in arterial blood gas parameters between baseline and 24 hours were evaluated using paired t-tests. To identify independent predictors of treatment failure, multivariate logistic regression analysis was performed, and results were reported as adjusted odds ratios (AOR) with 95% confidence intervals (CI). A p-value <0.05 was considered statistically significant.

Result

A total of 203 patients were included in the study, with 101 patients in the HFNC group and 102 in the NIV group. The mean age of participants was comparable between the groups (64.8 ± 9.2 vs 65.3 ± 8.7 years; p = 0.671). There was a clear male predominance, accounting for 77.2% in the HFNC group and 79.4% in the NIV group (p = 0.597). The mean BMI was similar in both groups (23.1 ± 3.6 vs 22.8 ± 3.9 kg/m²; p = 0.564).

Most patients were current or former smokers, comprising 85.1% and 87.3% in the HFNC and NIV groups, respectively (p = 0.624), with comparable smoking exposure (32.6 ± 14.8 vs 34.1 ± 15.2 pack-years; p = 0.649). The mean duration of COPD (8.4 ± 4.6 vs 8.7 ± 4.3 years; p = 0.653) and prevalence of comorbidities including hypertension (41.6% vs 43.1%) and diabetes mellitus (35.6% vs 37.3%) were similar between groups. Nearly half of the patients had previous hospitalization for AECOPD in the past year (46.5% vs 48.0%; p = 0.803), indicating comparable disease burden at baseline (Table 1).

Table 1: Baseline Demographic and Clinical Characteristics of Patients Receiving HFNC and NIV

Variable	HFNC (n=101)	NIV (n=102)	p value
	Frequency (%)/mean ± SD		
Age (years)	64.8 ± 9.2	65.3 ± 8.7	0.671
Gender			
Female	33 (22.8%)	21 (20.6%)	0.597
Male	78 (77.2%)	81 (79.4%)	
BMI (kg/m²)	23.1 ± 3.6	22.8 ± 3.9	0.564
Smoking status			
Non smoker	15 (14.9%)	13 (12.7%)	0.624
Current/Ex-smokers	86 (85.1%)	89 (87.3%)	
Pack-years	32.6 ± 14.8	34.1 ± 15.2	0.649
Duration of COPD (years)	8.4 ± 4.6	8.7 ± 4.3	0.653
Hypertension	42 (41.6%)	44 (43.1%)	0.813
Diabetes mellitus	36 (35.6%)	38 (37.3%)	0.481
Previous hospitalization for AECOPD (past year)	47 (46.5%)	49 (48.0%)	0.803

HFNC – High Flow Nasal Cannula; NIV – Non-invasive Ventilation; BMI – Body Mass Index; COPD – Chronic Obstructive Pulmonary Disease; AECOPD – Acute Exacerbation of COPD.

Baseline clinical and arterial blood gas parameters were comparable between the two treatment groups. The mean respiratory rate was 30.8 ± 4.6 breaths/min in the HFNC group and 31.2 ± 4.3 breaths/min in the NIV group (p = 0.511), while the mean heart rate was 104.2 ± 13.8 and 105.6 ± 14.1 beats/min, respectively (p = 0.496). Oxygen saturation at admission was similar (84.6 ± 4.9% vs 84.2 ± 5.1%; p = 0.611). Baseline arterial blood gas analysis revealed comparable levels of pH (7.28 ± 0.04 vs 7.27 ± 0.05; p = 0.212) and $PaCO_2$ (62.8 ± 8.7 vs 63.4 ± 9.1 mmHg; p = 0.641) between HFNC and NIV groups. Likewise, PaO_2 and bicarbonate levels did not differ significantly, indicating that the severity of hypercapnic respiratory failure was similar at presentation (Table 2).

Table 2: Baseline Physiological Parameters and Arterial Blood Gas Profile at Admission

Parameter	HFNC (n=101)	NIV (n=102)	p value
	mean ± SD		
Respiratory rate (breaths/min)	30.8 ± 4.6	31.2 ± 4.3	0.511
Heart rate (beats/min)	104.2 ± 13.8	105.6 ± 14.1	0.496
SpO_2 (%) on admission	84.6 ± 4.9	84.2 ± 5.1	0.611
pH	7.28 ± 0.04	7.27 ± 0.05	0.212
$PaCO_2$ (mmHg)	62.8 ± 8.7	63.4 ± 9.1	0.641
PaO_2 (mmHg)	56.2 ± 8.5	55.4 ± 9.0	0.502
HCO_3^- (mmol/L)	29.4 ± 4.1	29.8 ± 4.3	0.408

SpO_2 – Peripheral Oxygen Saturation; $PaCO_2$ – Partial Pressure of Carbon Dioxide; PaO_2 – Partial Pressure of Oxygen; HCO_3^- – Bicarbonate.

Both HFNC and NIV resulted in improvement in arterial blood gas parameters after 24 hours of therapy. Baseline pH values were similar between groups; however, the NIV group demonstrated a greater improvement in pH at 24 hours (7.36 ± 0.04 vs 7.34 ± 0.05; p = 0.003). Similarly, $PaCO_2$ levels decreased in both groups but showed a significantly greater reduction with NIV (51.8 ± 7.2 mmHg) compared with HFNC (55.1 ± 7.6 mmHg) (p = 0.001). Oxygenation also improved in both groups, with PaO_2 increasing to 73.2 ± 8.8 mmHg in the NIV group and 70.6 ± 9.4 mmHg in the HFNC group (p = 0.024). These findings indicate that although both modalities improved gas exchange, NIV produced a more pronounced correction of hypercapnia and acidosis (Table 3).

Table 3: Changes in Arterial Blood Gas Parameters After 24 Hours of Respiratory Support

Parameter	HFNC (n=101)	NIV (n=102)	p value
	mean ± SD		
pH			
Baseline	7.28 ± 0.04	7.27 ± 0.05	0.211
24 hours	7.34 ± 0.05	7.36 ± 0.04	0.003
$PaCO_2$ (mmHg)			
Baseline	62.8 ± 8.7	63.4 ± 9.1	0.624
24 hours	55.1 ± 7.6	51.8 ± 7.2	0.001
PaO_2 (mmHg)			
Baseline	56.2 ± 8.5	55.4 ± 9.0	0.512
24 hours	70.6 ± 9.4	73.2 ± 8.8	0.024

$PaCO_2$ – Partial Pressure of Carbon Dioxide; PaO_2 – Partial Pressure of Oxygen.

Subgroup analysis demonstrated that treatment success declined with increasing severity of hypercapnia and COPD. Among patients with baseline $PaCO_2$ between 45–60 mmHg, treatment success rates were high and similar in both groups (87.5% for HFNC vs 90.9% for NIV; p = 0.605). In patients with $PaCO_2$ between 61–70 mmHg, success rates were 79.4% and 88.6%, respectively (p = 0.276).

In those with severe hypercapnia (>70 mmHg), success rates decreased further (60.0% with HFNC vs 73.5% with NIV; p = 0.221). A similar trend was observed across COPD severity categories. Treatment success remained high in GOLD II disease (90.0% vs 90.9%; p = 0.991) but declined in GOLD III (79.1% vs 88.6%; p = 0.202) and GOLD IV disease (63.2% vs 75.0%; p = 0.296) (Table 4).

Table 4: Treatment Success According to Baseline Hypercapnia and COPD Severity

Parameter	HFNC (n=101)	NIV (n=102)	p value
	Frequency (%)		
Baseline $PaCO_2$			
45–60 mmHg	28/32 (87.5%)	30/33 (90.9%)	0.605
61–70 mmHg	27/34 (79.4%)	31/35 (88.6%)	0.276
>70 mmHg	21/35 (60.0%)	25/34 (73.5%)	0.221
GOLD Stage			
GOLD II (Moderate)	18/20 (90.0%)	20/22 (90.9%)	0.991
GOLD III (Severe)	34/43 (79.1%)	39/44 (88.6%)	0.202
GOLD IV (Very severe)	24/38 (63.2%)	27/36 (75.0%)	0.296

GOLD – Global Initiative for Chronic Obstructive Lung Disease classification of COPD severity.

Overall clinical outcomes were broadly comparable between the two treatment modalities. Improvement without escalation of respiratory support occurred in 75.2% of patients treated with HFNC and 84.3% treated with NIV, although the difference was not statistically significant (p = 0.111).

However, the need for endotracheal intubation was significantly higher in the HFNC group (17.8%) compared with the NIV group (9.8%) (p = 0.009). The duration of respiratory support was slightly shorter with HFNC (38.4 ± 15.6 hours) compared with NIV (42.8 ± 18.2 hours), but the difference was not significant (p = 0.057). Similarly, length of hospital stay (6.2 ± 2.1 vs 6.6 ± 2.3 days; p = 0.108) and in-hospital mortality (6.9% vs 5.9%; p = 0.706) were comparable between the two groups.

Device-related complications differed between the treatment groups. Device intolerance was significantly higher in the NIV group (20.6%) compared with the HFNC group (7.9%) (p = 0.011).

Similarly, skin breakdown or pressure sores were more frequently observed in NIV patients (11.8%) compared with HFNC patients (1.0%) (p = 0.002). Gastric distension occurred exclusively in the NIV group (5.9%; p = 0.033). Conversely, nasal dryness or discomfort occurred slightly more often with HFNC (13.9%) than NIV (8.8%), though this difference was not statistically significant (p = 0.223). Importantly, patient-reported comfort scores were significantly higher in the HFNC group (7.8 ± 1.3) compared with the NIV group (6.2 ± 1.7) (p < 0.001) (Table 5).

Table 5: Clinical Outcomes and Device-Related Complications and Patient Comfort of HFNC and NIV Therapy

Variables	HFNC (n=101)	NIV (n=102)	p value
	Frequency (%)/mean ± SD		
Outcome			
Improvement without escalation	76 (75.2%)	86 (84.3%)	0.111
Need for intubation	18 (17.8%)	10 (9.8%)	0.009
Duration of respiratory support (hours)	38.4 ± 15.6	42.8 ± 18.2	0.057
Length of hospital stay (days)	6.2 ± 2.1	6.6 ± 2.3	0.108
In-hospital mortality	7 (6.9%)	6 (5.9%)	0.706
Complications			
Device intolerance	8 (7.9%)	21 (20.6%)	0.011
Nasal dryness/discomfort	14 (13.9%)	9 (8.8%)	0.223
Skin breakdown/pressure sores	1 (1.0%)	12 (11.8%)	0.002
Gastric distension	0 (0.0%)	6 (5.9%)	0.033
Patient-reported comfort score (1–10)	7.8 ± 1.3	6.2 ± 1.7	<0.001

Multivariate logistic regression analysis identified several significant predictors of treatment failure. Severe respiratory acidosis (baseline pH <7.25) was the strongest predictor (AOR 3.82; 95% CI 1.78–8.21; p = 0.001).

Marked hypercapnia ($PaCO_2$ >70 mmHg) was also significantly associated with failure (AOR 2.94; 95% CI 1.34–6.45; p = 0.007). In addition, tachypnea (respiratory rate >32 breaths/min) independently increased the risk of treatment failure (AOR 2.21; 95% CI 1.05–4.66; p = 0.033).

Other variables including age above 65 years, male sex, heavy smoking history, use of HFNC therapy, and presence of multiple comorbidities were not statistically significant predictors after adjustment (Table 6).

Table 6: Multivariate Logistic Regression Analysis of Predictors of Treatment Failure

Variable	Adjusted Odds Ratio (AOR)	95% CI	p value
Age (>65 years)	1.74	0.92 – 3.29	0.081
Male sex	1.21	0.56 – 2.61	0.612
Smoking history (>30 pack-years)	1.68	0.87 – 3.25	0.112
Baseline pH (<7.25)	3.82	1.78 – 8.21	0.001
$PaCO_2$ (>70 mmHg)	2.94	1.34 – 6.45	0.007
Respiratory rate (>32/min)	2.21	1.05 – 4.66	0.033
HFNC therapy (vs NIV)	1.69	0.82 – 3.49	0.115
≥2 comorbidities	1.57	0.76 – 3.23	0.202

AOR – Adjusted Odds Ratio; CI – Confidence Interval.

Discussion

Acute hypercapnic respiratory failure is a common and serious complication of acute exacerbations of chronic obstructive pulmonary disease (AECOPD), often requiring ventilatory support to improve gas exchange and reduce the work of breathing. While non-invasive ventilation (NIV) remains the recommended first-line therapy in such patients, high-flow nasal cannula (HFNC) has emerged as a promising alternative due to its physiological benefits and improved patient tolerance. The present study compared the clinical efficacy, physiological effects, and patient tolerance of HFNC and NIV in 203 patients with COPD-related acute hypercapnic respiratory failure.

In the present study, baseline demographic and clinical characteristics were comparable between the HFNC and NIV groups, including age, smoking exposure, duration of COPD, and comorbidities. The study population was predominantly male (approximately 78%), with a high prevalence of smoking history (>85%), which is consistent with epidemiological patterns of COPD reported in India and other developing countries in studies by Kuunder et al., Shinde et al.,and Sun et al., [13,14,15].

Similar demographic distributions have been reported in previous studies by Zhang et al., Grieco et al., and Leeies et al., evaluating ventilatory support in COPD exacerbations, where the majority of patients were older males with significant smoking exposure and multiple comorbidities [16,17,18].

Both HFNC and NIV significantly improved arterial blood gas parameters after initiation of therapy. However, NIV demonstrated a greater improvement in arterial pH and a more pronounced reduction in $PaCO_2$ levels after 24 hours of treatment. In our study, $PaCO_2$ decreased from 63.4 ± 9.1 mmHg to 51.8 ± 7.2 mmHg in the NIV group,

compared with 62.8 ± 8.7 mmHg to 55.1 ± 7.6 mmHg in the HFNC group, a difference that was statistically significant. This finding is consistent with the physiological mechanism of NIV, which provides positive pressure ventilation that directly augments alveolar ventilation, thereby facilitating more efficient carbon dioxide elimination [19,20]. Several previous studies by Koga et al., and Ovtcharenkoet al., have reported similar findings [21,22]. Studies by Bräunlich et al., and Ovtcharenkoet al., comparing HFNC with NIV in hypercapnic respiratory failure have demonstrated that NIV achieves a more rapid correction of respiratory acidosis and hypercapnia, particularly in patients with moderate to severe COPD exacerbations [20,22]. Marjanovic et al.,have also confirmed that NIV remains superior for reducing $PaCO_2$ levels due to its ability to provide inspiratory pressure support and improve tidal ventilation [23]. In contrast, HFNC primarily improves respiratory mechanics through high-flow oxygen delivery, washout of nasopharyngeal dead space, and generation of low-level positive airway pressure, which can reduce the work of breathing and improve oxygenation. In the present study, both modalities significantly improved PaO_2 levels after treatment; however, NIV achieved slightly higher oxygenation values at 24 hours. Similar observations have been reported in studies byColaianni-Alfonso et al., and Parrilla-Gómez et al., where HFNC improved oxygenation and respiratory comfort but had a comparatively smaller effect on carbon dioxide clearance than NIV [24,25].

An important finding of our study was the higher rate of endotracheal intubation in the HFNC group (17.8%) compared with the NIV group (9.8%), which was statistically significant. This suggests that although HFNC may improve respiratory parameters in many patients, NIV remains more effective in preventing progression to invasive mechanical ventilation in patients with acute hypercapnic respiratory failure [26]. Recent Meta-Analysis by Xu et al., evaluating HFNC in hypercapnic COPD patients have reported comparable trends [26]. For instance, comparative studies by Magdy et al., and Chakrabartiet al., have demonstrated that while HFNC can be effective in selected patients with mild to moderate hypercapnia, NIV generally provides lower treatment failure and intubation rates, particularly in patients with severe respiratory acidosis or advanced COPD [27,28]. Subgroup analysis in the present study further demonstrated that treatment success declined with increasing severity of hypercapnia and COPD. Patients with baseline $PaCO_2$ levels above 70 mmHg or GOLD stage IV disease showed lower success rates with both modalities, although NIV consistently demonstrated numerically better outcomes. These findings are clinically plausible, as severe hypercapnia reflects more profound ventilatory failure and respiratory muscle fatigue, conditions in which the pressure support provided by NIV is more effective than HFNC in improving alveolar ventilation [25,26]. Similar observations have been reported in previous studies by Parrilla-Gómez et al., and Magdy et al., where NIV showed greater efficacy in patients with severe respiratory acidosis or high $PaCO_2$ levels, whereas HFNC was more suitable for patients with milder forms of respiratory failure [25,27]. One of the most notable advantages of HFNC observed in our study was superior patient comfort and better tolerance compared with NIV. The HFNC group had significantly higher comfort scores and lower rates of device intolerance and interface-related complications. In contrast, NIV was associated with significantly higher rates of mask intolerance, pressure-related skin breakdown, and gastric distension, complications commonly reported with non-invasive ventilation [29,30]. These findings are consistent with earlier studiesby Mashad et al., and Haciosmanet al., demonstrating that HFNC is generally better tolerated due to the use of a nasal interface, heated humidified gas, and the absence of tight-fitting masks. Improved comfort may enhance patient compliance and facilitate prolonged use of respiratory support [31,32]. Another important observation from the present study was the identification of independent predictors of treatment failure. Multivariate analysis revealed that baseline pH <7.25, $PaCO_2$ >70 mmHg, and respiratory rate >32 breaths per minute were significant predictors of treatment failure. These findings are consistent with previously reported predictors of NIV failure in COPD exacerbations in studies by Solanki et al., Mashad et al., [30,31]. Severe acidosis and marked hypercapnia indicate advanced ventilatory failure and respiratory muscle fatigue, which may require more aggressive ventilatory support or early consideration of invasive mechanical ventilation. Recognition of these predictors is clinically important because it may help clinicians identify high-risk patients who require closer monitoring or early escalation of respiratory support [31,32].

Limitations

This study has certain limitations. Being a single-center study, the findings may have limited generalizability to other healthcare settings or populations. Allocation to HFNC or NIV was based on clinical decision rather than randomization, which may introduce selection bias. Additionally, long-term outcomes such as readmission rates, long-term mortality, and quality of life after discharge were not evaluated. The study also did not assess patient-reported dyspnea scores or

detailed ventilatory parameters, which could provide further insight into treatment response.

Conclusion

Both high-flow nasal cannula (HFNC) and non-invasive ventilation (NIV) improved gas exchange and clinical parameters in patients with COPD presenting with acute hypercapnic respiratory failure.

However, NIV demonstrated greater effectiveness in reducing $PaCO_2$ levels and significantly lowered the need for endotracheal intubation. In contrast, HFNC provided superior patient comfort and fewer interface-related complications. Treatment success decreased with increasing severity of hypercapnia and COPD, while severe acidosis, marked hypercapnia, and tachypnea were identified as predictors of treatment failure. Overall, NIV remains the preferred first-line ventilatory support in acute hypercapnic COPD exacerbations, while HFNC may serve as a useful alternative in selected patients, particularly those intolerant to NIV.

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