HIGH-FLOW NASAL CANNULA (HFNC) VERSUS BILEVEL POSITIVE AIRWAY PRESSURE IN ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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A comparative study was conducted on COPD patients receiving HFNC or BIPAP to compare the effectiveness of high-flow nasal cannula (HFNC) and bilevel positive airway pressure (BIPAP) in treating the exacerbation of chronic obstructive pulmonary disease (COPD) patients. Oxygen saturation stability, patient comfort, and CO_2 reduction were measured. Data included oxygen saturation levels, patient comfort scores, and $PaCO_2$ levels. Statistical analysis used were t-tests and correlation coefficients with significance at $p < 0.05$. BIPAP significantly improved oxygen saturation (94.28% ± 2.63) but had a higher comfort index (2.30 ± 1.36), indicating poorer machine tolerance. HFNC effectively reduced $PaCO_2$ from 54.14mmHg to 47.06mmHg over time and provided greater comfort, improving the comfort score from 1.92 to 0.17. BIPAP shows a marked improvement in maintaining oxygen saturation, but the comfort index is higher, and the machine tolerance is poorer. HFNC can effectively reduce pCO2 over the time while providing more comfort to the patient.

Keywords: COPD, respiratory support, HFNC, BIPAP, oxygenation, ventilation.

I. INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of mortality worldwide, accounting for more than 3 million deaths annually. Acute exacerbations of COPD not only significantly impair patients' quality of life but also substantially increase healthcare costs and mortality rates. Respiratory support improves respiratory failure and reduces hospital admissions and mortality rates in severe COPD exacerbations.[1,2]

Two commonly used respiratory support methods are High-Flow Nasal Cannula (HFNC) and Bilevel Positive Airway Pressure (BIPAP). BIPAP has been proven effective in improving blood gas parameters and reducing respiratory effort in COPD patients. However, some studies suggest that BIPAP may cause discomfort and may not consistently achieve optimal efficacy in all patients.[3] In recent years, HFNC has emerged as a potential alternative with several advantages, including delivering higher airflow, increasing patient comfort, and improving oxygenation without needing a high-pressure mask.[4]

However, there is still a lack of direct comparative studies on the effectiveness of HFNC and BIPAP in treating acute COPD exacerbations. A survey by Frat et al. demonstrated that HFNC can improve oxygenation without increasing the treatment failure rate in patients with acute respiratory failure due to heart failure.[5] Another study showed that HFNC can effectively support respiration, helping to reduce hypoxia during

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breathing in patients with respiratory failure.[6] Although these initial findings suggest positive potential, further studies are needed to determine the benefits and effectiveness of HFNC compared to BIPAP in treating acute COPD exacerbations.

This study aimed to compare the efficacy of high-flow nasal cannula (HFNC) and bilevel positive airway pressure (BiPAP) in patients with acute exacerbations of chronic obstructive pulmonary disease (COPD). Specific objectives were to evaluate improvements in oxygen saturation (SpO2), reduction in arterial partial pressure of carbon dioxide (PaCO2), patient level of comforts, and treatment success rates within 48 hours of initiating respiratory support. The study results will provide important scientific and practical insights for clinicians to select the most appropriate respiratory support method and optimize treatment effectiveness for patients with acute COPD exacerbations.

II. MATERIALS AND METHODS

1. Subjects

The study included hospitalized patients with acute exacerbation of chronic obstructive pulmonary disease (COPD) and moderate respiratory failure, eligible for non-invasive respiratory support based on clinical criteria (e.g., SpO_2 < 92%, $PaCO_2$ > 45mmHg).

Inclusion criteria

Patients diagnosed with COPD according to GOLD criteria, experiencing an acute exacerbation (increased dyspnea, increased sputum production, or sputum color changes), and having moderate respiratory failure. Moderate exacerbation classification based on the Rome proposal:

Patients meeting at least three out of five criteria:

(1) Dyspnea VAS score ≥ 5.

(2) Respiratory rate ≥ 24 breaths per minute.

(3) Heart rate ≥ 95 beats per minute.

(4) SpO_2 < 92% on room air (or the patient's usual oxygen dose) AND/OR a decrease of >3% (if previously known).

(5) CRP ≥ 10 mg/L.

If arterial blood gas analysis was performed: PaO_2 ≤ 60mmHg and/or $PaCO_2$ > 45mmHg without respiratory acidosis.

Exclusion criteria

Patients were excluded if they had a history of prolonged non-invasive ventilation (NIV), acute failure of more than two organs, cardiac or respiratory arrest, unstable cardiovascular disorders, impaired consciousness, pneumothorax, anatomical abnormalities of the nasopharynx that hinder HFNC/BiPAP use, or if they refused to participate in the study.

2. Methods

Study design: This is a randomized controlled trial (RCT) comparing the efficacy of high-flow nasal cannula (HFNC) and bilevel positive airway pressure (BiPAP) in COPD patients with acute exacerbations.

Sample size and sampling method

The sample size (n = 176) was calculated to detect a 15% difference in treatment success rates (HFNC vs. BiPAP) with 80% power and alpha of 0.05, based on prior studies (e.g., Frat et al., 2015). Eligible patients were randomly assigned to HFNC or BiPAP groups using a sealed envelope method to ensure unbiased allocation.

Randomization method

A total of 176 sealed envelopes, each containing a numbered slip (1 – 176), were prepared by the principal investigator, who oversaw randomization. Patients were assigned to HFNC (n = 88) or BiPAP (n = 88) based on the sequence of drawn envelopes. These envelopes were placed in a container, and 88 envelopes were randomly drawn. The order of these 88 envelopes determined the sequence

of patients assigned to the HFNC group (Group 1). The remaining 88 envelopes determined the sequence of patients assigned to the BiPAP group (Group 2).

Study Parameters and Content

Arterial blood gas parameters: FiO_2, PaO_2, $PaCO_2$, SpO_2.

Vital signs: Respiratory rate, heart rate, blood pressure.

Primary outcomes included improvement in SpO_2 (target ≥ 92%), reduction in $PaCO_2$ (< 45mmHg), and patient comfort score (0 – 5 scale, 0 = maximum comfort). Secondary outcomes included respiratory rate, heart rate, and treatment failure rate (need for intubation or escalation). Patient comfort was assessed via a standardized questionnaire at 2, 12, 24, and 48 hours.

Clinical symptoms: Dyspnea severity, breathing level of comfort, respiratory effort signs.

Patient comfort: A 6-point scale (0: very comfortable to 5: very uncomfortable), based on patient self-report after respiratory support. The scale was explained by trained medical staff before scoring.

Treatment efficacy and failure rate: Evaluated based on oxygenation improvement and respiratory stability after applying HFNC or BiPAP within the first 24 hours.

Study Procedure

Following initial assessment, patients were randomized to HFNC (flow rate 30 – 60 L/min, FiO_2 titrated to SpO_2 ≥ 92%) or BiPAP (IPAP 10 – 20cmH_2O, EPAP 4 – 8cmH_2O, adjusted per patient tolerance). Parameters were recorded at 2, 12, 24, and 48 hours. Treatment failure (e.g., intubation) was documented. After respiratory support initiation, blood gas and vital sign parameters were recorded at 2 hours, 12 hours, 24 hours, and 48 hours. Any complications or signs of treatment failure were fully documented throughout the study. Treatment failure was defined as the need for intubation due to persistent hypoxemia (SpO_2 < 88% despite maximum support), worsening hypercapnia ($PaCO_2$ > 60mmHg with pH < 7.25), or signs of impending respiratory arrest.

Data analysis

Data were analyzed using independent t-tests for continuous variables (e.g., SpO_2, $PaCO_2$) and chi-square tests for categorical variables (e.g., treatment success rates), with significance set at $p < 0.05$. Descriptive statistics (means, SD) were also reported.

3. Research ethics

All patients were fully informed about the study's objectives, methods, and their rights before participation. They were required to sign a written informed consent form before enrolling in the study.

The study was approved by the Biomedical Ethics Committee of Hanoi Medical University (Approval number: 841GCN-HDDDNCYSH-DHYHN, dated May 11, 2023).

III. RESULTS

Table 1. Study population characteristics

Characteristics	HFNC (n = 88)	BIPAP (n = 88)	Total (n = 176)
Mean age (SD)	70.8 (10.2)	73.5 (8.8)	72.1 (9.6)
Male (%)	55.7%	68.2%	61.9%
Body mass index (BMI)	23.5 (3.2)	24.1 (3.5)	23.8 (3.4)
Smoking history (%)	85%	55%	70%
Comorbidity rate (%)	55%	40%	47.50%

Table 1 showed that the average age in the BiPAP group (73.5 ± 8.8 years) was higher than in the HFNC group (70.8 ± 10.2 years), but the difference was not significant (p = 0.08, independent t-test). The proportion of males was higher in the BIPAP group. The average BMI was similar between the two groups. The smoking history rate and the comorbidity rate were both higher in the HFNC group than in the BIPAP group.

Table 2. General clinical parameters by COPD group

Clinical parameters	HFNC (n = 88)	BIPAP (n = 88)	p value*
	Mean (SD)		
Fraction of inspired oxygen (FiO_2) (%)	28.20 (4.31)	30.99 (4.34)	0.01
Blood (pH)	7.42 (0.14)	7.41 (0.04)	0.52
Partial pressure of CO_2 in arterial blood ($PaCO_2$) (mmHg)	50.26 (9.07)	53.13 (9.15)	0.03
Bicarbonate concentration (HCO_2) (mEq/L)	32.89 (5.64)	34.18 (4.49)	0.04
Oxygen saturation (SpO_2) (%)	92.91 (6.97)	94.28 (2.63)	0.02
Heart rate (beats/min)	97.29 (11.39)	99.28 (11.19)	0.09
Systolic blood pressure (mmHg)	127.29 (12.56)	129.89 (7.80)	0.07
Diastolic blood pressure (mmHg)	70.77 (9.20)	73.24 (6.84)	0.06
Respiratory rate (breaths/min)	24.00 (10.31)	23.90 (1.82)	0.93
Patient level of comfort (scale 0-5)	0.76 (0.84)	2.30 (1.36)	0.01

** independent t-tests*

Table 2 showed that the FiO_2 (p = 0.01), $PaCO_2$ (p = 0.03), bicarbonate concentration (p = 0.04), SpO_2 (p = 0.02), heart rate (p = 0.09), systolic (p = 0.07), and diastolic blood pressure (p = 0.06) were higher in the BiPAP group than in the HFNC group, with significant differences for FiO_2, $PaCO_2$, bicarbonate, and level of comfort SpO_2 (p < 0.05, independent t-tests).

Table 3. Comparison of clinical parameters over time (T0 to T5, n=176)

Clinical parameters	T0	T1	T2	T3	T4	T5
FiO_2 (%)	28.80 (4.69)	28.90 (4.77)	28.86 (3.24)	28.80 (4.30)	28.23 (4.32)	25.63 (3.40)
Blood pH	7.43 (0.08)	7.42 (0.05)	7.41 (0.04)	7.40 (0.32)	7.44 (0.04)	7.43 (0.03)
$PaCO_2$ (mmHg)	54.14 (10.40)	50.94 (9.97)	50.21 (9.05)	49.83 (8.32)	49.39 (8.77)	47.06 (5.99)
HCO_2 (mEq/L)	34.21 (6.45)	32.70 (6.49)	32.44 (5.77)	33.12 (5.82)	32.97 (4.75)	31.91 (4.01)

Clinical parameters	T0	T1	T2	T3	T4	T5
SpO_2 (%)	88.52 (7.09)	92.73 (1.46)	94.08 (1.21)	94.49 (1.33)	93.76 (10.31)	94.00 (10.32)
Heart rate (beats/min)	110.59 (10.16)	103.83 (8.68)	97.75 (6.59)	93.64 (6.40)	90.51 (7.67)	87.44 (9.14)
Systolic blood pressure (mmHg)	132.08 (14.70)	129.19 (10.85)	126.51 (8.76)	126.64 (9.74)	125.33 (14.31)	123.99 (14.26)
Diastolic blood pressure (mmHg)	75.23 (9.82)	71.73 (10.33)	69.03 (7.80)	70.25 (8.38)	69.46 (8.60)	68.91 (8.65)
Respiratory rate (breaths/min)	27.02 (1.36)	24.47 (1.01)	25.50 (21.32)	22.49 (1.04)	22.45 (7.80)	22.00 (7.80)
Patient level of comfort (scale 0-5)	1.92 (0.57)	1.20 (0.53)	0.90 (0.48)	0.31 (0.53)	0.17 (0.55)	0.17 (0.55)

Table 3 showed that FiO_2 and HCO_2 levels gradually decreased over time. $PaCO_2$, heart rate, systolic and diastolic blood pressure, and respiratory rate also showed a decreasing trend. SpO_2 increased significantly from T0 to T3 and then stabilized. Blood pH remained relatively stable throughout. Patient level of comfort improved significantly over time, with the highest level of comfort recorded at T4 and T5.

Table 4. Changes in clinical parameters over time between COPD groups (HFNC vs. BIPAP)

Clinical parameters	HFNC (n = 88)	BIPAP (n = 88)	Comparison between COPD groups
FiO_2 (%)	28.80 -> 25.63	31.55 -> 30.59	BIPAP maintained higher FiO_2 levels with less variation
Blood pH	7.43 -> 7.43	7.40 -> 7.42	Both groups maintained stable pH
$PaCO_2$ (mmHg)	54.14 -> 47.06	55.97 -> 51.50	HFNC showed a greater reduction in $PaCO_2$
HCO_3 (mEq/L)	34.21 -> 31.91	34.88 -> 34.23	HFNC had a more significant reduction in HCO_3
SpO_2 (%)	88.52 -> 94.00	91.61 -> 95.41	Both groups improved SpO_2, with BIPAP achieving higher levels
Heart rate (beats/min)	110.59 -> 87.44	112.72 -> 92.55	HFNC showed a more rapid decrease in heart rate
Systolic blood pressure (mmHg)	132.08 -> 123.99	132.32 -> 129.31	HFNC had a more significant drop in systolic blood pressure

Clinical parameters	HFNC (n = 88)	BIPAP (n = 88)	Comparison between COPD groups
Diastolic blood pressure (mmHg)	75.23 -> 68.91	76.55 -> 71.68	HFNC had a more pronounced reduction in diastolic blood pressure
Respiratory rate (breaths/min)	27.02 -> 22.00	26.07 -> 23.03	HFNC showed a greater reduction in respiratory rate
Patient level of comfort (scale 0-5)	1.92 -> 0.17	3.20 -> 1.69	BIPAP had a higher level of comfort, but both groups showed improvement

Table 4 showed that BIPAP maintained higher FiO_2 levels with less variation, while HFNC showed a greater reduction in $PaCO_2$, HCO_2, heart rate, and blood pressure. SpO_2 improved in both groups, with BIPAP achieving higher levels. Respiratory rate decreased more in the HFNC group. Patient comfort improved in both groups, but BIPAP had a consistently higher level of comfort.

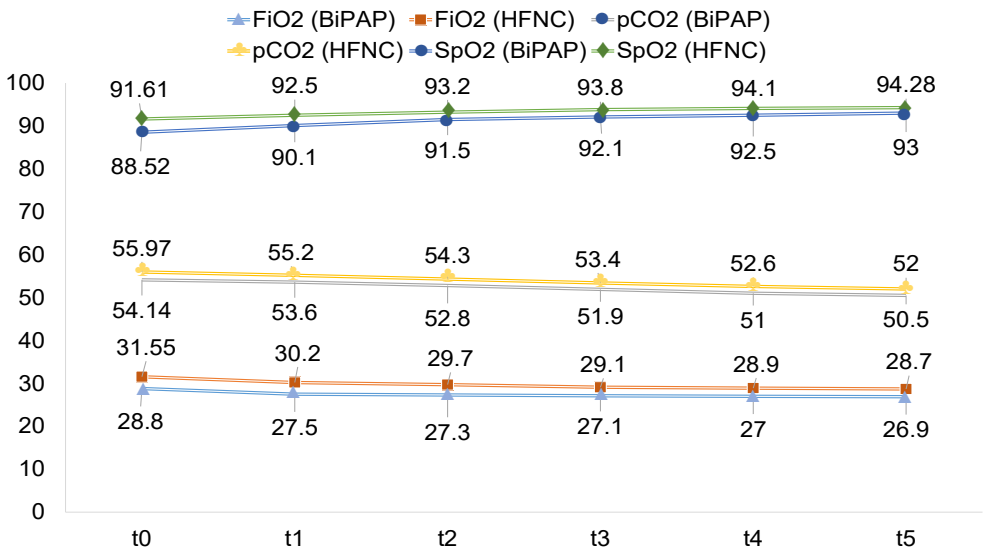

Chart 1. Changes in blood gas and vital signs over Time

Figure 1 illustrated that the SpO_2 levels increased steadily over time in both groups, with BIPAP consistently achieving higher values than HFNC. $PaCO_2$ levels decreased more noticeably in the HFNC group than in the BIPAP group. FiO_2 levels remained relatively stable, but BIPAP maintained higher values throughout the observation period.

IV. DISCUSSION

This study's results highlight the differences in the effectiveness of two non-invasive respiratory support methods, HFNC and BIPAP, regarding respiratory and circulatory parameters in patients with chronic obstructive pulmonary disease (COPD). The improvement

in oxygen saturation (SpO_2) in the BiPAP group was significantly more stable compared to the HFNC group ($p = 0.02$, independent t-test), likely due to BiPAP's continuous positive airway pressure mechanism. This can be explained by the continuous positive airway pressure mechanism of BIPAP, which enhances gas exchange and optimizes blood oxygenation. According to Xie et al., BIPAP has been proven effective in improving oxygen saturation, reducing the risk of respiratory failure, and preventing hypoxemia in COPD patients.[7] The stability of SpO_2 in the BIPAP group reflects a better response to patients' oxygen demands, contributing to improved treatment quality and a reduced risk of complications related to hypoxemia.

On the other hand, HFNC demonstrated an advantage in reducing $PaCO_2$ compared to BIPAP. This mechanism can be attributed to the high gas flow provided by HFNC, which enhances ventilation, facilitates CO_2 removal from the airways, and improves CO_2 elimination. A study by Rittayamai et al. also emphasized that HFNC effectively reduces CO_2 levels by generating high gas flow, decreasing physiological dead space, and promoting more efficient ventilation.[8] Reducing $PaCO_2$ is crucial in preventing respiratory acidosis, aiding COPD patients improve alveolar ventilation, and minimizing distressing respiratory symptoms.

The difference in FiO_2 levels between the two groups is also noteworthy. The BIPAP group maintained stable FiO_2 levels, reflecting more effective oxygen delivery and better treatment control. This stability may be due to BIPAP's continuous positive airway pressure mechanism, which improves synchronization between the patient's breathing and the ventilator, thereby optimizing oxygen uptake. In contrast, the HFNC group showed a gradual decrease in FiO_2, suggesting that the high gas flow of HFNC allows patients to self-regulate their oxygen needs while reducing the risk of dependence on ventilator-supplied oxygen.

The gradual decrease in respiratory rate in both groups may indicate an improvement in patients' respiratory status. According to a study by Lee et al., HFNC and BIPAP help reduce respiratory workload, decrease breathing effort, and alleviate discomfort during respiration. This effect is evident in the progressive reduction in respiratory rate over time in both treatment groups.[9] Additionally, the gradual decrease in the comfort score in both groups suggests improved respiratory sensation as patients adapted better to the applied respiratory support method over time.

From a circulatory perspective, systolic and diastolic blood pressure and heart rate gradually decreased in both groups, reflecting more excellent circulatory stability as patients' respiratory conditions improved. This finding aligns with the study by McEvoy et al., which demonstrated that reducing respiratory load alleviates cardiovascular strain, particularly in severe COPD patients who often experience pulmonary hypertension and right heart failure.[10] Reducing heart rate and blood pressure is clinically significant in managing cardiovascular complications in COPD patients, especially those requiring non-invasive respiratory support. This improvement helps reduce the risk of cardiac strain and related complications, enhancing overall cardiopulmonary stability in these patients.

The study results also indicate that comfort scores gradually decreased in both groups, with the BIPAP group reporting higher comfort levels. This suggests that BIPAP may provide greater ease, likely due to its adjustable pressure support, which helps reduce breathing

discomfort. According to a study by Rochwerg et al., BIPAP helps alleviate respiratory stress, enhances patient comfort, and improves treatment adherence. However, HFNC also offers advantages, particularly for patients with milder respiratory failure, as it maintains comfort throughout treatment.[11]

In summary, this study highlights the differences in the mechanisms and effectiveness of the two non-invasive respiratory support methods, HFNC and BIPAP. HFNC is more effective in reducing CO_2 levels and supporting ventilation, particularly in patients who can maintain independent breathing and good consciousness levels. BIPAP, on the other hand, is more suitable for patients requiring higher respiratory support, as it provides more stable oxygen delivery and improves oxygen saturation. These findings have important clinical implications for personalizing treatment strategies for COPD patients, optimizing treatment efficacy, and minimizing complications. Future studies should focus on evaluating the long-term effectiveness of each method while also considering factors such as treatment adherence and patient quality of life after receiving non-invasive respiratory support.

V. CONCLUSION

This randomized controlled trial compared HFNC and BiPAP in COPD patients with acute exacerbations. The BiPAP group demonstrated significantly higher oxygen saturation (SpO_2, $p = 0.02$) but higher discomfort scores ($p < 0.01$), indicating poorer device tolerance. Conversely, HFNC significantly reduced arterial partial pressure of carbon dioxide ($PaCO_2$, $p = 0.01$) and improved patient comfort ($p < 0.01$), making it effective for ventilation support in moderate respiratory failure.

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