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High-Flow Nasal Oxygen versus Non-Invasive Ventilation in Acute Hypoxemic Respiratory Failure: A Comparative Study

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ABSTRACT

Introduction: Acute hypoxemic respiratory failure (AHRF) is a common cause of intensive care unit admission and is associated with significant morbidity and mortality. High-Flow Nasal Oxygen (HFNO) has emerged as an alternative to Non-Invasive Ventilation (NIV) by providing heated, humidified oxygen at high flow rates with improved patient comfort and physiological benefits. The present study compared the clinical effectiveness, physiological response, treatment outcomes, and device-related complications of HFNO and NIV in patients with acute hypoxemic respiratory failure.

Materials and Methods: This prospective comparative observational study was conducted over one year from May 2024 to May 2025 and included 150 adult patients with acute hypoxemic respiratory failure. Patients were managed with either HFNO (n=75) or NIV (n=75) according to institutional treatment protocols. Baseline demographic characteristics, physiological parameters, SOFA and APACHE II scores were recorded. Clinical response, oxygenation indices, respiratory parameters, requirement for endotracheal intubation, duration of ICU and hospital stay, mortality, successful weaning, and device-related complications were evaluated. Data were analyzed using SPSS version 26.0, with a p-value <0.05 considered statistically significant.

Results: Baseline demographic and clinical characteristics were comparable between the two groups. HFNO demonstrated significantly greater improvement in respiratory rate, oxygen saturation, PaO_2/FiO_2 ratio, and dyspnea score during the early treatment period (all $p<0.05$). Patients receiving HFNO had significantly shorter ICU stay (6.3 ± 2.9 vs. 7.8 ± 3.5 days; $p=0.006$) and hospital stay (10.8 ± 4.3 vs. 12.5 ± 5.1 days; $p=0.031$). Although intubation, successful weaning, ICU mortality, and hospital mortality favored the HFNO group, these differences were not statistically significant. HFNO was associated with significantly fewer device-related complications and better patient tolerance than NIV.

Conclusion: HFNO provided superior early physiological improvement, shorter ICU and hospital stay, and significantly better tolerability compared with NIV while maintaining comparable rates of intubation and mortality. HFNO may therefore be considered an effective first-line non-invasive respiratory support strategy for appropriately selected patients with acute hypoxemic respiratory failure.

Keywords: *Acute hypoxemic respiratory failure; High-flow nasal oxygen; Non-invasive ventilation; Oxygen therapy; Intensive care.*

INTRODUCTION

Acute hypoxemic respiratory failure (AHRF) is a common medical emergency encountered in emergency departments and intensive care units and is associated with substantial morbidity and mortality [1]. It is characterized by severe impairment of oxygenation resulting from various underlying conditions such as pneumonia, acute respiratory distress syndrome (ARDS), sepsis, pulmonary edema, and other diffuse parenchymal lung diseases [2]. Prompt recognition and appropriate respiratory support are essential to improve oxygenation, reduce the work of breathing, prevent respiratory muscle fatigue, and avoid progression to invasive mechanical ventilation, which carries additional risks including ventilator-associated pneumonia, prolonged intensive care unit (ICU) stay, and increased mortality [3].

Non-invasive ventilation (NIV) has long been used as a first-line modality for managing selected patients with acute respiratory failure by improving alveolar ventilation and reducing respiratory effort [4,5]. However, its effectiveness in patients with de novo hypoxemic respiratory failure remains variable, with treatment failure frequently related to poor patient tolerance, discomfort from the mask interface, air leaks, gastric insufflation, and delayed recognition of clinical deterioration [6]. These limitations have prompted the exploration of alternative non-invasive oxygen delivery systems that provide effective respiratory support while improving patient comfort and compliance [7].

High-flow nasal oxygen (HFNO) has emerged as an effective modality for delivering heated and humidified oxygen at high flow rates with precise control of the inspired oxygen concentration [8]. By generating a low level of positive airway pressure, reducing anatomical dead space, improving mucociliary clearance, and meeting patients' inspiratory flow demands, HFNO enhances oxygenation while remaining well tolerated [9,10]. Several clinical studies have demonstrated favorable physiological effects and improved patient comfort with HFNO, although evidence comparing its effectiveness with NIV in patients with acute hypoxemic respiratory failure continues to evolve, with varying results regarding intubation rates, mortality, and other clinical outcomes [11-13].

Given the increasing use of HFNO in routine clinical practice and the ongoing uncertainty regarding its comparative benefits over NIV, further evaluation of these modalities is warranted. The present study aimed to compare the clinical effectiveness, physiological response, treatment outcomes, and device-related complications of High-Flow Nasal Oxygen and Non-Invasive Ventilation in adult patients with acute hypoxemic respiratory failure.

MATERIALS AND METHODS

This prospective comparative observational study was conducted in the Department of Respiratory Medicine and Intensive Care over a period of one year, from May 2024 to May 2025. The study included 150 adult patients diagnosed with acute hypoxemic respiratory failure (AHRF) who required non-invasive respiratory support and fulfilled the predefined eligibility criteria. Eligible patients were allocated to receive either High-Flow Nasal Oxygen (HFNO) (n=75) or Non-Invasive Ventilation (NIV) (n=75) as the initial mode of oxygen therapy based on the treating physician's clinical judgment and institutional treatment protocol. Written informed consent was obtained from all participants or their legally authorized representatives prior to enrolment. Institutional Ethics Committee approval was obtained before commencement of the study.

Adult patients (≥18 years) presenting with acute hypoxemic respiratory failure, defined by clinical features of respiratory distress with hypoxemia requiring advanced oxygen support, were included in the study. Patients with hypercapnic respiratory failure requiring immediate invasive mechanical ventilation, hemodynamic instability requiring vasopressor support, altered sensorium impairing airway protection, facial trauma preventing the use of NIV or HFNO interfaces, do-not-intubate orders, pregnancy, or refusal to participate were excluded. Baseline demographic data, including age, sex, body mass index, smoking status, and associated comorbidities such as diabetes mellitus, hypertension, chronic kidney disease, and coronary artery disease, were recorded for all participants.

Clinical assessment was performed at admission and throughout hospitalization. Baseline physiological parameters including respiratory rate, heart rate, peripheral oxygen saturation (SpO_2), arterial blood gas analysis (PaO_2), PaO_2/FiO_2 ratio, Sequential Organ Failure Assessment (SOFA) score, and Acute Physiology and Chronic Health Evaluation II (APACHE II) score were documented before initiation of respiratory support. Following initiation of HFNO or NIV, respiratory rate, oxygen saturation, PaO_2/FiO_2 ratio, and dyspnea score were reassessed at predefined intervals, including 1 hour and 6 hours, to evaluate early physiological response. Patients were monitored for the need for endotracheal intubation, duration of intensive care unit (ICU) stay, duration of hospital stay, successful weaning from respiratory support, ICU mortality, hospital mortality, and device-related complications including facial skin breakdown, claustrophobia, poor tolerance, gastric distension, air leak, and nasal dryness.

All collected data were entered into Microsoft Excel and analyzed using 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 HFNO and NIV groups were performed using the independent Student's *t*-test for continuous variables and the Chi-

square test or Fisher's exact test for categorical variables, as appropriate. Multivariable logistic regression analysis was performed to identify independent predictors of treatment failure, with results expressed as adjusted odds ratios (ORs) and 95% confidence intervals (CIs). A two-tailed *p* value of <0.05 was considered statistically significant.

RESULTS

A total of 150 patients with acute hypoxemic respiratory failure were enrolled and equally allocated to the HFNO group (n=75) and the NIV group (n=75). The mean age of participants was comparable between the HFNO and NIV groups (58.6 ± 13.4 vs. 59.9 ± 12.8 years; p=0.562). Males constituted the majority of patients in both groups (61.3% vs. 64.0%). There were no statistically significant differences in body mass index or the prevalence of major comorbidities, including diabetes mellitus, hypertension, chronic kidney disease, coronary artery disease, and smoking history (all p>0.05), indicating that the two groups were well matched at baseline. (Table 1)

Table 1. Baseline demographic and clinical characteristics of the study participants

Variable	HFNO (n=75)	NIV (n=75)	P value
Age (years), Mean ± SD	58.6 ± 13.4	59.9 ± 12.8	0.562
Male, n (%)	46 (61.3)	48 (64.0)	0.734
Female, n (%)	29 (38.7)	27 (36.0)	
BMI (kg/m²), Mean ± SD	25.4 ± 3.7	25.8 ± 4.0	0.608
Diabetes mellitus, n (%)	28 (37.3)	31 (41.3)	0.618
Hypertension, n (%)	35 (46.7)	38 (50.7)	0.626
Chronic kidney disease, n (%)	8 (10.7)	10 (13.3)	0.612
Coronary artery disease, n (%)	11 (14.7)	13 (17.3)	0.663
Smoking history, n (%)	27 (36.0)	30 (40.0)	0.614

Baseline physiological and disease severity parameters were similar between the two treatment groups. The mean respiratory rate, heart rate, oxygen saturation (SpO_2), arterial oxygen tension (PaO_2), PaO_2/FiO_2 ratio, SOFA score, and APACHE II score did not differ significantly between patients receiving HFNO and those receiving NIV (all p>0.05), confirming comparable clinical severity prior to initiation of respiratory support. (Table 2)

Table 2. Baseline clinical and respiratory parameters

Variable	HFNO (n=75)	NIV (n=75)	P value
Respiratory rate (breaths/min)	31.2 ± 4.5	30.8 ± 4.8	0.581
Heart rate (beats/min)	108.6 ± 15.7	110.2 ± 16.4	0.544
SpO_2 (%)	86.3 ± 4.1	86.8 ± 4.5	0.472
PaO_2 (mmHg)	57.6 ± 8.2	58.4 ± 7.8	0.519
PaO_2/FiO_2 ratio	132.5 ± 34.8	134.8 ± 36.2	0.691
SOFA score	5.6 ± 2.1	5.8 ± 2.3	0.633
APACHE II score	17.8 ± 4.6	18.1 ± 4.9	0.741

Patients treated with HFNO demonstrated significantly greater improvement in respiratory parameters following initiation of therapy. Compared with the NIV group, the HFNO group exhibited lower respiratory rates at both 1 hour (26.5 ± 3.8 vs. 27.8 ± 4.1 breaths/min; p=0.041) and 6 hours (22.3 ± 3.4 vs. 24.5 ± 3.8 breaths/min; p=0.001). Furthermore, HFNO resulted in significantly higher oxygen saturation (95.7 ± 2.4% vs. 94.2 ± 2.8%; p=0.002), improved PaO_2/FiO_2 ratio (218.4 ± 48.6 vs. 198.5 ± 44.8; p=0.010), and greater improvement in dyspnea scores (4.3 ± 1.2 vs. 3.7 ± 1.3; p=0.008), indicating superior early physiological response. (Table 3)

Table 3. Comparison of respiratory parameters following initiation of therapy

Variable	HFNO (n=75)	NIV (n=75)	P value
Respiratory rate at 1 hour (breaths/min)	26.5 ± 3.8	27.8 ± 4.1	0.041
Respiratory rate at 6 hours (breaths/min)	22.3 ± 3.4	24.5 ± 3.8	0.001
SpO_2 at 6 hours (%)	95.7 ± 2.4	94.2 ± 2.8	0.002
PaO_2/FiO_2 ratio at 6 hours	218.4 ± 48.6	198.5 ± 44.8	0.010
Dyspnea score improvement	4.3 ± 1.2	3.7 ± 1.3	0.008

Although the proportions of patients requiring endotracheal intubation (21.3% vs. 32.0%), ICU mortality (14.7% vs. 20.0%), hospital mortality (16.0% vs. 21.3%), and successful weaning from respiratory support (78.7% vs. 68.0%) favored the HFNO group, these differences did not reach statistical significance (all p>0.05). However, patients managed with HFNO experienced significantly shorter ICU stays (6.3 ± 2.9 vs. 7.8 ± 3.5 days; p=0.006) and shorter overall hospital stays (10.8 ± 4.3 vs. 12.5 ± 5.1 days; p=0.031) compared with those receiving NIV. (Table 4)

Table 4. Clinical outcomes in the two study groups

Outcome	HFNO (n=75)	NIV (n=75)	P value
Endotracheal intubation, n (%)	16 (21.3)	24 (32.0)	0.139
ICU mortality, n (%)	11 (14.7)	15 (20.0)	0.390
Hospital mortality, n (%)	12 (16.0)	16 (21.3)	0.404
ICU stay (days), Mean ± SD	6.3 ± 2.9	7.8 ± 3.5	0.006
Hospital stay (days), Mean ± SD	10.8 ± 4.3	12.5 ± 5.1	0.031
Successful weaning from respiratory support, n (%)	59 (78.7)	51 (68.0)	0.138

HFNO was associated with significantly fewer device-related adverse events than NIV. Facial skin breakdown, claustrophobia, poor tolerance requiring interruption of therapy, gastric distension, and air leak occurred significantly less frequently in the HFNO group than in the NIV group (all $p<0.05$). Although nasal dryness was observed more commonly with HFNO (13.3% vs. 6.7%), the difference was not statistically significant ($p=0.177$). These findings suggest that HFNO was better tolerated than NIV. (Table 5)

Table 5. Device-related complications and adverse events

Complication	HFNO (n=75)	NIV (n=75)	P value
Facial skin breakdown, n (%)	2 (2.7)	15 (20.0)	<0.001
Claustrophobia, n (%)	3 (4.0)	17 (22.7)	<0.001
Poor tolerance requiring interruption, n (%)	6 (8.0)	18 (24.0)	0.008
Gastric distension, n (%)	1 (1.3)	8 (10.7)	0.034
Air leak, n (%)	0 (0.0)	5 (6.7)	0.022
Nasal dryness, n (%)	10 (13.3)	5 (6.7)	0.177

Multivariable logistic regression identified an APACHE II score greater than 20 (adjusted OR=3.21, 95% CI: 1.42–7.18; $p=0.005$) and a baseline PaO_2/FiO_2 ratio below 120 (adjusted OR=2.87, 95% CI: 1.28–6.42; $p=0.010$) as independent predictors of treatment failure. Increasing age, diabetes mellitus, and use of NIV instead of HFNO were not independently associated with treatment failure after adjustment for confounding variables (all $p>0.05$). (Table 6)

Table 6. Multivariable logistic regression analysis for predictors of treatment failure

Variable	Adjusted Odds Ratio	95% Confidence Interval	P value
APACHE II score >20	3.21	1.42–7.18	0.005
PaO_2/FiO_2 ratio <120	2.87	1.28–6.42	0.010
Age >65 years	1.69	0.83–3.42	0.152
Diabetes mellitus	1.34	0.65–2.75	0.426
NIV (vs HFNO)	1.74	0.89–3.38	0.104

DISCUSSION

The present study compared the effectiveness of High-Flow Nasal Oxygen (HFNO) and Non-Invasive Ventilation (NIV) in 150 patients with acute hypoxemic respiratory failure. Both groups were comparable with respect to baseline demographic characteristics, comorbidities, physiological parameters, and disease severity scores, thereby minimizing baseline confounding. Our findings demonstrated that HFNO resulted in significantly greater improvement in oxygenation and respiratory parameters during the initial hours of therapy, with significantly higher SpO_2 and PaO_2/FiO_2 ratios and lower respiratory rates compared with NIV. These physiological benefits can be attributed to the ability of HFNO to deliver heated and humidified oxygen at high flow rates, reduce anatomical dead space, improve mucociliary clearance, and generate a low level of positive airway pressure. Similar findings were reported by Frat et al. in the landmark FLORALI trial, which demonstrated superior oxygenation, improved patient comfort, and reduced respiratory effort with HFNO compared with NIV and conventional oxygen therapy in patients with acute hypoxemic respiratory failure [14]. Likewise, a recent systematic review and network meta-analysis by Okano H et al. supported the role of HFNO as an effective non-invasive respiratory support strategy, particularly in improving physiological outcomes in selected patients with de novo hypoxemic respiratory failure [15].

Although lower rates of endotracheal intubation, ICU mortality, hospital mortality, and higher rates of successful weaning were observed in the HFNO group, these differences did not achieve statistical significance. However, HFNO was associated with significantly shorter ICU and hospital stays, suggesting more rapid clinical recovery and earlier stabilization. These findings are broadly consistent with the FLORALI study, where HFNO did not significantly reduce overall intubation rates but demonstrated improved survival among patients with more severe hypoxemia [14]. Similarly, Pan JT et al. reported that non-invasive respiratory support strategies, including HFNO, may reduce progression to invasive mechanical ventilation in appropriately selected patients, although mortality benefits remain inconsistent across studies because of variations in patient populations, disease severity, and treatment protocols [16]. Therefore, our

findings further support the use of HFNO as an effective first-line respiratory support modality without compromising important clinical outcomes.

An important observation in the present study was the significantly better tolerability of HFNO compared with NIV. Patients receiving HFNO experienced substantially fewer device-related complications, including facial skin breakdown, claustrophobia, poor tolerance, gastric distension, and air leaks, while the incidence of nasal dryness was low and comparable between groups. Improved comfort and interface tolerance have consistently been recognized as major advantages of HFNO over mask-based NIV, facilitating prolonged uninterrupted therapy and potentially improving treatment adherence. Similar observations were reported by Frat et al. and have been reaffirmed in subsequent systematic reviews, which consistently demonstrated higher patient comfort and fewer interface-related adverse events with HFNO than with NIV [14]. Better tolerance may also contribute to reduced nursing interventions and greater patient acceptance in routine intensive care practice.

Multivariable logistic regression analysis in the present study identified an APACHE II score greater than 20 and a baseline PaO_2/FiO_2 ratio below 120 as independent predictors of treatment failure, emphasizing that underlying disease severity remains a stronger determinant of clinical outcome than the choice of non-invasive respiratory support alone. This finding is consistent with previous studies demonstrating that severe hypoxemia and higher illness severity scores are associated with an increased likelihood of intubation and mortality despite optimal non-invasive respiratory support [14-16]. Overall, the present study adds to the growing body of evidence supporting HFNO as an effective, well-tolerated, and safe alternative to NIV in patients with acute hypoxemic respiratory failure, offering superior early physiological improvement and shorter ICU and hospital stays while maintaining comparable rates of intubation and mortality.

CONCLUSION

High-Flow Nasal Oxygen (HFNO) is an effective and well-tolerated non-invasive respiratory support modality for patients with acute hypoxemic respiratory failure. Compared with Non-Invasive Ventilation (NIV), HFNO provided significantly better early improvement in oxygenation and respiratory parameters, reduced intensive care unit and hospital stay, and was associated with fewer device-related complications while demonstrating comparable rates of endotracheal intubation, successful weaning, and mortality. These findings suggest that HFNO represents a safe and effective first-line alternative to NIV in appropriately selected patients with acute hypoxemic respiratory failure. Further large-scale, multicenter randomized controlled trials are warranted to validate these findings and establish definitive recommendations for its routine clinical use.

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REFERENCES

1. Bay P, de Prost N. Diagnostic approach in acute hypoxemic respiratory failure. J Intensive Med. 2024;5(2):119-126. doi: 10.1016/j.jointm.2024.09.003.
2. Ketcham SW, Sedhai YR, Miller HC, Bolig TC, Ludwig A, Co I, Claar D, McSparron JI, Prescott HC, Sjoding MW. Causes and characteristics of death in patients with acute hypoxemic respiratory failure and acute respiratory distress syndrome: a retrospective cohort study. Crit Care. 2020;24(1):391. doi: 10.1186/s13054-020-03108-w.
3. Wu D, Wu C, Zhang S, Zhong Y. Risk Factors of Ventilator-Associated Pneumonia in Critically III Patients. Front Pharmacol. 2019 May 9;10:482. doi: 10.3389/fphar.2019.00482.
4. Mas A, Masip J. Noninvasive ventilation in acute respiratory failure. Int J Chron Obstruct Pulmon Dis. 2014 Aug 11;9:837-52. doi: 10.2147/COPD.S42664. PMID: 25143721; PMCID: PMC4136955.
5. Cavalleri MA, Barbagelata E, Scudeletti M, Nicolini A. Effectiveness of non-invasive ventilation in acute respiratory failure of obese patients: A brief narrative review. Ital J Med. 2018;12(1):1-7. doi:10.4081/itjm.2018.916.
6. Chawla R, Dixit SB, Zirpe KG, Chaudhry D, Khilnani GC, Mehta Y, Khatib KI, Jagiasi BG, Chanchalani G, Mishra RC, Samavedam S, Govil D, Gupta S, Prayag S, Ramasubban S, Dobariya J, Marwah V, Sehgal I, Jog SA, Kulkarni AP. ISCCM Guidelines for the Use of Non-invasive Ventilation in Acute Respiratory Failure in Adult ICUs. Indian J Crit Care Med. 2020;24(Suppl 1):S61-S81. doi: 10.5005/jp-journals-10071-G23186.
7. Cammarota G, Simonte R, De Robertis E. Comfort during non-invasive ventilation. Front Med (Lausanne). 2022;9:874250. doi:10.3389/fmed.2022.874250.

8. Petkar S, Wanjari D, Priya V. A Comprehensive Review on High-Flow Nasal Cannula Oxygen Therapy in Critical Care: Evidence-Based Insights and Future Directions. Cureus. 2024 Aug 6;16(8):e66264. doi: 10.7759/cureus.66264.
9. Spicuzza L, Schisano M. High-flow nasal cannula oxygen therapy as an emerging option for respiratory failure: the present and the future. Ther Adv Chronic Dis. 2020 May 13;11:2040622320920106. doi: 10.1177/2040622320920106.
10. Bruni A, Garofalo E, Cammarota G, Murabito P, Astuto M, Navalesi P, Luzza F, Abenavoli L, Longhini F. High Flow Through Nasal Cannula in Stable and Exacerbated Chronic Obstructive Pulmonary Disease Patients. Rev Recent Clin Trials. 2019;14(4):247-260. doi: 10.2174/1574887114666190710180540.
11. Pachisia AV, Govil D. High Flow, High Hope: HFNO in Acute Hypoxemic Respiratory Failure. Indian J Crit Care Med. 2024 Aug;28(8):726-728. doi: 10.5005/jp-journals-10071-24779. Epub 2024 Jul 31. PMID: 39239190; PMCID: PMC11372679.
12. Leeies M, Flynn E, Turgeon AF, et al. High-flow oxygen via nasal cannulae in patients with acute hypoxemic respiratory failure: A systematic review and meta-analysis. Syst Rev. 2017;6:202. doi:10.1186/s13643-017-0593-5.
13. Grieco DL, Menga LS, Cesarano M, et al. Effect of helmet noninvasive ventilation vs high-flow nasal oxygen on days free of respiratory support in patients with COVID-19 and moderate to severe hypoxemic respiratory failure: The HENIVOT randomized clinical trial. JAMA. 2021;325(17):1731-43. doi:10.1001/jama.2021.4682.
14. Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, Prat G, Boulain T, Morawiec E, Cottereau A, Devaquet J, Nseir S, Razazi K, Mira JP, Argaud L, Chakarian JC, Ricard JD, Wittebole X, Chevalier S, Herbland A, Fartoukh M, Constantin JM, Tonnelier JM, Pierrot M, Mathonnet A, Béduneau G, Delétage-Métreau C, Richard JC, Brochard L, Robert R; FLORALI Study Group; REVA Network. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. N Engl J Med. 2015 Jun 4;372(23):2185-96. doi: 10.1056/NEJMoa1503326. Epub 2015 May 17. PMID: 25981908.
15. Okano H, Sakuraya M, Masuyama T, Kimata S, Hokari S. Respiratory support strategy in adults with acute hypoxemic respiratory failure: a systematic review and network meta-analysis. JA Clin Rep. 2022 May 6;8(1):34. doi: 10.1186/s40981-022-00525-4. PMID: 35522380; PMCID: PMC9072760.
16. Pan JT, See KC. Criteria for stopping high-flow nasal oxygen for acute hypoxemic respiratory failure: A systematic review of randomized controlled trials. Acute Crit Care Pract Sci (APS). 2024;2:23. doi:10.1007/s44254-024-00060-8.