ORIGINAL ARTICLE

Outcome of Early Initiation of High-flow Nasal Oxygen Therapy among Pneumonia Patients Presenting with Acute Hypoxemic Respiratory Failure

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Abstract

Background: High-flow nasal oxygen (HFNO) therapy is an upcoming and beneficial modality for patients with acute hypoxemic respiratory failure (AHRF).

Objectives: To evaluate whether early use of HFNO in pneumonia patients with AHRF can reduce the need for invasive ventilation.

Patients and methods: In this prospective, randomized controlled trial, 160 patients who fulfilled the criteria were included. The patient's characteristics, sequential organ failure assessment score, and simplified acute physiology score were recorded. Respiratory rate (RR), and oxygenation parameters (PaO_2/FiO_2), and RR-oxygenation index at selected time intervals were collected and analyzed. The primary outcome was the number of patients who needed intubation. Secondary outcomes included length of intensive care unit (ICU) and hospital stay and mortality at day 28.

Results: The rate of intubation was not statistically significant between the two groups 15 vs 18.7%; difference 3.7% [(95% confidence interval (CI): 2.5–5.7%]. In 48-hour time periods, the mean PaO_2/FiO_2 ratio was significantly increased in the HFNO group compared with the non-invasive ventilation (NIV) group. The RRs and heart rate (HR) showed a significant decrease in the HFNO group.

The length of ICU and hospital stays was not different between both groups. No significant differences were found in mortality rates between the HFNO and NIV groups 9 (11.2%) and 10 (12.5%), with 1.3% (95% CI: 0.7–3.8%) ($p = 0.21$). Multivariate analysis demonstrated that low baseline PaO_2/FiO_2, Respiratory rate-oxygenation index (ROX index) ≤ 5.4 measured at 12 hour and high severity scores were independent risk factors for intubation.

Conclusion: Treatment with HFNO did not reduce the need for intubation among patients with pneumonia-induced AHRF, despite the improved PaO_2/FiO_2 observed with HFNO compared with NIV.

Keywords: Acute hypoxemic respiratory failure, High-flow nasal oxygen, Pneumonia.

Clinical trial no: NCT05809089

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Highlights

This study reflects the beneficial effect of using high-flow nasal oxygen (HFNO) therapy for patients with acute hypoxemic respiratory failure (AHRF) and whether early use of HFNO in pneumonia patients with AHRF can reduce the need for invasive ventilation. The observations from this study indicate that treatment with HFNO did not reduce the need for intubation, despite the improved PaO_2/FiO_2 observed with HFNO as compared with Non-invasive ventilation (NIV). This may be more applicable in respiratory intensive care units (ICUs) and emergency departments.

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Introduction

Acute hypoxemic respiratory failure is a frequent major health problem in patients with pneumonia caused by bacterial or viral pneumonia, accompanied by in-hospital mortality. Several clinical observations have suggested that the early application of HFNO in the ICU setting might be more successful in avoiding intubation and a worse prognosis.[1–4]

The use of HFNO in patients with AHRF related to pneumonia is associated with decreased breathing, improved oxygenation, and the avoidance of endotracheal intubation with sedation and concomitant hemodynamic effects.

In addition, the warmed and humidified gas in HFNO improves patient comfort and tolerance. Moreover, HFNO impedes expiratory flow, producing distending pressure similar to continuous positive airway pressure (CPAP) or positive end expiratory pressure (PEEP).[5]

Although these patients have the potential to benefit from early respiratory support, there is little evidence supporting the efficacy of HFNO in the early management of patients with AHRF.

Hence, it is necessary to discriminate between those who will succeed with HFNO and those who will fail as early as possible. In 2015, the FLORALI trial revealed that HFNO is a safe substitute for

conventional oxygen delivery or NIV in patients with AHRF and showed a mortality benefit and increase in ventilator-free days for the group treated with HFNO.[1]

Recently, the respiratory rate-oxygenation (ROX) index as a simple marker, [defined as the ratio of pulse oximetry (SpO_2)/fraction of inspired oxygen (FiO_2) to respiratory rate (RR)] was proposed to predict the outcome of HFNO in pneumonia patients with AHRF. However, the predictive performance and the optimal values of the ROX index largely varied across studies.[6,7]

Thus, we conducted this study among pneumonia patients admitted to the ICU with AHRF to determine whether high-flow oxygen therapy, compared with noninvasive ventilation therapy, can reduce the need for invasive ventilation and improve outcomes.

Patients and Methods

This prospective, randomized, controlled trial was carried out from March 2022 to May 2024 at Assiut University Hospital. The study was approved by the Faculty of Medicine Ethics Committee, Assiut University.

Pneumonia adult patients (age >18 years) with AHRF were eligible for this study after conventional oxygen therapy failure.

According to the previously published studies,[6,7] the criteria for diagnosing AHRF were defined as the presence of a RR ≥25 breaths/min with SpO_2 ≤92%, and/or the partial pressure of arterial oxygen (PaO_2) to FiO_2 ratio ≤300 mm Hg despite conventional oxygen therapy at 10 L/min delivered for at least 60 minutes.

Patients requiring urgent intubation, those with recent facial or cranial trauma or surgery, decreased consciousness [Glasgow coma scale (GCS) of 11 or less], severe hemodynamic instability, severe ventricular arrhythmia or myocardial ischemia, tracheotomy, active gastrointestinal bleeding, and inability to clear respiratory secretions were excluded.

Community-acquired infection refers to an infection that occurred in a community setting; hospital-acquired infection is acquired ≥48 hours after hospital admission. The pathogen was defined as any agent cultured from samples collected within 48 hours or at the time of diagnosis. The empirical therapy was adjusted based on drug susceptibility testing or the recommendations of relevant guidelines.[8,9]

Patients were randomized to receive either HFNO or NIV respiratory support throughout the hospitalization period. Randomization was stratified by a laboratory scientist using shuffled, sealed envelopes.

Interventions

In the HFNO group (Optiflow; Fisher & Paykel Healthcare, Auckland, New Zealand), high-flow device was utilized. The humidifier temperature was set at 37°C via large-bore nasal prongs. The flow was initialized at 35 L/min and titrated to a maximum of 50 L/min as determined by patient comfort. FiO_2 was titrated to maintain SpO_2 ≥ 90%.

Non-invasive ventilation was delivered with an oral-nasal face mask (ZS-MZ-A Face Mask; Shanghai Zhongshan Medical Technology Co., Shanghai, China) using bilevel positive airway pressure (BiPAP spontaneous-mode; Respironics Inc., Murrysville, PA, USA). The initial BiPAP settings were adjusted with a pressure support level targeting a tidal volume of 6–8 mL/kg; inspiratory positive airway pressure was initiated at 10–12 cm H_2O, and expiratory positive airway pressure started at 4–5 cm H_2O. FIO_2 was adjusted to maintain SpO_2 ≥90%.[10]

The patients were advised to use respiratory support for a minimum of 16 hours a day with short breaks to receive meals, scheduled medications, or nursing care.

Demographic details include age, sex, sequential organ failure assessment (SOFA) score,[11] simplified acute physiology score (SAPS II),[12] and infection source and type (i.e., community- or hospital-acquired). Respiratory rate and oxygenation parameters in terms of oxygenation index (PaO_2/FiO_2) and ROX index index[7] [ROX index calculated as $SpO_2/(FiO_2 \times RR)$] were recorded at 0, 2, 12, 24, and 48 hours after initiation of therapy.

Clinical outcomes measures (length of HFNO therapy, hospital stay, and mortality) were monitored. Subjective dyspnea was measured at 24 and 48 hours using a modified Borg scale of 0 = no dyspnea to 10 = maximal dyspnea.[13]

The primary objective is to assess the proportion of patients who required endotracheal intubation within 72 hours after randomization.

The determined criteria for endotracheal intubation were established as follows to avoid delayed intubation:[14] (1) signs of persistent or worsening respiratory failure, defined by at least two of the following criteria: A RR ≥ 40 cycles/min, lack of improvement of signs of respiratory-muscle fatigue, development of excessive tracheal secretions, acidosis with a pH below 7.35, SpO_2 ≤90%; (2) hemodynamic instability (defined by systolic blood pressure ≤90 mm Hg, mean blood pressure ≤65 mm Hg, or requirement for a vasopressor; (3) and deterioration of mental status.

Once a patient fulfilled these criteria, the final decision for intubation was made by the attending physician with the consent of the family members.

The secondary endpoints included improvement of respiratory exchanges compared to baseline (time frame: Hospital admission until the achievement of clinical stability) arterial blood gas evaluation; ICU and in-hospital mortality; and lengths of ICU and hospital stays.

Statistical Analysis

Sample Size Estimation

A network analysis of several randomized controlled trials (RCTs) that studied different noninvasive oxygenation strategies in AHRF patients showed that 24.3% of patients experienced HFNO failure (i.e., intubation).[15] Based on a previous study,[16] the rate of ICU death was expected to be 33.0%. Hence, with a power of 80% and a type I error rate of 5% (two-sided), the calculated sample size was 160 patients in the present study. All statistical analyses were performed using IBM SPSS for Windows software (version 25.0; IBM Corp., Armonk, NY, USA).

Values were presented as mean and standard deviation using the Mann–Whitney *U*-test for comparison between the two study groups. The qualitative data were compared between the two groups using the χ^2-test, and the quantitative data were compared using the Student's *t*-test. A *p*-value < 0.05 was considered significant.

Two-way ANOVA test was used in the overall comparisons of repeated measures over time. Comparisons between each measure at baseline and each time point after starting HFNO or NIV therapy were then performed with the Wilcoxon test for paired samples. Receiver operating characteristics curves were used to identify a cut-off point in the ROX index to predict intubation in logistic regression.

Multiple logistic regression analyses were performed to examine the variables associated with intubation. A difference

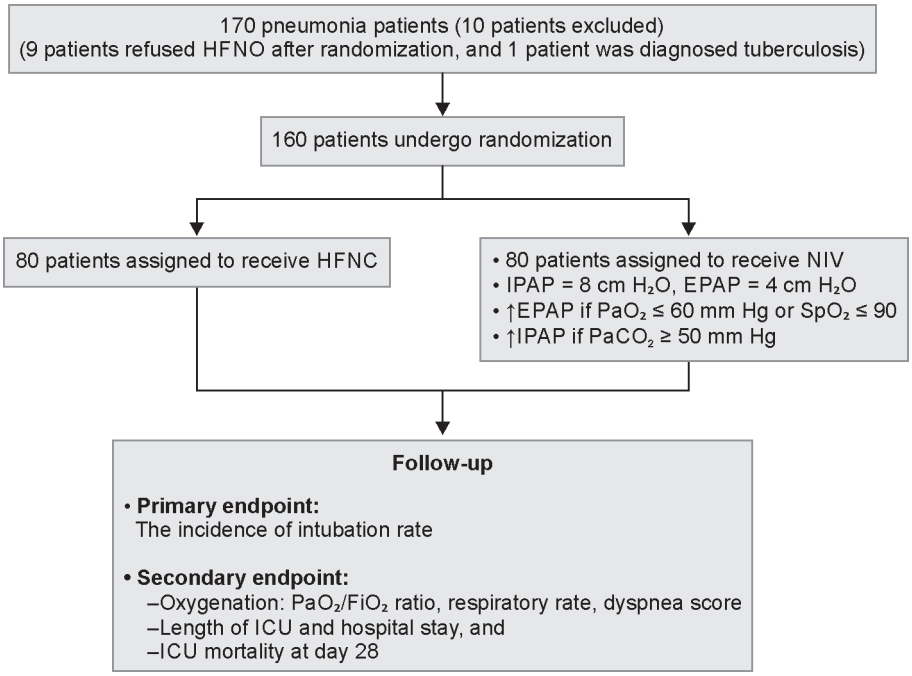

Fig. 1: CONSORT flowchart of the study

was considered statistically significant when the alpha probability was >0.05.

Results

Patients' Characteristics

Between March 2022 and May 2024, 170 pneumonia patients were admitted to the respiratory intensive care unit who fulfilled the criteria of pneumonia with AHRF. Of these 170 patients, nine refused HFNO after randomization to the HFNO group and one was diagnosed as having tuberculosis. Thus, a total of 160 patients were included; 80 patients were allocated to the HFNO group and 80 patients were allocated to the NIV group (Fig. 1).

Baseline patients' characteristics were similar (Table 1). Community-acquired pneumonia presented in 90% of the HFNO group and 91.2% of the NIV group. Respiratory tract cultures were found to be positive for bacteria in 27.5 and 17.5% of patients and were positive for fungus in 6.2 and 2.5% of patients in the HFNO and NIV groups, respectively. No significant differences were observed between both groups regarding severity scores.

Physiological Changes between the HFNO and NIV Groups

As shown in Table 2, the time course of the PaO_2/FiO_2 ratio, arterial blood gases, and respiratory frequency. There was an improvement in PaO_2/FiO_2 over time in both groups. In the HFNO group, PaO_2/FiO_2 became significantly higher than in the HFNO group at 2 hours after randomization and remained stable for the first 48 hours. The FiO_2 in both groups shows a similar value.

The RRs and heart rate (HR) improved with time in both groups, with a significant decrease in the HFNO group as compared with the NIV group. No differences between the two groups existed for the time course of arterial pH, or partial pressure of arterial carbon dioxide ($PaCO_2$). Also, significant differences were observed in the ROX index after 12 hours of HFNO therapy.

Table 1: Patients characteristics and severity scores

	HFNO group (n = 80)	*NIV group (n = 80)*	*p-value*
Sex (male) no. (%)	49 (61.2%)	31 (38.7%)	0.21
Age	55.2 ± 12.3	62.4 ± 11.6	0.21
Smoking, no. (%)	42 (52.5%)	38 (47.5%)	0.41
Type of pneumonia, no. (%)			
Community-acquired	72 (90%)	73 (91.2%)	0.32
Hospital-acquired	8 (10%)	7 (8.7%)	0.21
Positive culture of pathogen, no. (%)	35 (43.7%)	20 (25%)	0.01
Bacteria from the respiratory sample	22 (27.5%)	14 (17.5%)	0.17
Blood culture	8 (10%)	4 (5%)	0.01
Fungus from the respiratory sample	5 (6.2%)	2 (2.5%)	0.01
Virus	12 (15%)	10 (12.5%)	0.21
Comorbidity no. (%)			
Hypertension	38 (47.5%)	30 (37.5%)	0.32
Diabetes mellitus	48 (60%)	40 (50%)	0.12
Coronary heart disease	12 (15%)	10 (12.5%)	0.21
Chronic heart failure	8 (10%)	6 (7.5%)	0.31
Cancer	4 (5%)	3 (3.7%)	0.42
Cerebrovascular disease	1 (1.2%)	1 (1.2%)	0.23
Severity scores			
SOFA score on admission	4.27 ± 1.56	4.09 ± 1.91	0.45
SAPS II on admission	45 ± 20	42 ± 16	0.23

SAPS II, simplified acute physiologic score II; SOFA, sequential organ failure assessment score; $p \leq 0.5$ was considered statistically significant

Table 2: Comparisons of physiological parameters between HFNO and NIV groups

	HFNO group (n = 80)	*NIV group n = 80*	*p1*
Heart rate (beat/minute)			
Baseline	120 ± 13.2	120 ± 12.7	0.42
2 H	111 ± 10.3	110.6 ± 9.8	0.01
12 H	98.2 ± 9.4	110.1 ± 10.3	0.01
24 H	94.8 ± 8.7	95.5 ± 8.6	0.01
48 H	93.2 ± 7.5	95.3 ± 8.3	0.01
P2	0.01	0.02	0.01[a]
RR (breath/minute)			
Baseline	34 ± 12.2	33 ± 13.5	0.41
2 H	28 ± 10.3	29.4 ± 12.3	0.01
12 H	23.3 ± 4.5	24.4 ± 5.4	0.01
24 H	22.3 ± 5.4	23.3 ± 5.7	0.01
48 H	20.1 ± 3.4	23.4 ± 4.2	0.01
P2	0.01	0.01	0.01[a]
PaO_2/FiO_2			
Baseline	232.7 ± 33.8	231.8 ± 32.5	0.41
2 H	246.5 ± 40.5	224.07 ± 34.7	0.01
12 H	244.5 ± 42.9	230.6 ± 34.1	0.01
24 H	247.0 ± 44.3	238.6 ± 36.6	0.01
48 H	265.0 ± 48.3	250.2 ± 38.3	0.01
P2	0.01	0.02	0.01[a]
pH			
Baseline	7.44 ± 0.05	7.45 ± 0.05	0.43
2 H	7.44 ± 0.03	7.42 ± 0.04	0.62
12 H	7.42 ± 0.03	7.43 ± 0.02	0.23
24 H	7.39 ± 0.05	7.39 ± 0.05	0.21
48 H	7.42 ± 0.03	7.42 ± 0.03	0.31
P2	0.24	0.42	0.23[a]
$PaCO_2$, mm Hg			
Baseline	34.5 ± 5.8	33.5 ± 4.9	0.04
2 H	34.9 ± 5.9	34.5 ± 5.7	0.11
6 H	36.7 ± 5.6	34.6 ± 5.6	0.01
12 H	36.8 ± 6.8	36.5 ± 6.4	0.21
24 H	37.9 ± 5.5	37.8 ± 5.6	0.24
P2	0.01	0.02	0.01[a]
ROX index			
Baseline	5.8 ± 1.1	5.4 ± 1.2	0.74
2 H	5.8 ± 1.2	5.4 ± 1.2	0.32
6 H	6.9 ± 1.0	5.4 ± 1.2	0.01
12 H	6.9 ± 1.4	5.8 ± 1.1	0.01
24 H	7.4 ± 1.3	5.8 ± 1.1	0.01
P2	0.01	0.02	0.01[a]

Results are means ± SDs. a, for overall comparisons of differences between groups over time; FiO_2, fraction of inspired oxygen; P1, for comparisons of differences between groups at each time point; P2, for overall comparisons of differences in each group over time; PaO_2, arterial partial pressure of oxygen; $PaCO_2$, partial pressure of arterial carbon dioxide; RR, respiratory rate; ROX index, respiratory rate-oxygenation index

Main Outcome

As shown in Table 3, the rate of intubation was needed in 12 (15%) patients allocated to HFNO and in 15 (18.7%) patients who received NIV. The rate of intubation was not statistically significant between the two groups (15 vs 18.7%; difference 3.7%; 95% CI: 2.5–5.7%). The criteria identifying causes of intubation were not different between groups.

There was a significant difference in PaO_2/FiO_2 ratio between groups in the first 24 H [HFNO: 247.0 ± 44.3; NIV: 238.6 ± 36.6; mean difference: −8.4 (95% CI: −5.0–2.5); $p = 0.01$]. At 48-hour periods, the mean PaO_2/FiO_2 ratio showed higher values in the HFNO group.

Dyspnea at both 24 and 48 hours was very low in both groups, corresponding to either no (score = 0) to very slight (score = 1) dyspnea. The median (IQR) dyspnea scores at 24 hours were 0 (0–2) in the HFNO group and 1 (0–2) in the NIV group ($p = 0.09$). At 48 hours, the median (IQR) dyspnea scores were 0 (0–1) for the HFNO group and 1 (0–3) for the NIV group ($p = 0.008$); this difference is

Table 3: Outcome variables, length of stay, and mortality

Outcome variables	*HFNO group (n = 80)*	*NIV group (n = 80)*	*Difference between groups (95% CI)*	*p-value*
Need for intubation, no. (%)	12 (15%)	15 (18.7%)	3.7 (2.5–5.7)	0.31
Oxygenation (PaO_2/FiO_2 ratio), mean				
24 H	247.0 ± 44.3	238.6 ± 36.6	–8.4 (–5.0 to 2.5)	0.01
48 H	265.0 ± 48.3	250.2 ± 38.3	–14.8 (–9.9 to –17.4)	
Dyspnea score, median (IQR)				
24 H	0 (0–2)	1 (0–2)	–	0.09
48 H	0 (0–1)	1 (0–3)	–	
RR, mean				
24 H	22.3 ± 5.4	23.3 ± 5.7	1 (–0.74 to 2.8)	0.85
48 H	20.1 ± 3.4	23.4 ± 4.2	3.3 (1.38–4.2)	0.01
Length of stay				
Intensive-care unit stay (days)	10.6 ± 6.3	11.5 ± 7.4		0.32
Hospital stay (days)	12.2 ± 9.3	12.5 ± 8.4		0.22
Mortality				
Intensive-care unit mortality	8 (10%)	9 (11.2%)	1.2 (0.8–3.8)	0.21
Hospital mortality	8 (10%)	9 (11.2%)	1.2 (0.8–3.2)	0.23
Mortality at 28 days	9 (11.2%)	10 (12.5%)	1.3 (0.7–3.8)	0.21

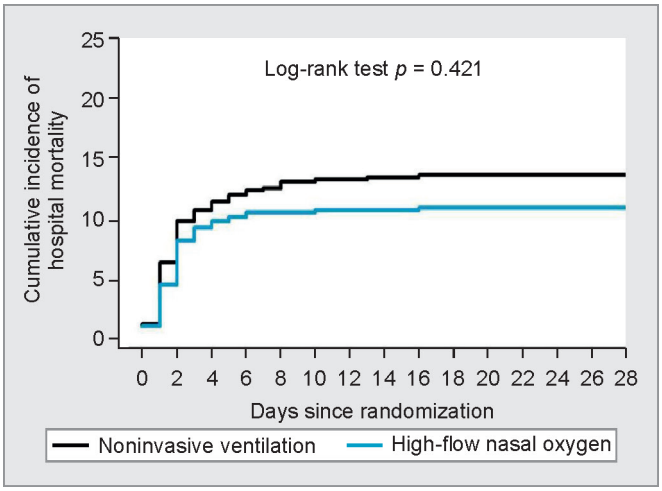

Fig. 2: Kaplan–Meier curve analysis for cumulative incidence of hospital mortality

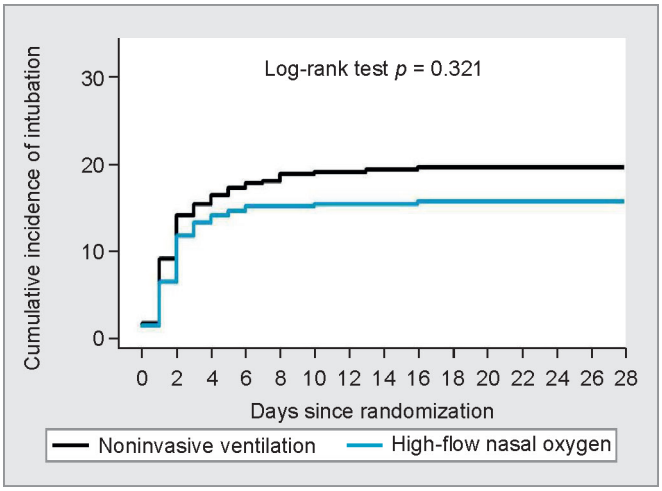

Fig. 3: Kaplan–Meier curve analysis for cumulative incidence of intubation rate

not clinically relevant. Furthermore, there was a clinically significant difference in RR between the two groups were observed at 48 hours [HFNO: 20.1 ±3.4; NIV: 23.4 ± 4.2; mean difference: 3.3 (95% CI: 1.38–4.2; $p = 0.01$)].

The length of ICU and hospital stays was not different between both groups. No significant differences were found in mortality rates between the HFNO and NIV groups [9 (11.2%) and 10 (12.5%), with 1.3% (95% CI: 0.7–3.8) ($p = 0.21$)].

No statistically significant difference was found between the two groups in need of intubation and overall hospital mortality using the log-rank test (Figs 2 and 3). The factors associated with intubation were lower baseline PaO_2/FIO_2 (OR: 3.5; 95% CI: 1.2–4.2) and a high severity score (OR: 2.2; 95% CI: 1.5–4.3). Moreover, the ROX index less than 5.4 measured at 12 hours (OR: 3.24; 95% CI: 1.34–12.74; $p < 0.01$) was a consistently associated predictor of intubation (Table 4).

Table 4: Multiple logistic regression analysis of the association of intubation

Variables	*Adjusted OR (95% CI)*	*p–value*
Low baseline PaO_2/FIO_2	3.5 (1.2–4.2)	0.01
High severity score	2.2 (1.5–4.3)	0.01
Presence of comorbidity	1.9 (1.2–8.4)	0.42
RR > 35 bpm	3.4 (1.5–6.9)	0.32
12 H ROX index ≤ 5.4	3.24 (1.34–12.74)	0.01

Discussion

High-flow nasal oxygen has now assumed a central role in the management of AHRF. Therefore, this RCT designed to evaluate initiating HFNO in AHRF-induced pneumonia could decrease the need for invasive mechanical ventilation compared to NIV.

The primary outcome analysis of our study showed that the use of HFNO therapy in pneumonia-induced AHRF, compared to NIV, HFNO did not reduce the need for intubation or mortality in pneumonia-induced AHRF. The rate of need for intubation is lower than expected in our study. This may reflect that patients are being included in a very early stage of mild hypoxemia. Furthermore, no differences were observed in hospital and ICU length of stay or mortality rate at 28 days.

A randomized trial conducted by Frat et al. comparing HFNO with standard oxygen and intermittent sessions of facemask NIV showed no significant effects on the rate of endotracheal intubation in the overall population, but a reduction in the intubation rate was observed among a subgroup of patients with $PaO_2/FiO_2 \leq 200$ mm Hg treated with HFNO.[1]

Early studies comprising pneumonia patients with acute respiratory failure treated with NIV. In Agarwal's study, who investigated patients presented with pneumonia to determine factors associated with NIV failure, NIV may be used appropriately and not delay intubation. The overall failure rate was 43.8%, and there were significant differences in failure rates between ARDS severity groups according to the Berlin definition (mild 18.9%, moderate 73%, and severe 83.3%), and factors associated with NIV failure were a low baseline PaO_2/FiO_2 ratio, the presence of septic shock, and the severity of ARDS. The authors speculated that the higher failure rate in patients with pneumonia was due to difficulty clearing secretions, reduced pulmonary compliance, and nonhomogeneous gas exchange.[17,18] The overall ICU mortality rate was 37.1%, and the factors associated with ICU mortality were a high Acute Physiology and Chronic Health Evaluation II (APACHE II) score, a low baseline PaO_2/FiO_2, the presence of septic shock, and the severity of ARDS. The authors reported that the mortality rate for mild hypoxemia was significantly lower (20.3%) when compared with moderate and severe hypoxemia. Their study highlights the significant risk of NIV failure when used in patients with moderate and severe hypoxemia, whereas it supports the idea that in the absence of septic shock, patients with mild hypoxemia (PaO_2/FiO_2 more than 200) may be successfully managed with NIV.[18]

A meta-analysis studied the mortality rate in patients with AHRF, comparing HFNO to conventional oxygen therapy and NIV. They found that mortality remains unaffected, but the HFNO seems to be better tolerated than conventional oxygen therapy by the patients.[19] Whereas another study suggests that the HFNO may reduce the intubation rate, this finding may be specific to high-risk patients (defined by APACHE II or SAPS II scores).[20]

We demonstrated that PaO_2/FiO_2 was significantly higher than the baseline level in the HFNO group compared with the NIV group at 2 hours after initiation of therapy, and this trend remained for the first 48 hours, similar to previous studies.[10,21] Thus, HFNO was more efficient than NIV in elevating PaO_2/FiO_2 in pneumonia patients with AHRF. However, despite an initial improvement in arterial oxygenation, the use of HFNO did not result in changes in the intubation rate. In our study, the average usage duration of HFNO was more than 16 hours per day. Despite this supportive time dose, we did not show a positive effect on the avoidance of intubation.

The important feature of the HFNO application is its mechanism that allows accurate delivery of FiO_2, flushes the upper airways, yielding a washout of dead space, and provides low and variable levels of positive pressure in the airways, generating a mild PEEP effect.[22,23] As compared with standard oxygen, HFNO decreases the work of breathing, inspiratory effort, and RR, resulting in an improvement in oxygenation and comfort.[24] These physiological effects make HFNO the most promising technique for first-line oxygen therapy in patients with high-flow demands, such as those affected by AHRF.

In this study, there was no improvement in dyspnea score in the HFNO group compared to the NIV group. Noteworthy, dyspnea levels in both groups were nil or very slight. We demonstrated a reduction in RR and HR in the HFNO group. Despite not being a reliable index of effort, the RR remains the most used surrogate predictor for the need for intubation. Several clinical studies have demonstrated a causal relationship between persistent high respiratory effort and NIV failures.[25,26] Persistently high inspiratory effort and RR are attributed to treatment failure and the need for intubation[27,28] Conversely, a preliminary RCT investigated HFNO usage among patients with mild to moderate hypoxaemic respiratory failure, and they found no improvement in oxygenation.[29] No studies have reported the usefulness of HFNO for lowering the intubation rate in patients with AHRF due to pneumonia. However, several clinical trials have been published, demonstrating a reduction in the need for mechanical ventilation and mortality in patients due to COVID-19.[30–32] The inclusion of pneumonia patients with very early stages of hypoxemia may in turn reduce progression to lung injury, ARDS, and mortality.

The main strength of our study is its high homogeneity; only pneumonia-induced AHRF patients were included in this study. Moreover, sputum culture was routinely performed for every patient. Although the positive culture rate is low, most patients were treated with guideline-compliant antibiotics and improved.

Among the limitations of this study, the most important was the technical inability to blind the treating team. The lack of blinding can contribute to bias, especially when clinical judgment affects an outcome that is being evaluated. Because of the sample size, randomization cannot guarantee the balance of the distribution of confounders between the two groups. Lastly, it was conducted in a single tertiary hospital, thus our findings might not be generalizable to other settings.

Conclusion

High-flow nasal oxygen did not significantly reduce the rate of intubation. Given the findings reported in this study, HFNO seems to be a beneficial strategy for improving oxygenation and reducing the work of breathing in pneumonia-induced AHRF.

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