Original Article

Use of High-Flow Nasal Oxygen in Critically Ill Adults with Respiratory Failure: A Single-Center, Retrospective, Descriptive Study

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Abstract

Background: High-flow nasal oxygen (HFNO) therapy is an upcoming modality used among patients with respiratory failure. The utility of this equipment in intensive care units (ICUs) is undergoing global scrutiny through trials. This article provides descriptive detail about its usage and factors affecting its outcome in an Indian ICU setting. **Aims:** The aim is to assess the use of HFNO therapy in managing respiratory failure in an ICU setting. **Settings and Design:** This is a single-center, retrospective, descriptive study in a tertiary care teaching hospital. **Patients and Methods:** All data of patients who received HFNO therapy between August 2015 and April 2017 were extracted from hospital medical records. Association of HFNO therapy failure rates with age, sequential organ failure assessment (SOFA) score, diagnosis, PaO_2/FiO_2, $PaCO_2$, and duration of HFNO therapy was analyzed. Data were also analyzed for association of HFNO therapy duration with ICU length of stay and ICU mortality. **Results:** No significant relation was found between HFNO failure and age, diagnosis, SOFA score, PaO_2/FiO_2, or $PaCO_2$ levels at initiation of HFNO therapy. Increased HFNO therapy failure rate was found in the first 2 days of HFNO therapy (40.4%) when compared to HFNO therapy use >2 days (8.7%) ($P = 0.006$). No significant association was found between duration of HFNO therapy use and length of stay or mortality in the ICU. **Conclusions:** HFNO is an effective technique to manage respiratory failure in the ICU setting. Severe hypoxia and hypercapnia may effectively be managed using HFNO therapy. Most HFNO therapy failures occur as early as 48 h after initiation of therapy. Prolonged HFNO therapy use does not prolong ICU stay or affect patient mortality.

Keywords: High-flow nasal oxygen therapy, intensive care unit, respiratory failure

Introduction

Respiratory failure has been successfully managed using high-flow nasal oxygen (HFNO) therapy, and data regarding usage and clinical benefits are available for developed countries.[1] The reliable accuracy with which HFNO therapy offers high FiO_2 levels has led to the increased acceptance of this equipment among intensive care units (ICUs) worldwide. In India, HFNO therapy is emerging as a popular mode of delivering high oxygen flow to patients. However, there is a paucity of data available concerning the successful use of HFNO therapy in Indian ICU setting.

The aim of this study was to assess the use of HFNO therapy in managing respiratory failure in an ICU setting. Our objectives were to identify the association of demographic particulars and severity of hypoxemia or hypercapnia with the failure of HFNO therapy. In this article, we also examine the association of duration of HFNO therapy with HFNO therapy failure rates, length of ICU stay, and mortality among patients with respiratory failure in the ICU.

Patients and Methods

After obtaining institutional ethics committee and research committee approval, extraction of data was done from hospital medical records of adult patients admitted to the ICU of a single tertiary teaching hospital from August 2015 to April 2017. Data of patients who were administered HFNO therapy

Access this article online

Quick Response Code:

Website: www.ijrconline.org

DOI: 10.4103/ijrc.ijrc_3_19

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How to cite this article: Paul J, Mathews V, Babu A, Thekkeyil A, Paul C. Use of high-flow nasal oxygen in critically Ill adults with respiratory failure: A single-center, retrospective, descriptive study. Indian J Respir Care 2019;8:111-5.

Received: 03-02-2019 **Revised:** 11-03-2019 **Accepted:** 17-03-2019

were analyzed for demographic details, etiology and severity of primary illness, HFNO treatment particulars, and outcome of treatment. Patients with inadequate data or treatment limitations were excluded.

HFNO therapy was applied to patients admitted to the ICU with respiratory distress (tachypnea, dyspnea, oxygen saturation <90%) in spite of administration of oxygen by face mask at flow rates up to 12 L/min. The equipment used to deliver HFNO therapy at our center was AIRVO™2 by Fisher and Paykel Healthcare. The equipment is shown in Figure 1. In the adult settings of this equipment, FiO_2 levels can be titrated between 0.21 and 0.95 and flow rates can be titrated between 30 L/min and 70 L/min. Failure was defined as conversion to Non-Invasive ventilation (NIV) or mechanical ventilation during the ICU stay.

Demographic details including age, sequential organ failure assessment (SOFA) score, primary diagnosis, and oxygenation and ventilation status of patients in terms of PaO_2/FiO_2 and $PaCO_2$ values at initiation of HFNO therapy were analyzed for differences between those who succeeded or failed HFNO therapy. Association of failure of HFNO therapy, length of stay, and mortality with HFNO therapy duration was assessed.

Statistical analysis was performed using IBM SPSS Statistics Version 23, IBM, Armonk, New York, United States of America. Fisher and Paykel healthcare, East Tamaki, Auckland,New Zealand. All normally distributed quantitative variables have been expressed in terms of mean and standard deviation and analyzed using two-tailed Student's *t*-test. Quantitative variables that do not follow normal distribution have been expressed in terms of median and range and analyzed using Mann–Whitney U-test. All qualitative data have been expressed in terms of frequency and percentage and analyzed using Chi-square test or Fisher's exact test, wherever applicable.

Results

During the study period, a total of 92 patients received HFNO therapy in the study area. Seventeen patients were excluded from the study due to inadequate medical records or treatment limitation. Of 75 patients who were included, 23 (30.7%) required conversion to NIV or invasive mechanical ventilation for their management whereas 52 patients (69.3%) were maintained solely on HFNO therapy. Consort diagram is provided in Figure 2.

Age, SOFA score, P/F ratio, and $PaCO_2$ values at the initiation of HFNO therapy were comparable between patients who required only HFNO and patients who failed HFNO therapy. The results are depicted in Table 1.

The primary diagnosis of patients included in the study were chest trauma (n = 21), sepsis (n = 14), abdominal surgery (n = 13), cardiac failure (n = 8), pancreatitis (n = 7), and others (n = 12). No significant difference was found in success rates between different groups (P = 0.880).

Success rates were analyzed between groups of varying hypoxia and hypercapnia. Increasing hypoxia and hypercapnia were associated with more failures. Increasing PaO_2/FiO_2 levels were associated with increasing success rates. There was a marked decrease in success rates (47%) at $PaCO_2$ values >45 mmHg compared to 78% success rates when $PaCO_2$ values were >35 mmHg. However, the results were not statistically significant. The results are displayed in Tables 2 and 3.

Failure rates were analyzed between patients who required up to 2 days of HFNO therapy and those who required >2 days of therapy. The use of HFNO therapy for ≤2 days was associated

Table 1: Association between failure rates and age, sequential organ failure assessment score, PaO_2/FiO_2 ratio, $PaCO_2$ values at the initiation of high-flow nasal oxygen

	Mean±SD		*P*
	Success	Failure	
Age	45.98±17.53	50.83±18.48	0.281
SOFA score	3.67±2.56	4.09±1.91	0.489
PaO_2/FiO_2 ratio	242.92±95.04	216.87±85.02	0.262
$PaCO_2$	36.09±5.84	38.64±6.78	0.102

SD: Standard deviation, SOFA: Sequential organ failure assessment

Figure 1: AIRVO™2 in use

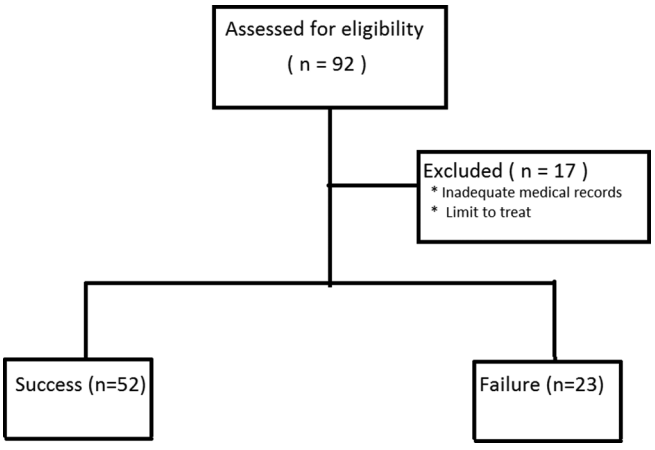

Figure 2: Consort diagram

with 40.4% failure as compared to HFNO therapy use >2 days which resulted in only 8.7% failure. Increased duration of HFNO therapy >2 days was associated with significantly lesser incidence of failure of HFNO therapy (P = 0.006). Most failures of HFNO therapy occurred in the first 2 days of treatment (91.3%). There was no significant difference in mortality (P = 0.422) or length of stay (P = 0.931) with relation to duration of HFNO therapy. The results are illustrated in Tables 4, 5 and Figure 3.

Discussion

HFNO therapy is a novel method that involves administering patients with heated, humidified oxygen at high FiO_2 levels with an additional advantage of improved compliance.[2] Ever since its introduction into clinical practice, the myriad uses of HFNO therapy have been studied in the emergency department, intensive care setting, and operating room.[3]

Table 2: Success rates associated with different levels of PaO_2/FiO_2 and high-flow nasal oxygen failure rate

PaO_2/FiO_2 (mmHg)	Success (%)	Failure (%)
<200	20 (65)	11 (35)
200-299	20 (71)	8 (29)
>299	12 (75)	4 (25)

P=0.727 (not significant)

Table 3: Success rates associated with different levels of $PaCO_2$ and high-flow nasal oxygen failure rate

$PaCO_2$ (mmHg)	Success (%)	Failure (%)
<35	21 (78)	6 (22)
35-45	28 (68)	13 (32)
>45	3 (47)	4 (53)

P=0.198 (not significant)

Table 4: Association of high flow nasal oxygen duration with failure rates, and mortality during intensive care units stay

Parameter	HFNO duration up to 2 days (%)	HFNO duration >2 days (%)	P
Failure rate	21/52 (40.4)	2/23 (8.7)	0.006*
Mortality	7/52 (13.7)	1/23 (4.3)	0.422

*Statistical analysis done using Fischer's exact test. HFNO: High flow nasal oxygen

Table 5: Association of high flow nasal oxygen duration with length of intensive care units stay

HFNO duration (days)	Total number	Median length of ICU stay	Range	P
≤2	52	6.5	28	0.931#
>2	23	7.0	22	

#Mann-Whitney U-test was used due to the nonnormal distribution of data. HFNO: High-flow nasal oxygen, ICU: Intensive care unit

In a series of prospective observational studies, Sztrymf *et al*. have found benefit in managing patients with respiratory failure in a French intensive care setting.[4] Parke *et al*. studied the utility of HFNO therapy in preventing escalation in respiratory support in patients following cardiac surgery. There was a significant difference in the rates of stepping-up of respiratory support among patients managed on high-flow nasal cannula (27.8%) versus those patients managed on standard care (45%).[5]

The FLORALI trial which was conducted among nonhypercapnic hypoxemic critically ill patients revealed decreased 28-day mortality rates in patients receiving HFNO therapy when compared to NIV or standard oxygen face mask. Patients on HFNO therapy also had significantly higher number of ventilator-free days.[6] The beneficial effects of HFNO therapy are seen as early as 15 min after initiation of HFNO therapy. They include increased oxygenation, reduced heart rate, respiratory rate, dyspnea scores, and accessory muscle use.[7] HFNO therapy has also been successfully used to maintain oxygenation during bronchoscopy and for preoxygenation before tracheal intubation among patients admitted in ICUs.[8,9] More evidence has been available on the utility of HFNO therapy in patients with Acute Respiratory Distress Syndrome (ARDS) and postextubation patients who are at high risk for reintubation.[10,11]

In this study, we analyzed the failure rates of HFNO therapy among adult patients in a 10-bedded adult critical care unit in an Indian tertiary care teaching hospital. 30.7% of patients who received HFNO therapy required an alternate mode, viz., NIV or invasive mechanical ventilation. This is comparable to the rates reported by Parke *et al*. Although the study conducted by Parke *et al*. was limited to cardiac surgery patients following extubation, our patient population included both surgical and medical patients who were admitted in the critical care unit with respiratory distress.[5] The use of HFNO therapy in preventing intubation in patients with chest trauma has not been studied previously. In our center, conversion to NIV or invasive mechanical ventilation was 33.3% among patients who were admitted with chest trauma (28% of patient population).

Conversion rates were not significantly different from patients with other diagnoses. Messika *et al*. studied the efficacy

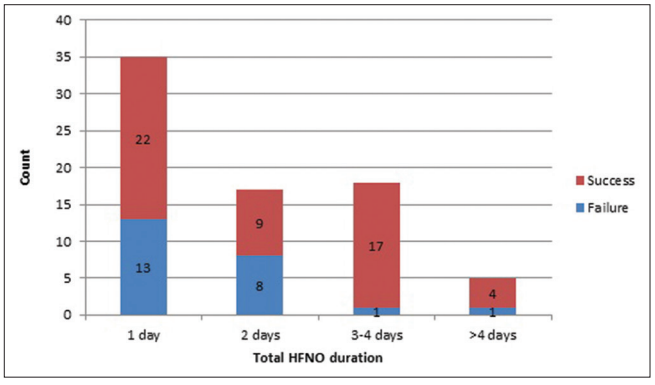

Figure 3: High-flow nasal oxygen duration

of HFNO therapy in patients with ARDS and reported an intubation rate of 40% among ARDS patients who were managed on high-flow nasal cannula.[10] Since our study included patients with sepsis who did not fit into ARDS, failure rates of HFNO therapy among patients with sepsis was much lower, i.e., 27%.

There was no significant association identified between age, diagnosis, SOFA score, and failure of HFNO therapy. Patients with lower PaO_2/FiO_2 levels had higher rates of failure of HFNO therapy. However, this difference between different categories of PaO_2/FiO_2 levels was not statistically significant. There were 35% failure rates in patients with PaO_2/FiO_2 levels <200 mmHg. This is similar to the findings of Stéphan *et al*., who found a failure rate of 27.5% with HFNO therapy in the same category of patients.[12]

Increasing levels of $PaCO_2$ were associated with increased failure rates of HFNO therapy. Most large randomized controlled trials of HFNO therapy excluded patients with hypercapnia ($PaCO_2$ > 45 mmHg). However, our study failed to reveal a significant difference in $PaCO_2$ values at the initiation of HFNO therapy between patients who were successful with HFNO therapy versus those who failed HFNO therapy. Although the number of patients with $PaCO_2$ > 45 mmHg was low (n = 7), it is hypothesized that high flow nasal oxygen washes out carbon dioxide and decreases the dead space.[13-15] HFNO therapy has been used in isolated cases to manage hypercapnic respiratory failure.[16]

In a study conducted by Kang *et al*., around 74% of failures associated with HFNO therapy occurred in the first 48 h.[17] Early failure of HFNO, defined as failure within the first 2 days of initiation of treatment, was 91.3% in our study. Among patients who received HFNO therapy for <2 days, 40.4% of patients failed HFNO therapy. However, only 8.7% failed HFNO therapy when HFNO duration prolonged >48 h. A significant difference in failure rates was found among patients who received HFNO therapy for ≤2 days and those who received HFNO therapy for >2 days (P = 0.006). This is evidence that adds to the fact that HFNO failures are detected within 48 h of initiation of therapy.

Kang *et al*. had also reported increased mortality among patients who were intubated following >2 days of treatment of HFNO therapy.[17] Our study did not reveal any significant difference in mortality or ICU length of stay between patients who were converted to other modes of ventilation before and after 48 h duration. This may be because, in the light of recent evidence, the practice at our center emphasized on watching out for predictors of HFNO therapy failure during the first 48 h of therapy. Earlier studies have confirmed that beneficial effects of high-flow nasal oxygen in terms of arterial oxygen pressures improve within 15 min of initiation of therapy and a significant increase was seen as early as 1 h.[18] Roca *et al*. introduced the ROX index which can be used to predict the need for mechanical ventilation during HFNO therapy failure as early as 12 h after initiation of therapy. ROX index (SpO_2/($Fi O_2$ × respiratory rate) ≥4.88 after 12 h of HFNO therapy predicted lower risks for mechanical ventilation.[19] Rello *et al*. also reported the identification of patients who are likely to fail HFNO therapy as early as 6 h from the initiation of treatment.[20]

Conclusions

HFNO therapy is effective in managing respiratory failure in ICU setting. It may be used to manage patients with severe hypoxemic and hypercapnic respiratory failure. HFNO therapy failure happens in the early rather than late stages of therapy, mostly within the first 48 h after the initiation. Future studies may be designed to validate the use of HFNO therapy in hypercapnic respiratory failure and to identify early predictors of HFNO failure.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Jubilee Mission Medical College and Research Institute, Thrissur - 680 005, Kerala, supported the study.

Conflicts of interest

There are no conflicts of interest.

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