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Original Research Article

Comparison of Non-Invasive Ventilation and High Flow Nasal Oxygen Therapy as Respiratory Support in patients with Acute Hypoxemic Respiratory Failure in ICU: A Prospective Observational Study

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Conflict of interest: Nil

Abstract:

Background and Objectives: This observational prospective study was carried out to assess and compare the outcome of non-invasive ventilation (NIV) and high-flow nasal cannula (HFNC) therapy as respiratory support in patients suffering from acute hypoxemic respiratory failure.

Methods: This study included 137 patients. The modality of respiratory therapy was determined by the treating physician, and 60 and 77 patients received HFNC and NIV as initial respiratory support, respectively. The patients were followed for 28 days or till death (whichever was earlier). The primary outcome was number of ventilator-free days and secondary outcomes were duration of respiratory support, need for intubation, and duration of ICU stay and hospital stay and 28-day mortality after initiation of respiratory support.

Results: It was observed that the number of ventilator-free days (primary outcome) at day 28 was similar in both HFNC group (median 28 days) and NIV group (median 28 days). The 28 day mortality was found to be lower in HFNC group (28.3%) than in NIV group (39%) but it was not statistically significant (p 0.26). The intubation rate was also lower in HFNC group (33.3%) compared with NIV group (48.1%) but this difference was not statistically significant (p 0.12). The duration of initial support with HFNC (3 days, IQR 3-7) was significantly less than with NIV (5 days, IQR 1.25-6; $p<0.05$). The duration of ICU stay [8 days (IQR 5-12) vs 13 days (IQR 7.5-17.5)] and hospital stay [13 days (IQR 11-18) vs 18 days (IQR 11-25)] was significantly lower in HFNC group compared with NIV group ($p<0.05$).

Conclusion: It is concluded that HFNC was a better modality of respiratory support, as its use is associated with shorter ICU and hospital stay, more number of support-free days and it is required for lesser duration than NIV, though there is no difference in number of ventilation-free days, endotracheal intubation rate, or mortality rate at day 28 from initiation of respiratory support.

Keywords: Acute Hypoxemic Respiratory Failure, Non-Invasive Ventilation, High Flow Nasal Oxygen Therapy, Respiratory Support.

Introduction

Acute respiratory failure and the subsequent need for respiratory support, is a frequent cause of admission of adults to an intensive care unit. For such patients, mechanical respiratory support is required owing to hypoxemia, ventilatory failure, or both, or for increased work of breathing. Respiratory support can be provided to the patient in either a non- invasive or invasive manner. Acute hypoxemic respiratory failure (AHRF) is characterised by an arterial oxygen tension (PaO2) lower than 60 mmHg with a normal or low arterial carbon dioxide tension (PaCO2), with a SpO2 corresponding to ~ 90%. [1] AHRF may be managed by supportive measures, such as increasing concentration and flow with or without positive pressure through either non-invasive or invasive interface, along with definitive therapy for treatment of the underlying cause. Invasive mechanical ventilation involves the insertion of an artificial airway (an endotracheal or tracheostomy tube). Although this is regarded as a life-saving treatment, it comes with multiple inherent risks to patients. These risks include development of ventilator- induced lung injury [2], ventilator-associated pneumonia [3], or need for sedation with or without paralysis resulting in ICU-acquired weakness [4] or longer ICU and hospital stay [5]. Invasive mechanical ventilation should be avoided whenever possible, yet in some cases, intubation and mechanical ventilation are unavoidable [6].

Non-invasive respiratory modality is the preferred method of respiratory support for acute hypoxemic respiratory failure that can be delivered via any of the following approaches.

- Oxygen delivery devices
- High-flow nasal cannula (HFNC)
- Non-invasive positive-pressure ventilation (NIV)

The type of delivery device chosen depends on the severity and the cause of the patient's acute respiratory failure, and each device has benefits and drawbacks that determine its usefulness in clinical practice.

The heated and humidified high-flow nasal cannula or, as most call it, high-flow nasal cannula (HFNC), is not just a standard nasal cannula turned up to deliver the oxygen at very high flow rates. It blends the oxygen and air, heat it to 37°C with a 100% relative humidity, and can deliver 0.21 - 1.00 fraction of inspired oxygen (FiO2) at flow rates of up to 60 liters (L)/min [7]. The flow rate and FiO2 can be independently titrated based on a patient's flow and FiO2 requirements. HFNC also has some drawbacks as it cannot provide and maintain high level of PEEP. PEEP is reduced significantly when the patient opens his mouth [8]. The maximum flow rate cannot exceed 60L/min, so when the inspiratory flow demand of the patient is more than this, air entrapment occurs as a result the desired FiO2 is not delivered [9].

NIV is used in patients who not only require supplemental oxygen but also need support for the mechanical process of ventilation. A blend of oxygen and air is delivered at a prescribed FiO2 via an interface, which is either a tight-fitting mask (nasal mask, oronasal mask, or full-face mask) or a helmet. Substantial available data show that NIV improves outcomes among patients requiring respiratory support owing to cardiogenic pulmonary oedema10. NIV is also used in immunocompromised patients with AHRF and in post-operative patients of abdominal surgeries developing acute respiratory failure [10].

Despite showing clear benefit for certain conditions, NIV inhibits mobilization, is associated with gastric distension with risk for vomiting and aspiration, restricts effective communication and oral nutrition, and is poorly tolerated by some patients owing to discomfort [11]. Both HFNC and NIV improve alveolar oxygenation, improve gas exchange, deliver high fraction of inspired oxygen (FiO2), generate positive pressure and provide washout of dead space in the upper airways and decrease work of breathing by unloading inspiratory muscles during acute respiratory failure. [9,10] In our study, we planned to observe the clinical outcomes in patients admitted to the ICUs of our institution during the study period, and requiring either NIV or HFNC.

Aims & Objective:

Aims: To observe which of the two, HFNC or NIV, is better as respiratory support in patients with acute hypoxemic respiratory failure.

Objectives:

Primary

- To study number of ventilator-free days at day 28 in patients receiving HFNC and NIV

Secondary

- To study the proportion of acute hypoxemic respiratory failure patients receiving either HFNC or NIV.
- To study the duration of respiratory support needed in patients receiving HFNC and NIV.
- To study the duration of ICU stay among patients receiving HFNC and NIV.
- To study the duration of hospital stay among patients receiving HFNC and NIV.
- To study the 28 day mortality in patients receiving HFNC and NIV.

Materials and Methods

This non-randomised prospective observational study was conducted between May 2021 and October 2021 in patients admitted to NH-RTIICS ITU-3, ITU-4, 5, 6 and CCU-1 who were be put on NIV or HFNC, with the last month's patient followed up till November 2021.

Eligibility criteria and participant recruitment procedures:

Inclusion Criteria:

1. Age above 18 years
2. SpO_2 less than 90% with conventional oxygen therapy.
3. PaO_2 – less than 60mm Hg with conventional oxygen therapy, with normal or low $PaCO_2$.
4. Receiving HFNC or NIV at the discretion of the clinician.

Exclusion Criteria:

1. Type 2 respiratory failure ($PaCO_2$ > 45mm Hg).
2. Patients with acute hypoxemic respiratory failure, not satisfying criteria for non-invasive ventilation.

3. Pregnant patients.

Methodology:

Written consent from the patients/ patients' relatives was taken before enrolling them for the study. Epidemiologic and baseline data were collected for each patient (heart rate, blood pressure, respiratory rate, SpO_2, PaO_2/FiO_2 ratio, provisional diagnosis, and modality of initial respiratory support – HFNC/ NIV). Patients were followed up till day 28 from initiation of the respiratory support or death (whichever earlier) and the data recorded were duration of respiratory support, duration of hospital stay and ICU stay, invasive mechanical ventilation required or not, number of ventilator free days, mortality occurred or not, any crossover in respiratory support as rescue therapy required or not, if required duration of such respiratory support, patients location at day 28 from initiation of the respiratory support.

The decision regarding treatment plan like cross over to other modality and initiation of invasive ventilation were taken by the treating physician and his team.

In case the patient is discharged from the hospital the patient were called over telephone to enquire about his (or her) condition at day 28 from initiation of respiratory support. All the data were tabulated in the data collection sheet.

The candidates who had received NIV as a rescue therapy among patients receiving HFNC initially were considered to be in HFNC group during final analysis of the outcome parameters. Similarly, the candidates who had received HFNC as a rescue therapy among patients receiving NIV initially were considered to be in HFNC group during final analysis of the outcome parameters.

Definition of Ventilator-free days at day 28 [12].

One point was given for each calendar day during the measurement period, *i.e.* from the first day of respiratory support initiation to day 28 that patients were both alive and free of invasive mechanical ventilation. Zero value was given for patients who died both before extubation and day 28.

A patient extubated on Day 2 of the study and remaining alive and free of the ventilator for the remainder of the 28-day study period would receive a ventilator-free day score of 26, whereas the patient receiving mechanical ventilation until death on Day 2 would receive a score of zero. In the same way respiratory support free days was calculated by giving one point for each calendar day during the hospital stay of the patients were both alive and free of respiratory support.

Zero value was given for patients who died before extubation and day 28 after initiation of respiratory support. After completion of data collection, the data was tabulated and analysed using appropriate statistical methods as described later.

There was no conflict of interest in conduction of this study.

Sample size calculation for comparing two independent groups (Mean)

Sample size calculation formula for comparing two group means is

$n = 2 *(z_\alpha + z_\beta)^2/ (\delta/\sigma)^2$

Where Z_α and Z_β are standard normal deviate at α and β respectively (Z_α =1.96 at 5% level and Z_β =0.84 at 80% power)

δ is the difference of mean (Mean 1-Mean 2)

σ is pooled SD of two samples [for equal sized group]

$\sigma = \sqrt{(\sigma 1^2 + \sigma 2^2)/2}$]

In the study conducted by Frat et al 2015 [12], it was observed that ventilation-free days (mean ± SD) in HFNC and NIV were 24±8 and 19±12 respectively.

Therefore, calculated sample size was

$n = 15.68*10.2^2 / 5^2$

$= 65.2 \approx 65$

Taking into consideration, ~10% probable dropout we needed to enroll minimum 72 patients per group.

Statistical Analysis Methods:

All continuous variables were presented as mean ± SD or median (IQR) as appropriate and will be compared between the groups by independent t-test for normally distributed data and by Mann-Whitney U test for non-normal data. All qualitative data were presented as numbers and percentages. Chi-square test or Fisher's exact test were used to see the difference between the groups for qualitative variables. For analyzing continuous variable which were not normally distributed in the same sample Sign Test was used. All p-value <0.05 were considered as statistically significant. Statistical software SPSS 21.0 was used for data analysis.

Results

During the study period 310 patients received respiratory support with HFNC or NIV in the hospital. Out of these, 154 patients were excluded as per exclusion criteria. 156 were included, out of which 9 patients left against medical advice while on respiratory support and 10 patients gave negative consent for mechanical ventilation after enrollment in the study. Among the included patients, 137 patients were taken up for the final analysis. (Figure 1)

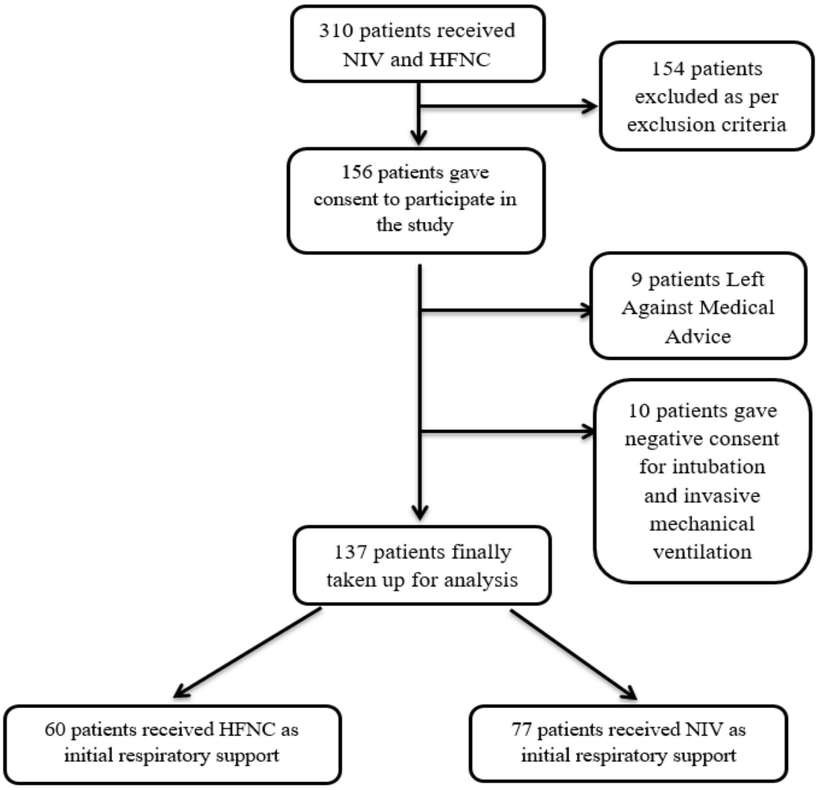

Figure 1: Flow Diagram

Out of 137 patients, 110 were male (80.29%) and 27 were female (19.71%).

Ages ranged from 18 to 88 years old, with a mean age of 54.30 ± 16.07 years. Out of 137 patients, 119 patients were suffering from COVID-19, 8 patients were suffering from lower respiratory tract infection, 5 patients were suffering from heart failure, rest of the patients were suffering from miscellaneous diseases like ARDS, pancreatitis, duodenal perforation.

Out of these 137 patients, 60 received HFNC (43.79%) and 77 received NIV (56.20%) as initial respiratory support. The baseline characteristics of all patients are summarized in Table 1.

Table 1: Baseline variables

	Total	HFNC (60)	NIV (77)	P-value
Age (Yrs)	54.30 ± 16.07	53.33 ± 17.94	55.05 ± 14.53	0.55
Sex (M: F)	110:27	50:10	60:17	0.57
Baseline PaO_2/FiO_2	77.28 ± 21.72	76.25±22.18	78.09±21.76	0.63

There was no difference between the HFNC group and the NIV group regarding the age and gender of the included patients; there was also no significant difference in baseline PaO_2/FiO_2 ratio and diagnosis between the two groups. The associated co-morbidities were diabetes mellitus, hypertension, and other co-morbidities (hypothyroid, ischemic heart disease, cerebrovascular accident, obesity, chronic cardiac disease, chronic kidney disease, post renal transplant, pancreatitis, Parkinsonism). The co-morbidities were also comparable in each group.

Table 2: Distribution of causes of acute hypoxemic respiratory failure among initial respiratory support groups

Diagnosis	HFNC	NIV	Total	P-value
COVID-19	50	69	119	0.14
ARDS	0	1	1	
LRTI	5	3	8	
Cardiac causes	5	0	5	
Others	0	4	4	
Total	60	77	137	

Table 3: Co-morbidities

Co-morbidities	HFNC (60)	NIV (77)	P-value
DM	14 (23.3%)	18 (23.4%)	1
HTN	19 (31.7%)	27 (35.1%)	0.814
Other comorbidities	14 (23.3%)	9 (11.7%)	0.11
No comorbidities	22 (36.7%)	35 (45.5%)	0.39

The PaO_2/FiO_2 were found to be significantly improved after 1 hour of application of HFNC as well as NIV but PaO_2/FiO_2 measured 1 hour after respiratory support showed better increase in HFNC group than in the NIV group, which was statistically significant ($p<0.05$).

Table 4: Median PaO_2/FiO_2 in the two groups before and after application of respiratory support.

Initial Respiratory Support	Median Baseline PaO_2/FiO_2 (IQR)	Median PaO_2/FiO_2 after 1 hour of initiation of Respiratory Support (IQR)	p-value
HFNC	82.5 (67.25,88.75)	129 (96.5,150)	<0.001
NIV	76 (55.5,90.0)	120 (92.5,135)	<0.001

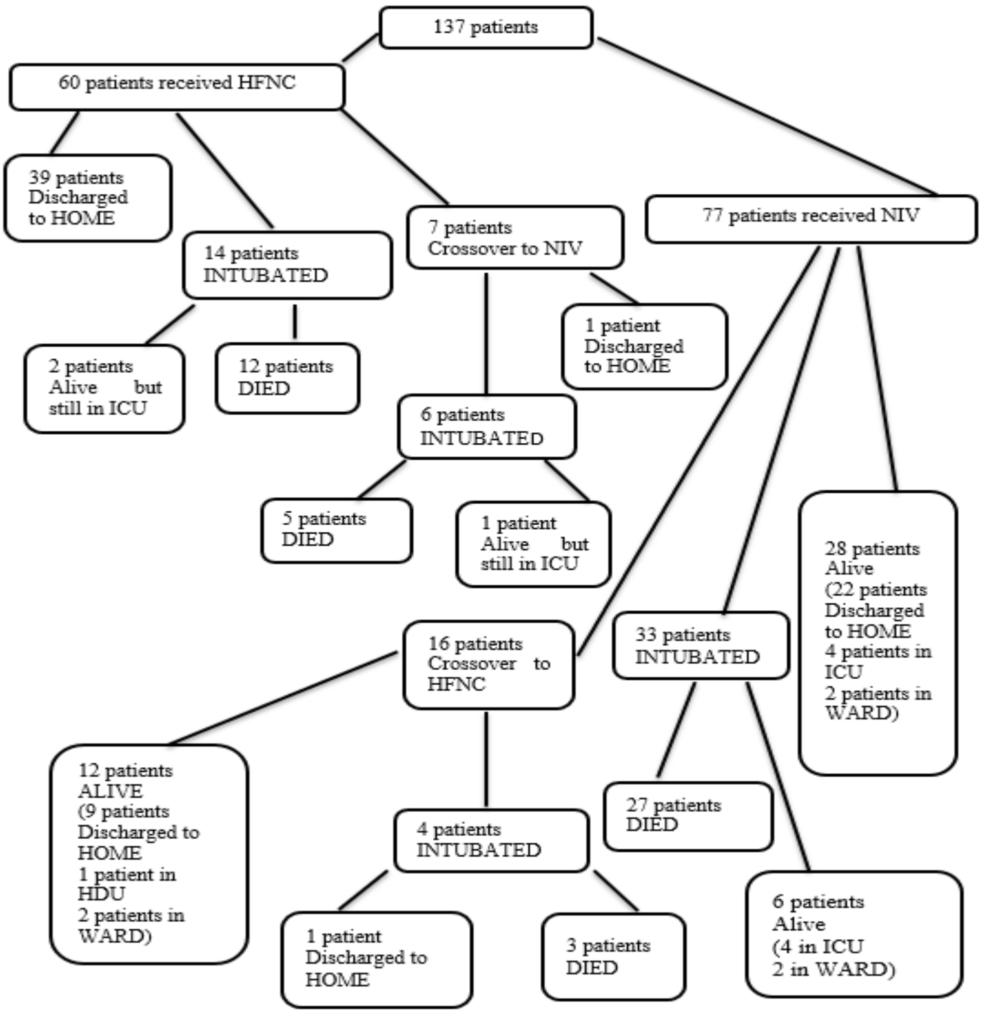

Figure 2. Outcome of the respiratory support

Among the 60 patients who received HFNC as the primary therapy for hypoxemia, 39 patients showed good response with no need to further escalate the respiratory support, and the median duration of initial respiratory support with HFNC was 3(1.25,6) days (Figure 2). 21 patients had progressive respiratory decompensation and failed therapy with HFNC, endotracheal intubation was done for 14 patients, and 7 patients were shifted to NIV as a rescue treatment, among whom 6 patients were intubated subsequently (Figure 2). The success rate of HFNC as initial therapy for acute hypoxemic respiratory failure was 65% (39 patient discharged to home), and total endotracheal intubation rate was 33.3% (20 patients), and mortality rate was 28.3% (17 patients) (Figure 2). The median duration of

ICU stay and hospital stay in patients receiving HFNC as initial respiratory support was 8(5,12) days and 13(11,18) days respectively. The mean and median ventilator free days in patients receiving HFNC as initial respiratory support were 19.07±12.99 days and 28 (0, 28) days respectively (Figure 2). Out of 60 patients receiving HFNC as initial support at day 28, 40 patients where at home (including 1 patient who crossed over to NIV), 3 were still in the hospital and 17 patients were dead. (Table 7) Among the 77 patients initially treated with NIV, 28 patients had favorable outcome at day 28(22 patients were discharged to home and 6 patients were still in hospital), and the mean duration of initial respiratory support was 5.74 ± 4.81 days (Table 5). 33 patients failed to improve with NIV and were intubated, and 16 patients did not tolerate NIV and were shifted to HFNC as a rescue therapy which was successful in 12 of them, while 4 patients were intubated (Figure 5). The success rate of NIV as initial therapy for acute hypoxemic respiratory failure was 28.5% (22 patients were discharged home), total endotracheal intubation rate was 48.1 % (37 patients), and mortality rate was 39.0% (30 patients). The median duration of ICU stay and hospital stay in patients receiving NIV as initial respiratory support was 13(7.5,17.5) days and 18(11,25) days respectively. The mean and median ventilator free days in patients receiving NIV as initial respiratory support were 15.32 ± 13.72 days and 28 (0, 28) days respectively (Table 5). Out of 77 patients receiving NIV as initial support at day 28, 32 patients where at home (including 10 patients who crossed over to HFNC), 15 were still in the hospital and 30 patients were dead. (Table 7)

Table 5: Outcome parameters represented as mean ± standard deviation, median and interquartile range and their respective p-values in the two Groups of Initial Respiratory Support.

	HFNC (60)	NIV (77)	P-value
P/f after 1 hour of Initial Respiratory Support	125.25±30.47 129(96.5,150)	114.27±31.12 120(92.5,135.5)	0.046
VAS after 1 hour of Initial Respiratory Support	0.57±1.05 0(0,1)	3.64±1.29 4(2.5,4.5)	<0.0001
Duration Initial Respiratory Support (Days)	4.32±3.47 3(1.25,6)	5.74±4.81 5(3,7)	0.022
ICU Stay (Days)	9.53±6.33 8(5,12)	13.18±7.21 13(7.5,17.5)	0.002
Hospital Stay (Days)	15.12±6.83 13(11,18)	18±8.14 18(11,25)	0.04
Ventilation free days	19.07±12.99 28(0,28)	15.32±13.72 28(0,28)	0.109
Support free Days	15.22±11.11 19(0,25.75)	10.75±10.62 12(0,22)	0.006

Table 6: Distribution of outcomes of the initial respiratory support at 28 days

Outcome	HFNC (60)	NIV (77)	P-value
Alive	43(71.7%)	47 (41%)	0.26
Cross-over	7 (11.7%)	16 (20.8%)	0.24
Invasive ventilation	20 (33.3%)	37 (48.1%)	0.12
Mortality	17 (28.3%)	30 (39%)	0.26

The VAS Score after 1 hour of applying HFNC were found to have significantly lower score when compared to patients receiving NIV.

The duration of initial respiratory support, ICU stay, hospital stay was significantly lower in the patients receiving HFNC as initial respiratory support when compared to NIV as initial respiratory support.

The ventilator free days, intubation rate, mortality at 28 days from initiation of respiratory support and patients requiring crossover were not significantly different in the two groups. (Table 5)

Table 7: Patient location at 28 Days after initiation of respiratory support

Location	HFNC (60)	NIV (77)
Home	40 (66.7%)	32 (41.6%)
Ward	0	6 (7.8%)
HDU	0	1 (1.3%)
ICU	3 (5%)	8 (10.4%)
Death	17 (28.3%)	30 (39%)

Discussion

Acute hypoxemic respiratory failure is one of the leading causes of ICU admission and mortality [13]. The four pathophysiological mechanisms that account for the AHRF seen in a wide variety of diseases are 1) ventilation/perfusion mismatch, 2) increased shunt, 3) diffusion impairment and 4) alveolar hypoventilation [14]. Ventilation/perfusion mismatch is the most common mechanism. It occurs when there is decreased ventilation to normally perfused alveoli or when there is a greater reduction in ventilation as compared to perfusion in certain lung units. With shunt, either intrapulmonary or intracardiac deoxygenated mixed venous blood bypasses ventilated alveoli, resulting in "venous admixture". Diseases that increase the diffusion pathway for oxygen from the alveolar space to the pulmonary capillaries, decrease capillary surface area or shorten the transit time of the blood through the pulmonary capillaries prevent complete equilibration of alveolar oxygen with pulmonary capillary blood [1]. The common causes of AHRF include pneumonia, pulmonary edema, ARDS, atelectasis, pulmonary embolism and pulmonary haemorrhage. Therapies for acute hypoxemic respiratory failure include treatment of the underlying cause and supportive measures like oxygen therapy (via variety of devices like nasal prongs, face mask, high flow mask, venturi mask, HFNC [15], NIV, invasive ventilation with or without neuromuscular blockade [16], inhaled vasoactive agents, prone positioning, extracorporeal life support [17].

In this study we tried to observe the difference between HFNC and NIV as respiratory support in patients with acute hypoxemic respiratory failure. Our study was conducted during the ongoing COVID-19 pandemic between May 2021 and October 2021. The number of patients developing acute hypoxemic respiratory failure had increased manifold during this pandemic. In our study the total number of AHRF patients due to COVID-19 outnumbered the other causes in critical care setting. The principle finding of our study was that there was no significant difference in number of ventilator-free days (primary outcome), rates of endotracheal intubation and mortality at 28 days between HFNC and NIV groups. The duration of respiratory support, ICU stay and hospital stay was significantly shorter in HFNC group as compared with NIV group. The VAS score after 1 hour of initiation of respiratory support was significantly less with the patients receiving HFNC compared to NIV. The PaO2/FiO2 ratio after 1 hour of initiation of respiratory support by either modality were improved compared to the baseline but this improvement was significantly better in patients receiving HFNC as initial support (as depicted in Table 4 and Table 5). The mean number of ventilation free days in our study was 19.07±12.99 days (median 28 days, IQR 0, 28) and 15.32±13.72 days (median 28 days, IQR 0, 28) in HFNC and NIV group respectively. There was no statistically significant difference between the groups. In the study conducted by Frat et al 2015 [12], the mean number of ventilator free days were 24±8 days and 19±12 days in HFNC and NIV groups respectively. This difference was statistically significant between the groups. We know that pathophysiology and clinical course of COVID-19 is a bit different from other causes of acute hypoxemic failure. This difference compared to our result, could be attributed to the fact that the study by Frat et al [12] was conducted in a pre- COVID-19 era. In contrast to this study, the majority of patients enrolled in our study had COVID-19 pneumonia.

The median PaO2/FiO2 after 1 hour of initiation of respiratory support in our study was found to be 129 (IQR 96.5, 150) and 120 (IQR 92.5, 135.5) in HFNC and NIV respectively, which was significantly more compared to baseline PaO2/FiO2 with both the modalities [median baseline PaO2/FiO2 was 82.5 (IQR 67.25, 88.75) and 76 (IQR 55.5, 90.0) in HFNC and NIV group respectively]. The median PaO2/FiO2 after 1 hour of initiation of respiratory support in our study was found to be higher in HFNC compared to NIV and it was statistically significant. In the study conducted by Frat et al [12] the mean PaO2/FiO2 after 1 hour was 133±73 and 183±83 in HFNC and NIV group and this difference was also found to be statistically significant. Shoukri et al [18] found the mean PaO2/FiO2 after 24 hours of therapy to be 225.67±44.33 and 241.53±49.43 in HFNC and NIV group respectively and there was no statistically significant difference between the two groups. The rise in P/f ratio in HFNC group was found to be higher in our study. This may be due to better compliance to awake proning in patients receiving HFNC than NIV.

The average rates of endotracheal intubation with invasive mechanical ventilation for patients who received HFNC and NIV were 33.3% and 48.1% respectively in our study. This finding is similar to the finding of Frat et al 2015 [12] where the intubation rate was 40% and 55% respectively in HFNC and NIV group. Nair et al 2021 [19] found the intubation rates at 48 hours to be 20% and 33% in HFNC and NIV respectively. The intubation rate at day 7 was 27.27% and 46.29% in HFNC and NIV group respectively. This was lower in comparison to our study because our intubation rates were calculated after a longer period of time (at day 28) compared to this study but the trend is similar to our study. In the study performed by Shoukri et al 2021 [18] the intubation rate was found to be 10.81% and 11.53% in HFNC and NIV group. The intubation rates in the study done by

Duan et al [20] were 17% and 15% in HFNC and NIV group respectively. The baseline PaO2/FiO2 in our study was 76.25±22.18 and 78.09±21.76 in HFNC and NIV. The intubation rates are found to be lower compared to ours, in the studies conducted by Shoukari et al [18] (baseline PaO2/FiO2 191.08 ± 37.83 and 190.38 ± 42.47 in HFNC and NIV respectively) and Duan et al [20] (baseline PaO2/FiO2 196 ± 46 and 165 ± 48 in HFNC and NIV respectively) as they had enrolled less sicker patients compared to our study. This is indicated by the mean baseline P/f ratio of these studies. All the above study results corroborate with the findings of our study that the difference in intubation rates among the HFNC and NIV groups was not statistically significant. The intubation rate in the study carried out by Coudroy et al [21] which involved only immunocompromised patients suffering from acute hypoxemic failure, intubation rates were 35% and 55% in HFNC and NIV group respectively, and this difference was statistically significant. Once again, this difference may be attributed to the fact that Coudroy et al [21] included only immunocompromised patients in their study.

The mean duration of respiratory support with HFNC in our study was 4.32±3.47 days, while the duration of treatment with NIV was 5.74±4.81days. The duration of respiratory support of our study was comparable with study conducted by Shoukri et al 2021 [18]. In their study mean duration of treatment with HFNC was 5.53 ± 1.11 days, while the duration of treatment with NIV was 5.86 ± 1.10 days. The median duration of respiratory support of our study was also comparable with study performed by Duan et al 2020 [20] where the median duration of respiratory support were 7.1 days (IQR: 3.5–12.2) and 7.3 days (IQR: 5.3–10.0) in HFNC and NIV group respectively.

The median duration of ICU stay assessed at day 28 in our study were 8 (IQR 5, 12) and 13 (IQR 7.5,17.5) in HFNC and NIV group respectively and it was found to be significantly lower in the HFNC group. In the study performed by Coudroy et al 2016 [21] which involved only immunocompromised patients suffering from acute hypoxemic failure, median duration of ICU stay was 7 (IQR 4,9) and 8 (IQR 5,13) in HFNC and NIV group respectively, where the difference between the groups was not statistically significant. In the study conducted by Frat et al 2015 [12] found mean length of ICU stay assessed at day 90 to be 10.7±15.8 days and 11.0±11.6 days in HFNC and NIV group respectively, among survivors. Among non-survivors it was 14.9±13.6 days and 15.7±13.7 days in HFNC and NIV group respectively and there was no statistically significant difference between the groups. The median duration of hospital stay assessed at day 28 in our study were 8 (IQR 5, 12) and 13 (7.5, 17.5) in HFNC and NIV group respectively, and it was found to be significantly lower in the HFNC group. The median length of hospital stay was analysed by Nagata et al [22], in the HFNC group it was 22 (IQR 14, 31.5) and 13 (IQR 9, 26) in patients receiving NIV. This study was conducted in early years after introduction of HFNC in clinical practice and in pre-COVID-19 period. This may have resulted in this difference of results between our study and that of Nagata et al 22. Support-free days at day 28 after initiation of respiratory support in our study was found to be higher in HFNC group compared to NIV group and this difference was statistically significant. This parameter has not been compared in any of the previous studies.

The mortality at day 28 in our study was found to be 28.3% and 39% in patients who received HFNC and NIV respectively as initial respiratory support. This difference was not statistically significant. Frat et al 2015 [12] found mortality at day 90 to be 12% and 28% in HFNC and NIV groups respectively. Duan et al 2020 [20] obtained a mortality of 4% and 8% in HFNC and NIV groups respectively, in their study. Shoukri et al 2021 [18] found a mortality rate of 2.7% and 3.8% in HFNC and NIV groups respectively.

Koga et al 2020 [23] found a 30-day mortality of 29% and 32% in the HFNC and NIV groups respectively. Nair et al 2021 [19] found a hospital mortality of 29.1% and 46.2% in HFNC and NIV groups respectively. None of these studies revealed any statistically significant difference between the patients who received HFNC or NIV with respect to mortality, which matches with the finding of our study. Coudroy et al 2016 [21] in his study on immunocompromised patients found a statistically significant difference in 28-day mortality (20% in NIV vs 40% in HFNC) between the two groups. This difference may be due to the fact that it was performed exclusively in immunocompromised patients.

VAS Score after 1 hour was found to be lower in HFNC group compared to NIV group and this difference was statistically significant. This indicates that HFNC is better tolerated as a modality of respiratory support.

Crossover rate in our study was 11.7% and 20.8% in patients receiving HFNC and NIV as initial respiratory support, respectively. In the study conducted by Shoukri et al 2021 [18] crossover was needed in 3 patients out of 37 patients in patients receiving HFNC initially and 2 patients out of 26 patients in patients receiving NIV. In the study conducted by Koga et al 2021 [23] crossover to NIV was needed in 54 patients out of 200 patients requiring HFNC initially and out of 378 patients requiring NIV initially only 2 required switch to

HFNC. In the study conducted by Duan et al 2020 [20] crossover to NIV from HFNC was required in 43% patients and crossover to HFNC from NIV was required in 8% cases. In our study the crossover rate from NIV to HFNC was found to be higher compared to the other studies, probably because the above studies were conducted either during initial days of COVID-19 pandemic or prior to the pandemic. In our study, 119 of 137 patients were suffering from COVID-19. The compliance of the patients to awake proning was observed to be very poor among the patients receiving NIV. However, with HFNC the compliance to awake proning was found to be much higher. Thus, the treating physicians were also keen to switch from NIV to HFNC, when patients were uncomfortable with awake proning on NIV. Out of 77 patients receiving NIV as initial support at day 28, 32 patients where at home, 15 were still in the hospital and 30 patients were dead. Out of 60 patients receiving HFNC as initial support at day 28, 40 patients where at home, 3 were still in the hospital and 17 patients were dead. None of the previous studies tried to analyse the location of the patient at day 28.

Our study was a prospective study and we were able to meet the target sample size of 135. We also followed the patients till 28 days from initiation of respiratory support even after hospital discharge. In this study we explored use of HFNC which is a new modality of non-invasive respiratory support for acute hypoxic respiratory failure in our institute, whereas there is better experience with use of NIV in this group of patients. Further studies are required to establish the superiority of one modality over the other.

Our study has certain limitations. Being a single-centre study, the sample size was limited. The study was non-randomised and observational in nature. It was conducted amidst the COVID-19 pandemic in India, leading to inclusion of high number of COVID-19 patients. The proportion of acute hypoxemic failure due to non-COVID illness was relatively less in our study population. So, the findings of this study may not be generalised to all other diseases causing acute hypoxemic respiratory failure.

Conclusion

It is concluded that HFNC was a better modality of respiratory support, as its use is associated with shorter ICU and hospital stay, more number of support-free days and it is required for lesser duration than NIV, though there is no difference in number of ventilation-free days, endotracheal intubation rate, or mortality rate at day 28 from initiation of respiratory support.

Reference

1. Roussos C, Koutsoukou A. Respiratory Failure. European Respiratory Journal 2003 22:3s-14s.
2. Gattinoni L, Carlesso E, Langer T. Towards ultraprotective mechanical ventilation. Current Opinion in Anesthesiology. 2012 Apr 1; 25(2):141-7.
3. Muscedere J, Dodek P, Keenan S, Fowler R, Cook D, Heyland D, VAP Guidelines Committee, Canadian Critical Care Trials Group. Comprehensive evidence-based clinical practice guidelines for ventilator-associated pneumonia: prevention. Journal of Critical Care. 2008 Mar 1; 23(1):126-37.
4. Morandi A, Brummel NE, Ely EW. Sedation, delirium and mechanical ventilation: the ‘ABCDE’ approach. Current opinion in critical care. 2011 Feb 1; 17(1):43-9.
5. Safdar N, Dezfulian C, Collard HR, Saint S. Clinical and economic consequences of ventilator-associated pneumonia: a systematic review. Critical care medicine. 2005 Oct 1; 33(10):2184-93.
6. Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. The Lancet. 2009 Jul 18; 374(9685):250-9.
7. Roca O, Riera J, Torres F, Masclans JR. High-flow oxygen therapy in acute respiratory failure. Respiratory care. 2010 Apr 1; 55(4):408-13.
8. Nishimura M. High-Flow Nasal Cannula Oxygen Therapy in Adults: Physiological Benefits, Indication, Clinical Benefits, and Adverse Effects. Respiratory Care 2016 Apr 1;61(4):529-541.
9. Chanques G, Riboulet F, Molinari N, Carr J, Jung B, Prades A, Galia F, Futier E, Constantin JM, Jaber S. Comparison of three high flow oxygen therapy delivery devices: a clinical physiological cross-over study. Minerva anestesiologica.2013 Jul 15;79(12):13 44-55.
10. Chawla R, Dixit SB, Zirpe KG, Chaudhry D, Khilnani GC, Mehta Y, Khatib KI, Jagiasi BG, Chanchalani G, Mishra RC, Samavedam S. ISCCM guidelines for the use of non-invasive ventilation in acute respiratory failure in adult ICUs. Indian journal of critical care medicine: peer-reviewed, official publication of Indian Society of Critical Care Medicine. 2020 Jan; 24(Suppl 1): S61.
11. Sluijs A. Non Invasive Ventilation; PROs and CONs. Netherlands Journal of Critical Care 2013 May; 7(2);27-29.
12. Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, Prat G, Boulain T, Morawiec E, Cottereau A, Devaquet J. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. New England

Journal of Medicine. 2015 Jun 4; 372(23): 2185-96.

13. Bellani G, Laffey JG, Pham T, et al. Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. JAMA. 2016;315(8):788–800.
14. Hall JB, Schmidt GA, Wood LD. Acute hypoxemic respiratory failureIn: Murray JF Nadel JA editors. Textbook of Respiratory Medicine Philadelphia, PA, Saunders. 2000,3rd edition ;2413–2442.
15. Hardavella G, Karampinis I, Frille A, Sreter K, Rousalova I. Oxygen devices and delivery systems. Breathe 2019 Sep;15(3):e108-e116.
16. Raoof S, Goulet K, Esan A, Hess DR, Sessler CN. Severe Hypoxemic Respiratory Failure: Part 2 - Nonventilatory Strategies. Chest 2010 Jun;137(6):1437-1448.
17. Munshi L, Walkey A, Goligher E, Pham T, Uleryk EM, Fan E. Venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome: a systematic review and meta-analysis. Lancet Respir Med. 2019 Feb;7(2):163-172.
18. Shoukri, A.M. High flow nasal cannula oxygen and non-invasive mechanical ventilation in management of COVID-19 patients with acute respiratory failure: a retrospective observational study. Egypt J Bronchol 2021 Mar; 15:17.
19. Nair PR, Haritha D, Behera S, Kayina CA, Maitra S, Anand RK, Ray BK, Soneja M, Subramaniam R, Baidya DK. Comparison of High-Flow Nasal Cannula and Noninvasive Ventilation in Acute Hypoxemic Respiratory Failure Due to Severe COVID-19 Pneumonia. Respiratory Care September 2021, respcare. 09130; DOI: 10.4187/respcare.09130.
20. Duan J, Chen B, Liu X, Shu W, Zhao W, Li J, Li Y, Hong Y, Pan L, Wang K. Use of high-flow nasal cannula and noninvasive ventilation in patients with COVID-19: A multicenter observational study. The American Journal of Emergency Medicine. 2020 Jul 29.
21. Coudroy R, Jamet A, Petua P, Robert R, Frat JP, Thille AW. High-flow nasal cannula oxygen therapy versus noninvasive ventilation in immunocompromised patients with acute respiratory failure: an observational cohort study. Annals of intensive care.2016 Dec; 6(1):1-1.
22. Nagata K, Morimoto T, Fujimoto D, Otoshi T, Nakagawa A, Otsuka K, Seo R, Atsumi T, Tomii K. Efficacy of high-flow nasal cannula therapy in acute hypoxemic respiratory failure: decreased use of mechanical ventilation. Respiratory care. 2015 Oct 1; 60(10):1390-6.
23. Koga Y, Kaneda K, Fujii N, Tanaka R, Miyauchi T, Fujita M, Hidaka K, Oda Y, Tsuruta R. Comparison of high-flow nasal cannula oxygen therapy and non-invasive ventilation as first-line therapy in respiratory failure: a multicenter retrospective study. Acute Med Surg. 2019 Sep 27; 7(1): e461.