

A retrospective observational study to determine the role of High Flow Nasal Oxygen in terms of recovery, mortality and need for invasive ventilation in COVID-19 cases

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Abstract

Background: Hypoxemic respiratory failure in COVID-19 is managed by conventional oxygen, High Flow Nasal Oxygen (HFNO), and invasive ventilation. Multiple studies have proven that using HFNO in the early stages of acute hypoxemia failure can lead to better outcomes and delay or avoidance of invasive ventilation. This observational study was conducted to further establish this hypothesis. Also, no difference was found in mortality rates between the usage of HFNO Conventional Oxygen Therapy. However, there are very limited studies comparing outcomes of HFNO and Invasive ventilation usage. Hence, this study was undertaken to gain insight into comparing HFNO and invasive ventilation. **Materials and Methods:** A retrospective data collection was performed from 06/05/2021 to 15/12/2021 after approval from the Institutional Ethics Committee. The collection was performed at MMFHA Ratna Hospital, Pune. All Indoor patient department files of positive cases of COVID first wave (2020) and second wave (2021) were screened. Reverse Transcription Polymerase Chain Reaction COVID-positive cases belonging to both genders, aged 18-100 years and where HFNO was part of management were selected, and data was extracted about socio-demographic data, clinical profile, and routine investigations advised, course of the patient in the hospital with respect to vital parameters, daily HFNO parameters, all the medications received, any other interventions if required, and the time points of taking patients off HFNO, the requirement of invasive ventilation, shifting out of Intensive Care Unit discharge, or death. Immunocompromised cancer patients and pregnant women were excluded. Outcomes were measured in terms of recovery, need for mechanical ventilation, and mortality. **Results:** Out of 700 cases screened, HFNO was used in 38 (5.4%) participants. The duration of HFNO ranged from less than one day to more than seven days. Of those 38, 30 (78.9%) received HFNO and 8 (21.05%) were shifted to mechanical ventilation. Out of these 30, eight (21.05%) expired on HFNO, eighteen (47.36%) were discharged, and four (10.52%) were shifted to another hospital on HFNO. All eight participants on mechanical invasive ventilation expired. **Conclusions:** In terms of recovery from HFNO use, discharge with a recovery rate was higher than mortality and the need for mechanical ventilation. The need for invasive mechanical ventilation was much lower in HFNO used participants (26 versus 8). All those on mechanical ventilation expired. HFNO can be a useful modality for oxygenation in COVID-19 patients. The exact role of HFNO in the trajectory of the management of hypoxemic respiratory failure due to COVID-19 needs to be defined.

Keywords: COVID-19, Acute Hypoxic Injury, HFNO, Mechanical Invasive ventilation

Introduction

SARS-CoV-2 causes COVID-19 which is a droplet infection. On 11th March 2024, the World Health Organization (WHO) declared it a pandemic. The respiratory symptoms form a major percentage, followed by gastrointestinal manifestations. Using High-Flow Nasal Oxygen (HFNO) requires guidance and expertise among the various modalities available to correct hypoxemic respiratory failure. The use of HFNO in the early stages of acute hypoxemia failure can lead to better outcomes and delay or avoidance of invasive ventilation⁽¹⁻³⁾. Also, no difference was found in

mortality rates between the usage of HFNO and Conventional Oxygen Therapy (COT)^(1,2). The European Society of Intensive Care Medicine and the European Respiratory Society recommended HFNO over COT in Acute Hypoxemic Respiratory Failure (AHRF)^(4,5). Surviving Sepsis Campaign (SSC) guideline 2021 by Society of Critical Care Medicine (SCCM) suggests weak but low-quality evidence supporting HFNO in ventilation strategies⁽⁶⁾. WHO recommends that candidates on HFNO need to be awake, alert, and cooperative. It clearly states that HFNO can delay the need for intubation; however, the success of HFNO requires early initiation, close monitoring, and experience⁽⁷⁾.

HFNO can be heated to 37° C. It can deliver Fraction of Inspired Oxygen (FiO₂) between 0.21 and 1.00% at the flow rate up to 60 liters (L)/min, with 100% relative humidity. The FiO₂ and flow rate can be independently titrated. These are based on the patient's flow and FiO₂ requirements. HFNO has few benefits when compared to various respiratory management techniques. It uses hot and humidified air, helping decreasing airway inflammation, can meet inspiratory demand, increase functional residual capacity, minimize oxygen dilution, and decrease dead space⁽⁸⁾. These reasons make HFNO a better choice in respiratory management. However, some disadvantages cannot be ignored, like delay in intubation, as it may mask patients' clinical condition and airborne transmission to health workers^(7,9).

Objective

To assess the role of HFNO in terms of recovery, mortality, and need for invasive ventilation in COVID-19 cases.

Materials and Methods

After taking Institutional Ethics Committee (IEC) approval, this retrospective observational study was conducted in a tertiary care hospital. All positive COVID-19 cases from the first and second waves were taken. Out of 700 cases, 38 participants were included in HFNO as respiratory therapy. All selected participants were 18 years and above of age and were admitted to a tertiary care hospital from the period of January 2020 to April 2021. Data collection commenced from 06/05/2021 to 15/12/2021. This study has been conducted according to the ethical standards laid down by Pharmaceuticals for Human Use Guideline for Good Clinical Practice (ICH GCP).

Sample size determination

Sample size was calculated based on the previously published study⁽¹⁰⁾ using the following formula:

$$n = z^2 \frac{pq}{(me)^2}$$

p = 0.667 (66.7%) (Published estimate of the incidence of good outcome),

q = 0.333 (33.3%) (1-p),

Z = 1.96 (Standard normal score at 95% confidence interval),

me = 0.15 (15.0%) (margin of error).

$n = 1.96 \times 2 \times 0.667 \times 0.333 / (0.15 \times 2) = 37.92$.

Thus, the minimum sample size was $37.92 \approx 38$.

Purposive sampling method was used.

Statistical Methods for Data Analysis

The IBM Statistical Package for Social Sciences (SPSS) version 24.0 was used for data analysis. The results were presented as number of cases (n) and percentage (%). The other variables (continuous data) were presented as Mean and Standard deviation (SD). Chi-square test or Fischer's Exact Probability test (2×2 table) was used to test statistical significance. P < 0.005 was considered statistically significant.

Data collection

A retrospective observational data collection was performed on positive COVID-19 cases with HFNO use, which were confirmed by Reverse Transcription Polymerase Chain Reaction (RT-PCR). All positive cases were determined on the basis of nasal and throat swab examination. The components of data collected were age, gender, pre-existing co-morbidities, number of days HFNO used, outcomes in terms of discharge with recovery, need for mechanical invasive ventilation, and mortality after HFNO use.

Results

Distribution of demographic and other clinical characteristics of COVID-19 cases studied

Among 38 cases, seven (18.4%) cases were in the age group of 40-49 years, nine cases (23.7%) were in the age group of 50-59 years followed by 13 cases (34.2%) were in the age group of 60-69 years and only three (7.9%) cases had age above 80 years. The mean age of cases studied was 61.5 years (SD 12.8 years). Of 38 cases studied, majority i.e., 29 cases (76.3%) were male and nine (23.7%) were female. The male-to-female ratio in the study group was 3.22:1.00. The proportion of HFNO users was found to be higher in male participants. Of 38 cases studied, 22 cases (57.9%) had diabetes, 22 cases (57.9%) had hypertension, five cases (13.2%) had Ischemic Heart Disease (IHD), three cases (7.9%) had hypothyroidism and six cases (15.8%) had other co-morbidities. An equal distribution of incidence was found in hypertension and diabetes use of HFNO (Table 1).

Table 1: Distribution of demographic and other clinical characteristics of COVID-19 cases treated using HFNO

Variables	No. of cases (n) (%)
Age group (in years)	
40-49	7 (18.4)
50-59	9 (23.7)
60-69	13 (34.2)
70-79	6 (15.8)
80	3 (7.9)
Gender	
Male	29 (76.3)
Female	9 (23.7)
Co-morbidity	
Diabetes Mellitus	22 (57.9)
Hypertension	22 (57.9)
Ischemic Heart Disease	5 (13.2)
Hypothyroidism	3 (7.9)
Other	6 (15.8)
HFNO duration	
<1 day	7 (18.4)
1-7 days	25 (65.8)
>7 days	6 (15.8)
Outcomes	
Expired	16 (42.1)
Discharged	18 (47.4)
Shifted to another hospital	4 (10.5)
Invasive ventilation used	
Yes	8 (21.1)
No	30 (78.9)

Of 38 cases studied, seven cases (18.4%) had HFNO duration less than one day, 25 cases (65.8%) had HFNO duration between 1–7 days, and six cases (15.8%) had HFNO duration more than seven days. Of 38 cases studied, 16 cases (42.1%) expired, 18 cases (47.4%) were discharged, and four cases (10.5%) were shifted to different hospitals for further clinical management. Of the 38 cases studied, eight cases (21.1%) required invasive ventilation, and 30 cases (78.9%) did not require invasive ventilation.

Incidence of mortality according to the HFNO duration

Of 32 cases who were given HFNO for less than seven days, 13 (40.6%) expired, 16 (50.0%) were discharged, and three (9.4%) were shifted to another hospital. Of six cases who were given HFNO for more than seven days, three (50.0%) expired, two (33.3%) were discharged, and one (16.7%) was shifted to another hospital. The distribution of incidence of mortality did not differ across groups of cases with different durations of HFNO (p -value>0.05) (Table 2).

Table 2: Distribution of incidence of mortality and the use of invasive ventilation according to the HFNO duration

Variable	High Flow Nasal Oxygen (HFNO) duration (in days)		
	≤7 days (n=32)	>7 days (n=6)	p - value
	n (%)	n (%)	
Outcomes			
Expired	13 (40.6)	3 (50)	0.72
Discharged	16 (50)	2 (33.3)	
Shifted to another hospital	3 (9.4)	1 (16.7)	
Invasive ventilation used			
Yes	7 (21.9)	1 (16.7)	0.99
No	25 (78.1)	5 (83.3)	

Incidence of use of invasive ventilation according to the HFNO

Of 32 cases who were given HFNO for less than seven days, seven (21.9%) required invasive ventilation. Of six cases that were given HFNO for more than seven days, one (16.7%) required invasive ventilation.

The distribution of incidence of the requirement of invasive ventilation did not differ significantly across various groups of cases with different durations of HFNO in the study group (p-value>0.05)(Table 2).

Discussion

The retrospective observational study was aimed at studying the various outcomes of HFNO usage and comparing them to mechanical ventilation. From our sample pool of 38 participants, 78.9% did not require mechanical invasive ventilation, whilst 21.1% required mechanical invasive ventilation. However, the incidence of mortality did not differ between the two modalities of therapy. The Florali trial (n=310) included randomized patients without pre-existing lung pathology⁽⁶⁾. Post hoc analysis revealed a significant reduction in intubation rates in HFNO arm (38%) and lower 90-day mortality with HFNO. Non-invasive Ventilation (NIV) increases rates of intubation and mortality compared to HFNO and COT among immunocompromised patients in SOHO trial (n=711) where intubation rate was low with HFNO (45%) when compared to standard oxygen (53%)⁽²⁾. Also, no significant difference was found in mortality rates when using HFNO or standard oxygen at 28 days⁽²⁾. Another epidemiological, clinical features and early outcomes of COVID-19 patients in India study (n=235) concluded that HFNO is considered to potentially delay or avoid intubation⁽⁹⁾.

A systematic study for measuring HFNO use in AHRF in patients with COVID-19 (n=1989) derived that HFNO may

reduce the need for invasive ventilation and escalation of O₂ therapy compared with COT but must be balanced with airborne transmission⁽¹¹⁾.

However, HOT-ER TRIAL, where 303 Randomized patients with pre-existing lung pathology [Chronic Obstructive Pulmonary Disease (COPD), asthma, heart failure] were included, emerged to conclude that no significant difference in rates of intubation at 24 hours and mortality at 90 days with HFNO versus COT. HFNO can be used if NIV is not tolerated as per an efficacy trial for HFNO use in AHRF⁽¹²⁾.

Our study inferred that recovery rates from HFNO use were higher than mortality, and there was a need for mechanical ventilation. Also, in those participants where HFNO was utilized, the need for mechanical ventilation was found to be lower.

Nevertheless, results should be interpreted with caution owing to the small sample size. Also, the difference between recovery (18) and mortality (16) was small, so it was difficult to conclude the role of HFNO. However, the complications were very few.

Limitations

This retrospective study had certain limitations. COT could not be monitored in comparison to HFNO and mechanical ventilation. Though co-morbidities were considered, specific consideration of existing lung pathology was not considered, which could be a major modulator in the outcome. The small sample size (n=38) remained an impediment to coming to firm conclusions.

Future recommendations

The use of HFNO in the management of hypoxemic respiratory failure needs to be more defined. Future studies are recommended to elucidate a subset of patients who may benefit from this therapy.

Conclusion

In terms of recovery from HFNO use, discharge with recovery rate was higher than mortality and need for mechanical ventilation. The need for invasive mechanical ventilation was much lower in HFNO used participants (26 versus 8). All those on mechanical ventilation expired. HFNO can be a useful modality for oxygenation in COVID-19 patients. The exact role of HFNO in the trajectory of the management of hypoxemic respiratory failure due to COVID-19 needs to be defined.

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Conflict of Interest: Nil

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Ethical consideration

Institutional Ethics Committee Approval was taken from Maharashtra Medical Research Society (MMRS), Joshi Hospital, Pune, Maharashtra. Protocol -2.0 (17.10.20) dated 14 January 2021

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Authors' Contribution

NJ: Conceptualization, Methodology, Project administration, Supervision, Visualization, Manuscript writing, editing and review; AB: Data Curation, Data acquisition, Supervision, Manuscript Writing, review and editing

Data availability statement

Data will be available with corresponding author on request.

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