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Evaluation of Early Institution of High Flow Nasal Oxygen Therapy in Type 1 Respiratory Failure in COVID 19 Patients - An Observational Study

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Abstract: ***Background: Type 1 respiratory failure is commonly seen in COVID 19 patients. High flow nasal oxygen was a new concept in management of ARDS. Heated humidified gas up to 37°C at high flow are delivered through nasal cannula using air/ oxygen blender. HFNO reduces the work of breathing by conditioning of gas by warming and humidifying it to physiological conditions. It is reported to be superior than COT and is as effective as NIV in patients with Type 1 respiratory failure. Aim and Objectives: To determine the efficacy of early institution of HFNO therapy on weaning in COVID 19 patients, to observe hemodynamic changes, number of days on and complications of HFNO. Methods: After obtaining institutional Ethical Committee and written informed consent from patients, prospective observational study was conducted on 70 COVID 19 positive patients (rapid antigen kit test or RT- PCR) aged 30-80 years with Type 1 respiratory failure (ABG- PaO2 & PaCO2) at COVID anaesthesia ICU, Nehru Hospital, Gorakhpur. 70 patients screened and put on nasal prongs on admission. 60 people, with mild or moderate ARDS were treated with HFNO. 10 patients with severe ARDS were excluded. Univariate logistic regression analysis was used to explore the association between predictors with risk of intubation. Analysis was done using SPSS software, version 24.0 Result: Out of 60 patients, who were treated with HFNO, 68.3%(41) were weaned off within 7 days, only 8.3%(5) patients required intubation, 11% (7) patients were expired. It was observed that the mean PaO2/ FiO2 ratio improved significantly (p<0.05) from admission (196.74+/- 49.92) to 30 minutes after admission (202.47+/- 49.52). Conclusion: Early institution of HFNO in COVID 19 patients with mild or moderate ARDS showed early and better recovery and patients can be successfully weaned off without requiring mechanical ventilation***

Keywords: High flow nasal oxygen therapy, Type 1 respiratory failure, ARDS management, COVID-19 patients

1. Introduction

SARS-CoV-2 emerged as a pandemic and has covered 0.94% of the population [1,2]. Novel corona virus infected pneumonia first emerged in Wuhan, China in December 2019. Commonly associated symptoms include fever, dyspnoea, cough, fatigue, myalgia and changes in chest X ray [2-4]. Some cases are associated with acute respiratory distress syndrome, sepsis, septic shock and multiorgan dysfunction.

The important risk factors associated with higher mortality in COVID 19 patients were old age, co- morbidities (diabetes mellitus, hypertension, COPD), higher SOFA score and d- dimer>1mcg/L. This infection can be transmitted from one person to another even in its incubation period [5-7].

Respiratory insufficiency or respiratory failure in COVID 19 infected patients may occur due to compromised diffusion capacity and ventilation perfusion mismatch [8]. Four types of respiratory failure are:

1) Type 1 respiratory failure (hypoxic)
2) Type 2 respiratory failure (hypercapnic)
3) Type 3 respiratory failure (post operatively)
4) Type 4 respiratory failure (following hypoperfusion and circulatory failure) [9]

Most common type of respiratory failure seen in COVID 19 patients is type 1 respiratory failure, followed by type 2 or a combination of both.

Hypoxemia is defined as PaO2<60mmHg in arterial blood or SpO2<90%. It is an inadequate oxygen level in the blood that occurs either due to low oxygen content at the arterial level or inadequate blood flow to the tissues [10].

Horowitz index (PaO2/FiO2) ratio is used to measure the degree of hypoxemia based on which ARDS is classified as mild, moderate and severe ARDS [11].

The first line treatment for hypoxemic respiratory failure is supplemental oxygen therapy. Factors that affect the alveolar oxygen delivery include the FiO2 delivered in supplemental flow, the device's interface with the patient, supplemental oxygen flow rate and inspiratory demand [13,14].

The various devices commonly used for conventional oxygen therapy includes:

1) Low flow devices
2) Intermediate flow devices

High flow nasal oxygen therapy has been developed over past two decades as a novel device for delivering oxygen at high flows. Heated humidified gas up to 37°C at high flow are delivered through nasal cannula using air/ oxygen blender. Air/ oxygen mixtures up to a flow of 60l/min at an adjustable FiO2 can be delivered by these devices [15]. Oxygen blender is used for the precise titration of FiO2 and it ranges from 0.21 to 1.0, independent of the flow. HFNO reduces the work of breathing by conditioning of gas by warming and humidifying it to physiological conditions. Better conductance and compliance are achieved due to conditioning of gas. It is reported to be superior than COT and is as effective as NIV in patients with Type 1 respiratory failure [16].

The aim of this study is to determine the efficacy of early institution of high flow oxygen therapy in type 1 respiratory failure in COVID 19 patients based on weaning, to observe hemodynamic changes, number of days on and complications of HFNO

2. Material and Methods

A prospective observational study was conducted after obtaining approval from ethical committee and informed and written consent on COVID 19 patients, aged 30-80 years, of either sex, with type 1 respiratory failure, at COVID ICU under department of anaesthesiology, Nehru hospital, Gorakhpur.

Exclusion Criteria:

1) Patients aged <30years
2) Hypercapnic patients (PaCO2>45mmHg)
3) Use of vasopressors on admission
4) Patients with severe ARDS on admission
5) Patients with uncontrolled respiratory comorbidities (COPD, ILD)
6) Glasgow Coma scale equal to or less than 12

70 COVID 19 patients (diagnosed to be positive by rapid antigen kit or RTPCR) who were admitted to COVID ICU were screened for the study. ABG was done immediately on admission when the patient was on nasal prongs or facemask. Out of these, 60 patients with mild or moderate ARDS were enrolled for the study. 10 patients were excluded as they has severe ARDS. These patients were instituted with High flow nasal oxygen therapy. After 30 minutes of HFNO application, an ABG was repeated and HFNC settings were adjusted accordingly. ABG was done twice daily for all the patients till 7 days of admission and vitals were charted 3 times a day.

All the patients were investigated for CBC, LFT, KFT, coagulation profile, procalcitonin, D-dimer, CRP, serum ferritin, CRP, LDH on alternate days. SOFA score was calculated on day 1, day 3, day 5 and day 7. All the patients were followed up for 7 days. Those patients who showed improvement in P/F ratio and SOFA score were weaned off from HFNO therapy gradually. HFNO therapy was managed based on current guidelines and expert suggestions. Rest of the management including intravenous antibiotics and other drugs as per ICMR guidelines were given to every patient, irrespective of patient's participation in the study.

The required data was entered in MS Excel spreadsheet (Microsoft Corp., WA, US) and analysis was done using SPSS software, version 24.0

It was observed that comparable number of males and females were included in the study and maximum percentage of the patients belonged to 41-50 years (36.67%) as compared to all the other age groups.

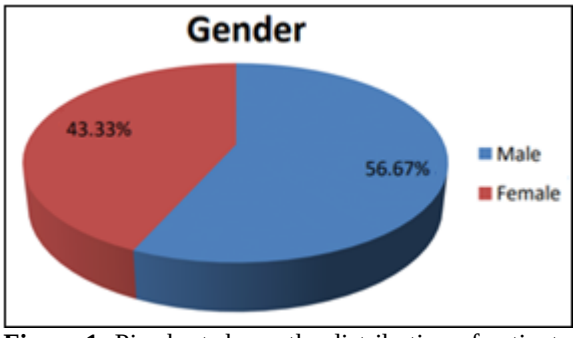

Figure 1: Pie chart shows the distribution of patients according to gender

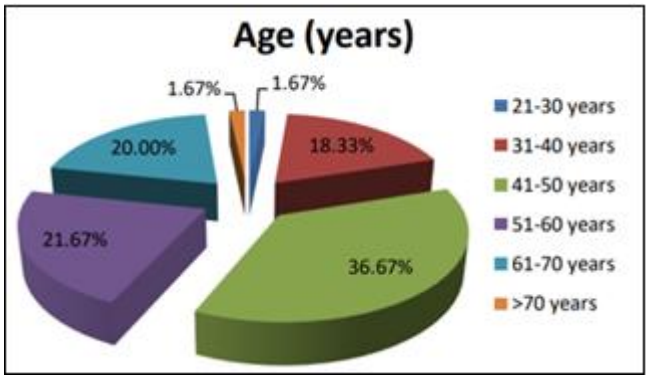

Figure 2: Pie chart show the distribution of patients according to different age group

Significant improvement in the P/F ratio on ABG was observed in the ABG taken after 30 minutes of institution of HFNO therapy. (PaO2/ FiO2 ratio on admission: 196.74, 30 minutes after HFNO: 202.47).

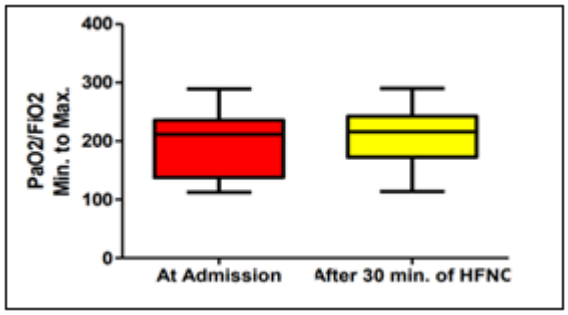

Figure 3: Whiskers box plot shows the PaO2/FiO2 on Admission and after 30 min. of HFNC institution

3. Observation and Result

Table 1: Comparisons of mean changes of PaO2/FiO2 on Admission and after30 min. of HFNC institution

	Mean	Median	Std. Deviation	Minimum	Maximum	Lower Limit	Upper Limit
PaO2/ FiO2 on admission	196.74	211.45	49.92	112.50	289.10	138.6	233.4
PaO2/ FiO2 after 30 minutes of HNFC institution	202.47	215.90	49.52	113.70	290.00	179.4	236.7236.7

$^{\perp}p< 0.001$*

*= Significant ($p<0.05$), $^{\perp}$= pair t test

It was also observed that P/F ratio improved significantly on the ABG over the period of 7 days in the patients in whom HFNO was instituted early on admission. (PaO2/FiO2 on day 1: 211.89 and on day 7: 254.71). Highest improvement in the P/F ratio was observed on day 5(266.00). It was also observed that maximum number of patients were also weaned off on day 5(n=13)

Table 2: The mean average of PaO2/FiO2 ratio from day 1 to day 7

Days	n	Mean P/F ratio	+ SD	F	p- value
Day 1	60	211.89	52.04	3.75	0.001*
Day 2	60	224.98	54.74		
Day 3	60	239.57	62.74		
Day 4	52	246.97	70.44		
Day 5	42	266.00	69.33		
Day 6	27	259.06	79.00		
Day 7	18	254.71	88.27		

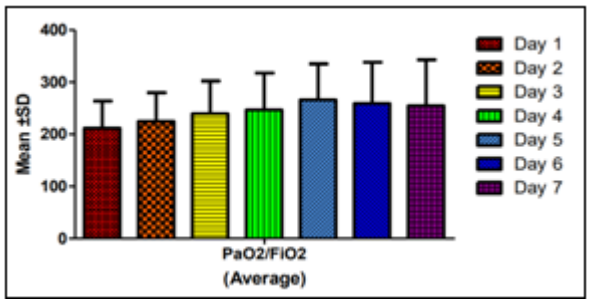

Figure 4: Bar chart shows the mean average of PaO2/FiO2 ratio from day 1 to day 7

The vitals of all the patients were observed from day 1 to day 7 and it has been observed that there was significant improvement in the Pulse rate (126.64 →84.64), mean arterial pressure (97.68→78.14) and respiratory rate (42.72→25.72).

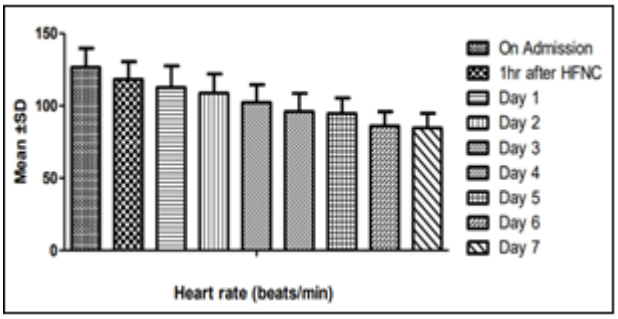

Figure 5: Shows heart rare

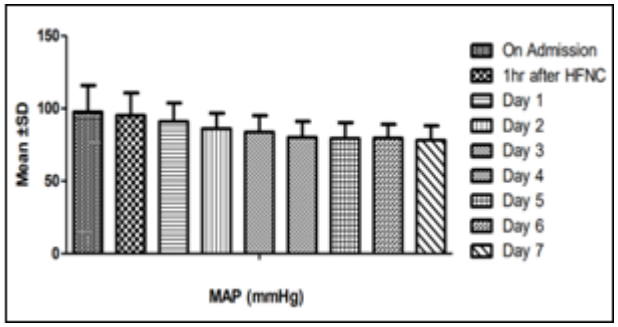

Figure 6: Shows mean arterial pressure

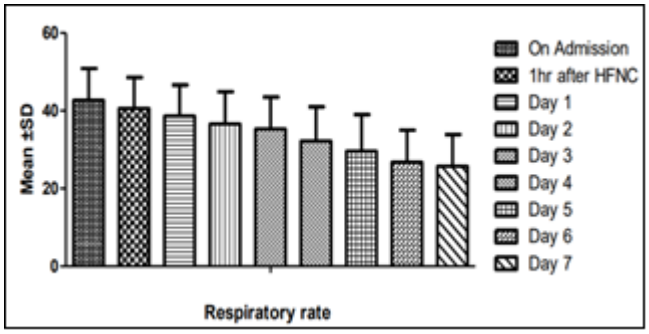

Figure 7: Shows Respiratory rate

At the end of day 7, it was found that 68.33% of the patients were successfully weaned from oxygen therapy, 11.67% of the patients included in the study were expired, 8.33% patients got intubated, 6.67% patients were not weaned off and 5% patients had other complications like hemodynamic instability, seizures, etc

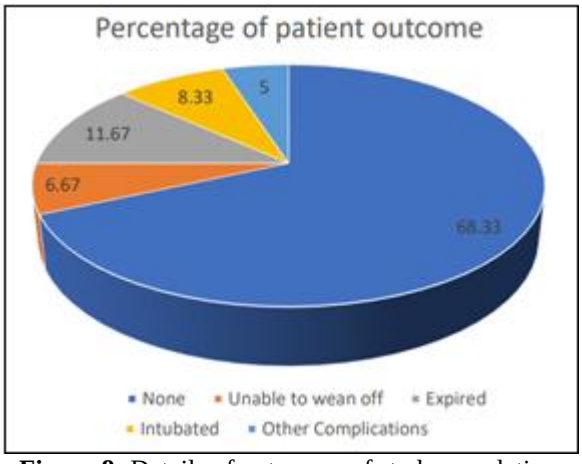

Figure 8: Details of outcomes of study population

Table 5: Outcome of study population

Outcome	n (n=60)	%
None	41	68.33
Expired	7	11.67
Intubated	5	8.33
Unable to wear off	4	6.67
Other Complications	3	5

The complications of HFNO observed in the present study were dry nose in 6.67% of the patients, nasal pain in 5% of the patients and throat irritation in 1.67% of the patients.

Table 6: Details of Complications associated with HFNC in study populations

Complications	n (n=60)	%
None	37	61.67
Dry Nose	4	6.67
Nasal Pain	3	5.00
Throat irritation	1	1.67

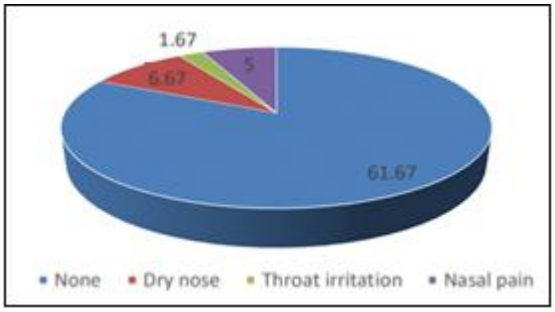

Figure 9: Complications associated with use of HFNC

Significant decrease in the mean SOFA score was observed from day 1 to day 7. (7.95→5.68).

Table 7: Mean SOFA score changes from day 1 to day 7

SOFA Score	N	Mean	± SD	F	p-value
Day 1	60	7.95	3.02	4.54	0.004*
Day 3	60	6.52	3.40		
Day 5	42	5.68	3.57		
Day 7	18	5.68	4.12		

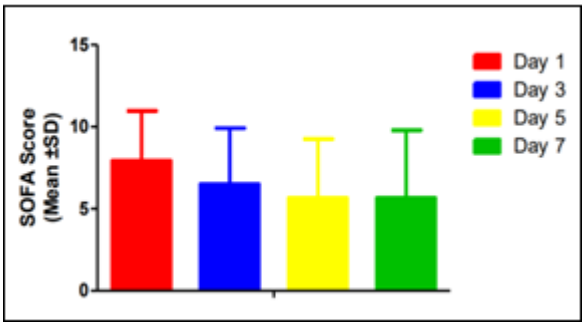

Figure 23: Bar chart shows the mean SOFA score changes from day 1 to day 7

4. Discussion

Acute respiratory failure is one of the most common presentations of COVID 19 infection and thus increases the need of ICU admission. Oxygen therapy remains the first line therapy in the management of these patients. Alveolar oxygen delivery depends on the supplemental oxygen flow rate, the FiO2 delivered in supplemental flow, the device's interface with the patient and the inspiratory demand. The HFNO overcomes the flow limitations of low and intermediate flow devices by delivering upto 60L per minute of warm, humidified gas via nasal prongs and thus can be used as an alternative to conventional oxygen therapy in such patients. High flow nasal oxygen via nasal cannula rapidly alleviates symptoms of hypoxemic respiratory failure and improves oxygenation by washing out the dead space, reducing oxygen dilution and nasopharyngeal resistance.

In our study, it has been observed that the P/F ratio significantly improved from admission to 30 minutes after institution of HFNO therapy. Significant improvement in the P/F ratio was also observed over 7 days of ICU admission. Corley et al., showed in their study that use of HFNO reduces the respiratory rate and improves oxygenation by increasing both EELV and tidal volume [17]. Mauri T et al., concluded that HFNO significantly decreased the respiratory rate and improved oxygenation in patients with acute hypoxemic respiratory failure [18].

Significant and progressive day wise improvement in the clinical status has been observed in the patients with early institution of HFNO in our study. Wang et al., however showed that 63% of the patients in their study showed HFNO failure [4].

Patients included in our study showed significant improvement in the hemodynamic status from admission till day 7. Kuwata et al., showed significant reduction in the heart rate, systemic vascular resistance and pulmonary vascular resistance. Similar findings were also observed with Masclans et al.

Spoletini G et al., showed that HFNO therapy was a well-tolerated alternative to standard oxygen therapy. In our study, it has been found that patients were comfortable and compliant with the use of HFNO despite the minor complications such as dry nose, nasal pain and throat irritation [19].

5. Limitations

Multiple organs were involved in the disease pathogenesis; hence P/F ratio alone cannot be used as a benchmark criterion for successful weaning of the patient.

The observation period was kept only for 7 days, due to the risk of COVID 19 infection to the observer and uncertainty of the natural history of the disease.

Study was done only in limited population- result not applicable for generalised population.

6. Conclusion

From our study, it can be concluded that early institution of High flow nasal oxygen therapy in COVID 19 patients with mild or moderate respiratory failure showed early and better recovery. It is very useful in the treatment of selected patients due to its ease of application and excellent patient tolerance.

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