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Research Article

Utility of High Flow Nasal Oxygen versus Non-Invasive Ventilation in Severe Covid-19 Pneumonia: Retrospective Comparative Analysis and Assessment in Present Scenario Patients

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ABSTRACT

Background: The pandemic of COVID-19 since its beginning has created havoc all-round the globe. The role of oxygen therapy remains constant. Various modalities have been studied for oxygen delivery to hypoxic patients but high flow nasal oxygen (HFNO) has lately gained importance in terms of non-invasive oxygen delivery, easy administration and great improvement in patient's recovery.

We conducted this retrospective analysis with the primary objective of looking for the proportion of patients who were successfully weaned off of HFNO or non-invasive ventilation (NIV) and the secondary aim was to look for duration of hospital stay and its effect on clinical recovery based on laboratory parameters.

Methods: All patients, positive for COVID-19 infection by real-time reverse transcriptase polymerase chain reaction (RTPCR) were admitted to covid ICU or ward with oxygen requirement and were treated with either NIV or HFNO were enrolled for the study. Patients were grouped under H group (HFNO) or N group (NIV). Daily ABG readings, chest x-ray, respiratory rate, hemodynamic parameters and urine output were noted on 12 hourly intervals. Any changes in above parameters along with need for intubation were assessed.

Results: Patients from both the groups showed significant improvement in their oxygen saturation by the fifth day of their treatment.

Fourteen patients from the NIV group and 10 from the HFNO group had saturation >90% by Day 5. Of those who presented with saturation of <85%, 2 out of 5 in the NIV group (40%) and 1 of the 2 patients in the HFNO group (50%) showed improvement in their oxygen saturation. The P/F was statistically comparable (p 0.928) in both groups. The levels of bio markers, and the improvement was comparable and correlated with clinical improvement as well.

Conclusion: We conclude that though HFNO is accepted better than NIV, the improvement in the respiratory status of the patient was comparable with both the treatment modalities and hence we do not recommend use of HFNO, especially in a situation of gross deficit of oxygen availability as compared to the exponential rise in the demand.

The pandemic of covid -19 since its beginning has created havoc all-round the globe. From the very first day of its diagnosis in China it has devastated a very large percentage of population and seems to be the largest pandemic of this century. Initially thought to be a simple viral illness, its rapid progression to severe form of acute respiratory distress syndrome (ARDS) and

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further causing hypoxic injury and mortality has been a matter of concern over the last two years [1].

Several modalities of therapies in the form of, antivirals, anthelminthic, steroids, anticoagulants and antibiotics have been studied and practiced since then, with no definitive proven treatment.

Despite all mentioned therapies, the hypoxic injury caused by the novel corona virus and the role of oxygen therapy remains constant [2-3]. Various modalities have been studied for oxygen delivery to hypoxic patients but high flow nasal oxygen (HFNO) has lately gained importance in terms of noninvasive oxygen delivery, easy administration and great improvement in patient's recovery [4].

As there are different phases of this pandemic in different areas of the globe, in India during the first wave the use of HFNO proved effective, while in unprecedented second wave when we experienced an explosive rise in the cases and faced acute shortage of oxygen, this study was conducted in the second wave of the pandemic to weigh the benefit of use of such high flows of oxygen in the face of limited availability.

We conducted this retrospective analysis with the primary objective of looking for the proportion of patients who were successfully weaned off of HFNO or non-invasive ventilation (NIV) and the secondary aim was to look for duration of hospital stay and its effect on clinical recovery based on laboratory parameters.

Methods

After obtaining institutional ethical committee approval and permission from the concerned authority the data was collected with respect to patients who were treated with either NIV or HFNO in our COVID ICU from April 2020 till April 2021. Ours is a retrospective observational single centric analysis conducted in Covid ICU and ward setup of a tertiary care hospital in complete accordance with the guidelines of Helsinki.

The data was collected from the medical records department (MRD) of our hospital. Both manual and electronic data was collected and tallied to rule out any missing information.

All patients, who tested positive for COVID 19 infection by real-time reverse transcriptase polymerase chain reaction (RTPCR) were admitted to covid ICU or ward with oxygen requirement and were treated with either NIV or HFNO as the primary line of treatment based on the following parameters were enrolled for the study (Figure 1).

- Arterial blood gas analysis
- Room air oxygen saturation 85-90%
- Respiratory rate >30

Depending upon which type of oxygen therapy was given to the patient, patient was grouped under H group (HFNO) or N group (NIV).

Daily ABG readings, chest x-ray, respiratory rate, hemodynamic parameters and urine output were noted on 12 hourly intervals.

Any changes in above parameters along with need for intubation were assessed.

Failure of intervention was defined as any upgradation of oxygen therapy in the form of invasive positive pressure ventilation (IPPV) or death on HFNO or NIV therapy.

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0. Categorical variables were compared using the Chi-square test or Fisher's exact probability test; continuous variables compared using unpaired t-test or Mann-Whitney U test. p values of < 0.05 were considered as statistically significant.

Results

In this retrospective study, we analyzed the case records of 32 patients, of which 22 were males (68.75%) and 10 were females (31.25%). Their ages ranged from 42 to 69 years. Of these, 20 patients received NIV and 12 received HFNO as the initial treatment. Both groups were comparable with respect to their baseline characteristics and demographic profile.

All the patients recruited in the study had moderate respiratory distress with saturation <90% and fiO2 requirement of >0.4 on admission. They were further categorized as follows, as per the severity of their disease on presentation:

For baseline SpO2 into two groups as those with SpO2 85-89% and those with SpO2 < 85%; and for baseline fiO2 requirement as those requiring fiO2> 0.8 and those with fiO2 requirement 0.4 -0.8.

Both groups were comparable with respect to baseline SpO2 (p 0.61) and oxygen requirement (p 0.258).

Patients from both the groups showed significant improvement in their oxygen saturation by the fifth day of their treatment.

Fourteen patients from the NIV group and 10 from the HFNO group had saturation >90% by Day 5. Of those who presented with saturation of <85%, 2 out of 5 in the NIV group (40%) and 1 of the 2 patients in the HFNO group (50%) showed improvement in their oxygen saturation. The remaining 3 patients in the NIV group and 1 patient in HFNO group were intubated by Day 5. All the patients who were intubated had presented with baseline saturation of <85%. By Day 10 all the unintubated patients, from both groups showed improvement in saturation to >90%. The patients once intubated were excluded from further study.

The oxygen requirement also showed similar trend of improvement in both the groups. On Day 10, only 1 patient in each group had oxygen requirement of >0.8. Both the groups were comparable with respect to the decrease in oxygen requirement when followed up to Day 10. (Table2)

The P/F ratio was <300 in 12 patients of NIV group (60%) and 7 patients of the HFNO group (58.33%), which was statistically comparable (p 0.928). Of these, only 1 patient from the NIV group and 2 from HFNO group, had persistent P/F ratio < 300 by Day 5. However, 3 patients from the NIV group and 1 patient from HFNO group, were intubated by this day. Remaining patients recovered and had P/F ratio of >300 by Day 5. Thus, with respect to the P/F ratio on day 5 and day 10; both the groups were comparable (p 0.711 for day 5 and p 0.764 for day 10).

Both the groups were comparable to baseline Respiratory rates (RR). 75% patients in each group had RR of 30-40/min and 25% had RR >40/min on admission. At Day 5, significant number of patients in the HFNO group showed an improvement in their tachypnea as compared to the patients in NIV group. 10 patients from the HFNO group; whereas 5 patients from the NIV group had RR of < 30/min on Day 5 (p 0.005). The RR was 30-40/min in 12 patients receiving NIV and 1 patient receiving HFNO (p 0.001). None of the patients, in any of the group had RR> 40/min on Day 5. The RR in all the unintubated patients was <30 / min on Day 10.

The levels of bio markers, namely S. Ferritin and C - reactive protein (CRP), were comparable on admission in both groups. The levels improved in all the patients and the improvement was comparable and correlated with clinical improvement as well (Table 3).

Table 1- Demographic parameters and comorbidities

	NIV (n=20)	HFNO (n=12)	P value
Age (yrs.)	66+1.43	0.68	0.68
Sex (M/F)	14:6	0.8414	0.8414
Comorbidities:			
HTN	9	5	0.857
DM	7	3	0.555
COPD	3	1	0.583
Cardiac	5	2	0.582
Other	1	0	0.19

NIV: Non-invasive ventilation, HFNO: High frequency nasal oxygen, HTN: Hypertension, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease.

Table 2- Comparison of respiratory parameters

Parameter	D1 NIV (n=20)	D1 HFNO (n=12)	P value	D5 NIV	D5 HFNO	P value	D10 NIV	D10 HFNO	P value
SpO2 (%)									
>/= 90%	0	0		14	10	0.711	17	11	0.764
85-89%	15	10	0.61	3	1	0.317	0	0	
<85% or intubated	5 (<85%)	2 (85%)	0.61	3 (Intubated)	1 (Intubated)	0.211			
FiO2									
<0.4	0	0	-	2	0	0.230	15	8	0.136
0.4-0.8	2	3	0.258	12	8	1.000	1	2	0.126
>0.8	18	9	0.258	4(3 intubated)	4 (1intubated)	0.502	1	1	0.764
RR (/min)									
<30	0	0	-	5	10	0.005	17	11	0.800
30 – 40	15	8		12	1	0.001	0	0	-
>40	5	4		0	0	-	0	0	-

SpO2: Oxygen saturation, fiO2: fractional oxygen requirement, RR: respiratory rate

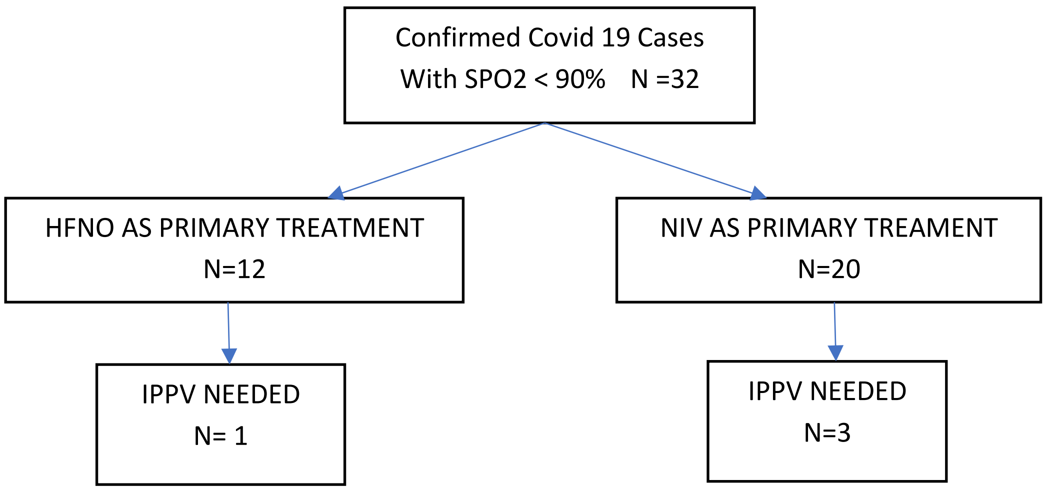
Table 3- Comparison of levels of biomarkers

Biomarker	D1 NIV (n=20)	D1 HFNO (n=12)	P value	D5 NIV	D5 HFNO	P value	D10 NIV	D10 HFNO	P value
S. Ferritin									
<250	1	0	0.406	6	2	0.372	16	10	0.800
250-500	4	4	0.136	9	7	0.170	1	1	0.764
>500	15	8	0.289	2	1	0.500	0	0	-
CRP									

<10	0	0	-	4	4	15	8
10-25	6	4		11	8	2	3
>25	14	8		2	0	0	0

S. Ferritin: Serum ferritin, CRP: C-reactive protein

Figure 1- Consort Flow Chart of the Study



Discussion

To the best of our knowledge this is the first study from the Indian subcontinent analyzing the efficacy of HFNO in comparison to NIV and also weighing the benefit of using HFNO in present scenario when everybody is facing the crisis of oxygen.

From our study it is very evident that, though the improvement of tachypnea was better with HFNO, its benefits in treatment of covid 19 ARDS is comparable with that of NIV when considering the objective parameters studied. This has also been proven by earlier conducted studies [5-7]. HFNO definitely reduces the need for intubation and invasive ventilation [8]. The improvement in tachypnea with HFNO could be attributed to several factors. The oxygen supplied is heated and humidified, hence tolerable as compared to a dry cool gas which would rapidly desiccate the nasal mucosa, causing an uncomfortable burning sensation. Also the soft, loosely fitting nasal interface that does not impede speech or oral intake as against the tight fitting mask used for NIV, which not only causes claustrophobia, but needs to be discontinued during feeds. The heat and humidification in HFNO also help to maintain hydration and mobility of secretions, preserving the muco-ciliary function. HFNO helps with oxygenation by flushing the nasopharynx during exhalation so that the air inhaled during the next inspiration is enriched with oxygenated HFNO gas. Also, compared with NIV which provides oxygen flows up to only 15 L/min, the high flow rate of HFNO comes closer to the inspiratory flow rates encountered in dyspneic patients, which may exceed 60 L/min [8].

NIV which has been the gold standard for ARDS since non covid era, surprisingly in covid times the percentage of patients initially on NIV requiring intubations and IPPV has been larger than those of HFNO [9-10].

In our study HFNO proved effective in management of covid 19 pneumonia with a very minimal need to upgrade the oxygen therapy. This may be attributable to the favorable physiologic effects of HFNO such as low-level positive end-expiratory pressure (PEEP) which keeps the alveoli open, washing out of nasopharyngeal dead space to improve ventilation efficiency, improvement in breathing patterns and enhancement of airway heating and humidification function [11-12].

However failure of HFNO was recorded in about 8.33 % of patients and all these patients succumbed to covid 19 pneumonia. All patients who succumbed were males and continued to have very high blood sugar levels throughout their hospital course. The time of hospital admission and uncontrolled blood sugar levels can be the cause for HFNO failure.

A larger percentage (15%) of patients with NIV treatment needed intubations which may be attributable to the defect in sealing effect by NIV mask, non-cooperation by the patients as NIV requires deep breathing efforts by the patients. High blood sugar levels stands as an independent factor common to both groups, causing rapid progression of the pulmonary function derangement.

Earlier studies conducted including few case reports and short case series describe the potential utility of

HFNO in treating covid 19 ARDS. It has been also used in treatment of pneumonia since pre covid era [5].

A meta-analysis conducted in pre covid era including 7 studies on patients with pneumonia describes the efficacy of HFNO in reducing intubation rates [13].

Our study was conducted not only in ICU setup but also included patients outside ICU setup as the massive surge in number of patients could not meet up the demand of ventilators and the critically ill patients had to be put on HFNO or NIV amongst the shortage of ventilators. Few patients were initially treated with HFNO in wards and were later shifted to ICU when they needed intensive care. With the oxygen delivery via HFNO their shifting through the green corridor became feasible and easy. Hence HFNO can be used for shifting critically ill patients while shifting on NIV is not that easy as it needs a ventilator which would require a continuous electric supply [14].

The total oxygen consumption with the use of HFNO and NIV also needs to be rationalized and the volume of used oxygen was definitely higher with HFNO (60-100 litres /min) than NIV. In the second wave, India faced a remarkable deficit in the demand versus the supply of oxygen owing to the rate of rise of cases and the sheer number of cases being admitted with moderate to severe respiratory affection and with comorbidities. We conducted this study to rationalize the deployment of HFNO as the treating modality for oxygen delivery. Usage of such high flows of oxygen, which is in effect, would have been used for other patients, is justified only and only if it saves lives. The results of our study however showed that HFNO did not have any advantage over NIV, to justify its use in a situation of shortage.

Even the study by Gregory et al suggested that the degree to which HFNO should be used and up-scaled to treat larger populations totally depends on the local oxygen capacity, delivery infrastructure and storage capacity of individual hospitals [15].

Another important aspect to be discussed in relation to HFNO and NIV is the safety with their use in terms of aerosol generation. Initially in the beginning of pandemic HFNO was considered a highly aerosol generating modality for oxygen delivery and its use was not recommended. However this recommendation had not much evidence and could not sustain [16]. Later HFNO was recommended for early and moderate hypoxic respiratory failure (HRF) cases where it in turn prevents unnecessary intubations and prevents transmission thus having a protective role in treatment of mild to moderate HRF. It is an important point of concern to be discussed with use of HFNO.

HFNO provides hot and humidified oxygen to covid 19 infected patients. Does this hot and humidified oxygen play certain role in these patients getting infected with mucormycosis which showed a rampant surge, is a question to be pondered upon.

Authors accept certain limitations of the study. It is a retrospective study with smaller sample size. But the sudden progression of the disease does not provide much time in hand to assess patients in pre ventilator period. Also the less number of available HFNO assembly limits its use.

Conclusion

We conclude that though HFNO is accepted better than NIV, the improvement in the respiratory status of the patient was comparable with both the treatment modalities and hence we do not recommend use of HFNO, especially in a situation of gross deficit of oxygen availability as compared to the exponential rise in the demand.

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