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Indian Journal of Clinical Anaesthesia

Journal homepage: www.ijca.in

Original Research Article

Trends in oxygen therapy in patients with moderate to severe COVID-19 admitted to the ICU

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ARTICLE INFO

Article history:
Received 07-02-2021
Accepted 09-03-2021
Available online 21-10-2021

Keywords:
COVID- 19
Oxygen therapy
ICU

ABSTRACT

Introduction: The most concerning complication of severe acute respiratory syndrome corona virus 2 (SARSCoV-2) pneumonia is acute hypoxemic failure. Though various antivirals, steroids, immunomodulators have been tried, oxygen therapy remains the mainstay of treatment.

Materials and Methods: After obtaining institutional ethical clearance, a prospective observational study was conducted on 102 COVID-19 positive patients aged 20 years and above, admitted in the ICU with moderate to severe disease. COVID-19 infection was confirmed by polymerase chain reaction or rapid antigen test. Data of two demographically comparable groups i.e., patients on HFNO and NIV was analysed outcome was defined as discharge from ICU, shift to other non-invasive modes of oxygen therapy, endotracheal intubation or death, and comfort level for each mode. The data was analysed using SPSS-16.0, Chi-square test and "t" value test were applied.

Results: Comparison of the mean number of invasive ventilator free days of HFNO and NIV was insignificant($p>0.05$). Among the patients on HFNO (high flow nasal oxygen) 49.09% were stepped down to NRB (non-rebreathing mask) whereas 7.27% went for intubation which is significant compared to NIV mask (non-invasive ventilation), where 13.64% were stepped down to HFNO and 34.09% were intubated ($p=0.000$).

Conclusion: Oxygen therapy with HFNO is associated with better outcome and less mortality when compared with NIV.

1. Introduction

Novel Corona Virus which had its epicentre in Wuhan, China became a pandemic and had resulted not only in global economic meltdown, also has resulted maximum morbidity and mortality even in developing countries. The pathophysiology and the ability of the virus to affect multiple systems has resulted in the pandemic to be called the great imitator of 2020.[1] It can be gastrointestinal disease-causing only diarrhoea and abdominal pain. It is reported to have caused heart failure, present as myocardial infarction, kidney disease, confusion, headaches, seizures, Guillain-Barre syndrome, fainting spells, new onset diabetic ketosis, and uncontrolled pre-existing diabetes. This makes it a incredibly difficult to diagnose and even harder to treat, although no established treatment is available and no vaccine is available to prevent the infection. Not only this, its droplet mode of infection is also challenged.

The portal of entry of the virus is eyes, nose, mouth etc the virus by its spike protein attaches itself with a specific receptor known as ACE2, on surface of cells the host. Predominantly affects the respiratory system presenting as pneumonia worsening as ARDS, septicaemia shock, resistant hypotension, multi-organ failure and thrombotic

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https://doi.org/10.18231/j.ijca.2021.098

effect in microcirculation.

Although research is on, early treatment with antiviral like Remdsevir, judicious use steroids and immune modulators or immunosuppressant is being tried and beneficial. The mainstay of treatment is oxygen therapy and the optimal administration of oxygen during the acute phase of the disease is important in preventing the morbidity and mortality. There are different modes of administering oxygen, invasive endotracheal intubation and mechanical ventilation was the usual mode of treatment. The COVID pneumonia responds to oxygen therapy with non-invasive methods, during the initial stages of disease.

Oxygen therapy varies according to the availability, patient acceptability and the ease of administration. Face masks, non-rebreather masks, nasal cannula, oxygen hoods, helmets, high flow nasal oxygen, Non-invasive ventilation are used as modes of oxygen therapy.

Invasive mechanical ventilation is not a benign intervention as it has number of associated complications including Ventilator associated pneumonias, excessive sedation, delirium, ICU acquired weakness, VILI. The study aims at finding the optimum mode of oxygen administration and the changing trends in oxygen administration during the course of this COVID pandemic.

The trivial dyspnea experienced by some patients with demonstrable hypoxemia has led to debates about the need for oxygen therapy. However, hypoxemia is a poor stimulus for dyspnea, and variation in symptoms associated with hypoxemia is unsurprising. Even for patients with minimal symptoms, available evidence does not support tolerating hypoxemia. A recent randomized trial comparing liberal (target oxygen saturation ≥96%) and conservative (target 88-92%) strategies for oxygen therapy in patients with ARDS was stopped early after it became clear that the conservative approach was unlikely to benefit patients and might cause harm. Recent guidance recommends a target oxygen saturation of 92-96% in adults with covid-19, using supplemental oxygen as needed.[2]

Some patients will require support beyond supplemental oxygen, and the choice between high flow nasal cannula, non-invasive positive pressure ventilation, or early intubation has been controversial. Issues include the need to protect healthcare workers from exposure to viral aerosols while providing optimal care for patients.[3]

1.1. *Primary objective*

Number of invasive ventilator free days (alive without mechanical ventilation).

1.2. *Secondary objectives*

The comfort of usage.

Transition from one mode to another mode of therapy.

Outcome: discharge/ death

2. Materials and Methods

This single-center, prospective, observational study was done at designated hospital to treat patients with SARS-CoV-2 pneumonia. We prospectively analyzed patients who had been diagnosed with SARS-CoV-2 pneumonia, according to WHO interim guidance, and who were admitted to the ICU. Laboratory confirmation of SARS-CoV-2 infection was performed by the local health authority.

2.1. *Data collection*

We reviewed clinical electronic medical records, nursing records, laboratory findings, and radiological examinations for all patients with laboratory confirmed SARS-CoV-2 infection. The admission data of these patients were collected. We collected data on age, sex, exposure history, chronic medical histories (chronic cardiac disease, chronic pulmonary disease, cerebrovascular disease, chronic neurological disorder, diabetes, malignancy, dementia, malnutrition, and smoking), symptoms from onset to hospital admission (fever, cough, dyspnoea, myalgia, malaise, rhinorrhoea, arthralgia, chest pain, headache, and vomiting), vital signs at ICU admission (heart rate, respiratory rate, blood pressure, saturation), oxygen therapy that was started upon admission to ICU.

Observational prospective study conducted on Patients who are admitted to ICU requiring oxygen therapy. Oxygen Saturation (SPO2) at the time of admission, the mode of therapy is started after clinically assessing the patient, four hourly monitoring of SPO2, heart rate, blood pressure comfort and ease of administration, blood analysis after 4 hours of oxygen therapy and on necessity basis. The comfort level of each patient with the mode of therapy was assessed using Visual Analogue scale. Complications associated with the therapy, and adverse effects are noted. Transition from one mode to another or requiring intubation and mechanical ventilation are recorded.[4]

2.2. *Inclusion criteria*

1. Age: 18 years and above.
2. Sex: male and female.
3. Requiring oxygen therapy.

2.3. *Exclusion criteria*

1. Impending cardiorespiratory arrest.
2. Glasgow coma scale less than 8
3. Absence of airway protective gag reflex.
4. Elevated intracranial pressure.
5. Tracheostomy
6. Upper airway obstruction.
7. Pregnancy.

The data was analysed using SPSS-16.0, Chi-square test and “t” value test were applied.

3. Results

The study included 102 patients among which, 70(68.6%) were males and 32(31.37%) were females. Patients in both groups were comparable on age basis (Table 1), with majority cluster around 40-60years (53%).

Table 1: Shows that the data of HFNO and NIV group is comparable on age basis

Age	N	Mean	Std. Deviation	" t " Value	P Value
HFNO	55	63.61818	68.80501	0.721	0.472
NIV	44	56.04545	11.51734		

Out of 102 patients, 57.8% (59 patients) were discharged, we call it as the survivor group and 42.2%. (43 patients) died i.e, the non-survivor group.

In the survivor group, maximum i.e., 67.79% (40 patients) were started on HFNO as the first line of therapy, 28.81% (17 patients) were started with NIV and 3.38% (2 patients) on combination of NIV+HFNO. Patients with HFNO as first line therapy, 67.5% were stepped down to NRB mask whereas, 30% had to be escalated to NIV and 2.5% to combination therapy.in patients with NIV, 52.9% were stepped down to NRB mask and 23.5% to HFNO whereas 23.5% were escalated to combination therapy. In the patients with combination as first line therapy, all were stepped down on their oxygen therapy.

In the non-survivor group, maximum i.e.62.79% (27 patients) were started on NIV as first line of therapy of which 40.74% patients were shifted to combination of NIV+HFNO and 59.25% got intubated. 34.88% (15 patients) were started with HFNO as first line of therapy, of which 73.33% had to be escalated to NIV, 6.66% to combination therapy and 20% got intubated. The primary objective i.e., Number of mechanical ventilation free days was comparable in both groups i.e., HFNO and NIV and no significant difference (p value 0.419) was obtained.(Table 2)

The comfort level of each patient was assessed using VAS (0 to 10) and it was found that patients using HFNO had significantly higher comfort level than with NIV. (Table 3) It is due to various factors such as HFNO being just a nasal canula, the patients were able to communicate easily, they were able to have food orally hence had better nutrition whereas patients with NIV had more discomfort due to the mask and high positive pressure.

The graph below depicts the transition from one mode to another in the patients who were started of HFNO and NIV as first line of therapy.(Figure 1)

The final outcome i.e., death or discharge was compared with the mode of oxygen therapy and it was observed that 27.27% of patients with HFNO as first-line of therapy have died whereas 61.36% of patients with NIV as first-line therapy have died. This shows that there is significantly reduced mortality with HFNO compared to NIV.(Table 4)

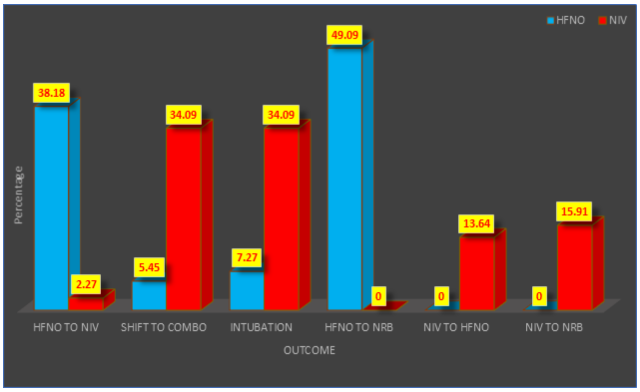

Fig. 1: Showing transition to different modes of oxygen therapy from HFNO (blue) and NIV (red)

When the median number of days of ICU stay and time required to shift to other mode of therapy was compared, it was found to be longer with HFNO than NIV.

In the non-survivors all patients (100%) were escalated to higher mode of oxygen therapy whereas, only 28% of survivors were escalated to higher modes.

1. 51.16% of non-survivors needed invasive ventilation, while none of the survivors (0%) required intubation.
2. It was observed that the survivors had a longer duration of ICU stay compared to non-survivors.(Table 5)
3. Patients with HFNO as first-line of intervention had better outcome and lesser mortality compared to NIV.

4. Discussion

During the first wave of covid pandemic 102 patients in ICU were studied, the number of invasive mechanical ventilation free days in patients on HFNO and NIV was comparable. When the comfort level of two groups was compared, it was found patients on HFNO had significantly higher comfort level than with NIV, the patients on HFNO were able to take care of their nutritional needs better compared to patients on NIV due to discomfort of the face mask and high positive pressure. Escalation of oxygen therapy to invasive ventilation was seen in 34.09% of patients in NIV group whereas, only 7.27 % of patients in HFNO group required intubation. When the death and discharge rate was compared in two groups, it was seen that there was significantly reduced mortality with HFNO compared to NIV.

HFNC oxygen delivery has already proved its value as an effective mode of noninvasive ventilatory support and has been gaining attention as a simple and well-tolerated alternative means of respiratory support for critically ill patients. NIV provides ventilatory support without the need of endotracheal tube, so that the patient remains awake. In one small retrospective case series from Wuhan, 72% of

Table 2: Showing the primary objective

	Group	N	Mean	Std. Deviation	" t " Value	P Value
No. of Invasive Ventilator Free Days	HFNO	55	0.709	2.551	0.811	0.419
	NIV	44	1.159	2.964		

Table 3: Comfort level with HFNO and NIV mask

	Group	N	Mean	Std. Deviation	" t " Value	P Value
Comfort Scale	HFNO	55	2.618	0.733	17.177	0.000
	NIV	44	5.227	0.774		

Table 4: Showing death or discharge with HFNO, NIV and COMBO i.e., combination therapy of HFNO+NIV

		HFNO		NIV		Combo		Total		CHI Square	P Value
		No.	%	No.	%	No.	%	No.	%		
Final	Death	15	27.27	27	61.36	1	33.33	43	42.16	11.749	0.003
	Discharge	40	72.73	17	38.64	2	66.67	59	57.84		
Total		55	100	44	100	3	100	102	100		

Table 5: Duration of ICU stay of survivor and non-survivor group

	Survivors		Non-survivors	
	ICU Stay (median)	Transition duration (median)	ICU Stay (median)	Transition duration (median)
HFNO	12	5	8.5	3.5
NIV	14	7	5	3

covid-19 patients given NIV died, although death rates were also high for patients intubated from the outset.[5]

Francois Stephan et al,[6] conducted study on HFNO vs NIV in hypoxemic non-covid patients after cardiothorathic surgery and found no significant differences in mortality with HFNO(6.8%) and NIV (5.5%).While in our study on covid patients a significant difference (p= 0.003) was found in mortality between patients on HFNO(27.27%) and NIV (61.36%). Massimo Antonelli et al[7] conducted a multiple-center survey on use in clinical practice of NIV as a first-line intervention for ARDS and concluded that it avoided intubation in 54% of patients and was associated with lower mortality rate (6%). In our study on covid cases, among patients with NIV as first-line intervention it was observed that 40.9% of patients were intubated but mortality rate was higher (61.36%).

5. Conclusion

Oxygen therapy with HFNO is associated with better outcome and less mortality when compared with NIV. Among the non-survivors significantly higher number of patients required invasive ventilation compared to survivors. The escalation of oxygen therapy was faster in non-survivors than survivors.

6. Source of Funding

None.

7. Conflict of Interest

The author declares no conflict of interest.

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Cite this article: Raghunath S S, Devanand B, Nizamuddeen B M, Bhaskar S B, Kothari P, Chand N K. Trends in oxygen therapy in patients with moderate to severe COVID-19 admitted to the ICU. *Indian J Clin Anaesth* 2021;8(Special Issue):10-14.