Feasibility of Non-Rebreather Masks and Nasal Cannula as a Substitute for High Flow Nasal Oxygen in Patients with Severe COVID-19 Infection

mehmet kabak (mehmetkabak8@hotmail.com)
Mardin state Hospital https://orcid.org/0000-0003-4781-1751
Baris Cil
Mardin State Hospital

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Abstract

Objective: Severe pneumonia and respiratory failure may develop in patients with coronavirus infection, placing a very significant burden on healthcare systems due to the need for both emergency and intensive care treatment. Therefore, treatment of hypoxemia is a clinical priority in the treatment of such patients. In this regard, newer strategies such as High Flow Nasal Oxygen (HFNO) and non-invasive mechanical ventilators that can provide non-invasive high fraction of inspired oxygen are gaining clinical significance.

Our objective was to compare oxygen supply by HFNO with Non-Rebreather Masks and Nasal Cannula (NRMs + NC) in terms of treatment costs and mortality in a group of COVID-19 patients requiring intensive care unit admission.

Material and Methods: This was a retrospective and single-center study involving 54 patients who were admitted to an Intensive Care Unit with a diagnosis of COVID-19 infection between July 2020 and August 2020.

Results: HFNO was compared with NMRs + NC in terms of mortality and duration of hospital stay. The two groups were comparable in age (p=0.45), gender (p=0.33), and mortality (p=0.43). Also, there was no significant difference in oxygen saturation at admission (p=0.63), duration of intensive care (p=0.35), total length of hospital stay (p=0.057), and need for invasive mechanical ventilator (p=0.39) between the study groups.

The levels of WBC (p=0.36), platelets (p=0.12), lymphocytes (p=0.98), CRP (p=0.11), pro-calcitonin (p=0.20), D-dimer (p=0.74), ferritin (p=0.14), urea (p=0.74), and creatinine (p=0.35) were also similar between the two groups.

Conclusion: Oxygen support by NRMs + NC was comparable to HFNO in terms of mortality, need for invasive mechanic ventilation, length of intensive care, and length of hospital stay. We believe that NRMs + NC may represent an inexpensive and easily accessible therapeutic substitute for HFNO, particularly when the risk of transmission and costs related with HFNO use are considered.

Introduction

COVID-19 has become a major global public health problem in the past year (1). In particular, patients with acute respiratory distress syndrome (ARDS) may develop severe respiratory failure and need intensive care unit admission. In these patients, hypoxemia is associated with more rapid disease progression and increased mortality. Obviously, a more severe disease course is associated with a major healthcare burden as a result of the need for both emergency and intensive care. Therefore, strategies aimed at correcting the hypoxemia have gained clinical significance (2). In this regard, newer approaches such as High Flow Nasal Oxygen (HFNO) and non-invasive mechanical ventilators that can deliver non-invasive high fraction of inspired oxygen have become increasingly important.

HFNO provides nasal oxygen support of up to 40-60 L/min, at appropriate temperature and humidity. The air is exhaled, since the mouth of the patient remains open. HFNO leads to high oxygenation, reducing the respiratory difficulty and need for oxygen (3). On the other hand, the approximate cost of HFNO per patient is around 140-150 US$, resulting in a high cumulative cost due to increasing number of COVID-19 patients admitted for intensive care.

Non-rebreathing masks (NRMs) are very safe in prevention of the spread of droplets and they can provide oxygen support up to 90% at a flow rate of up to 15 L/min. In order to maintain the reservoir bag inflated, the minimum oxygen flow rate should be 8 to 10 L/min so that t hypercapnia can be prevented by blocking entry of exhaled air into the bag (3). Nasal cannula (NC) can provide oxygen at 40-45% at flow rates of 5 to 6 L/minute and represents a very important means of oxygen support for patients with mild hypoxia. It is possible to administer near 100% oxygen at a flow rate of 20 L/min, when NRM and nasal cannula are used in combination, providing a high level of nasal and oral oxygen support. The approximate cost of combined use of NRM and nasal cannula (NRMs + NC) is 1-2 US$ per patient, representing a widely available and practical method for oxygen support.

Based on the above-mentioned data, our objective was to compare HFNO with NRMs + NC in terms of cost ant mortality in a group of COVID-19 patients admitted to our intensive care unit.

Materials And Methods

This retrospective single-center study involved a total of 54 patients admitted to our intensive care unit due to COVID-19 infection between July 2020 and August 2020. The study protocol was approved by the Scientific Research Commission of the Turkish Ministry of Health. Patient related data such as age, gender, comorbid conditions, saturation at the time of presentation, length of intensive care unit admission (days), total length of hospital stay (days), type of oxygen support administered, discharge status, use of invasive mechanical ventilation, and certain laboratory parameters (urea, creatinine, C-Reactive Protein (CRP), D-dimer, ferritin, and pro-calcitonin) were recorded and analyzed.

Inclusion criteria were as follows:

- Bilateral diffuse infiltration or ≥ 50% involvement of the total lung area in Computed Tomography
- No need for mechanical ventilation support at presentation
- SpO2 of < 88% despite maximum nasal oxygen support
- COVID-19 PCR (polymerase chain reaction) test positivity
- D-dimer > 500 and ferritin > 500, or presence of cytokine storm

Exclusion criteria were as follows:

- Presence of invasive mechanical ventilator support at presentation
- CT involvement of < 50% in lungs

- Requirement only for nasal oxygen
- COVID-19 PCR test negativity
- Absence of cytokine storm
- Patients who were referred to another healthcare facility after presentation
- Pregnant women

All patients had diffuse ARDS and received oxygen support by HFNO or NRMs + NC. They also received wide spectrum antibiotics, low molecular weight heparin, low dose steroids, high dose vitamin C, vitamin D, and tocilizumab.

Study data were analyzed using SPSS (Statistical Package for Social Sciences) for Windows, 23.0. Normal distribution of the parametric data was evaluated by the Shapiro-Wilk test. Non-parametric data were compared using chi-square test, while parametric data were compared by Student's *t* test. A *p* value of < 0.05 at 95% confidence interval was considered statistically significant.

Results

A total of 54 patients were included, who were classified into two groups; those who received oxygen by HFNO and by NRMs + NC. The mean age in the HFNO group was 62.30 ± 15.73 years, and 7 (26.9%) of these patients were female, and 19 (73.1%) were male. Hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), and chronic renal failure (CRF) were present in 16 (61.5%), 3 (11.5%), 3 (11.5%), 2 (7.7%), 1 (3.8%), and 1 (3.8%) of these patients, respectively. Seventeen patients (64.4%) were discharged, while 9 (34.6%) died. The mean age in the NRMs + NC group was 65.28 ± 13.32 years, with 11 (39.3%) and 17 (60.7%) being female and male, respectively. HT, DM, CAD, COPD, asthma, and CRF were present in 16 (57.1%), 7 (25%), 2 (7.1%), 4 (14.3%), 2 (7.1%), and 1 (3.8%) of the patients, respectively. Twenty-one patients (75%) were discharged, and 7 (25%) died (Table 1).

No statistically significant difference was found between the two groups in terms of age (p=0.45), gender (p=0.33), and mortality (p=0.43). Also, there were no significant difference in oxygen saturation at admission (p=0.63), duration of intensive care (p=0.35), total length of hospital stay (p=0.057), and need for invasive mechanical ventilator (p=0.39) between the study groups (Table 2).

The levels of White Blood Cells (WBC) (p=0.36), platelets (p=0.12), lymphocytes (p=0.98), CRP (p=0.11), pro-calcitonin (p=0.20), D-dimer (p=0.74), ferritin (p=0.14), urea (p=0.74), and creatinine (p=0.35) were also similar between the two groups (Table 3).

Discussion

Severe hypoxemia may be observed in patients who develop severe ARDS due to COVID-19 pneumonia. Provision of adequate oxygenation has proven to be a major challenge in these patients, and failure to do

so may lead to increased need for invasive mechanical ventilation and duration of hospital stay, with consequent increase in mortality rates and treatment costs. The present study comparing oxygen support by HFNO and by NRMs + NC found that both modalities were comparable in mortality, duration of intensive care unit stay, length of hospital stay, and need for invasive mechanical ventilation.

HFNO can deliver a 40 to 60 L/min of oxygen flow via a nasal cannula and has been reported to reduce the need for mechanical ventilation and mortality as well as the duration of intensive care unit stay (4-7). Also, HFNO was found to be an effective therapeutic modality in subjects with ARDS of mild to moderate severity (8). On the other hand, it has been suggested that HFNO may not be safer than non-invasive mechanical ventilators and it requires rooms with negative pressure (9). Pinkham and colleagues observed that the size of the nasal cannula is an important consideration, with narrower cannula increasing the resistance, and thus failing to provide adequate oxygen due to the lack of sufficient pressure and flow rate (10). Furthermore, others reported that HFNO should be avoided, since it may be associated with viral spread (11, 12). On top of these, the cost of HFNO per patient is approximately 150-160 US$, leading to significant cumulative costs due to the increasing number of patients admitted to intensive care units.

Hypoxemia represents one of the most important determinants of the clinical outcome in patients with COVID-19 pneumonia. Provision of adequate oxygenation both before and during intensive care unit admission is of critical importance for improving the course of disease. Since it may not be possible to utilize HFNO support for each patient due to increased burden in intensive care units, we administered oxygen via NRMs + NC in a group of patients. During their subsequent course, no desaturation or tachypnea was observed in our patients, and even some benefited more from NRMs + NC support than from HFNO. Furthermore, NRMs + NC was associated with a faster discharge rate from the intensive care unit. Our clinical observations also suggested that provision of NRMs + NC early in the course of the disease could also reduce the need for admission to intensive care unit. It should also be borne in mind that the cost of NRMs + NC per patient is approximately 1-2 US$.

Main limitations of our study include the small sample size and absence of scoring for the thoracic tomography findings.

Conclusion

In conclusion**,** oxygen support by NRMs + NC was at least as effective as HFNO in COVID-19 patients in terms of mortality, need for invasive mechanic ventilation, duration of intensive care unit stay, and length of hospital stay. We believe that NRMs + NC may represent an inexpensive and more accessible means for oxygen supply as compared to HFNO, particularly when one considers the viral transmission risk and high acquisition cost of the latter. However, further studies are required to confirm our initial observations.

Abbreviations

COVID-19: Coronavirus disease 2019; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; HFNO: High Flow Nasal Oxygen NRMs+NC: NonRebreathing Masks +Nasal Cannula

Declarations

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Authors' contributions

All authors had full access to all of the data in the study and take responsibility for the integrity of the data. LJ has written the letter. The authors read and approved the fnal manuscript. **Funding**

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Availability of data and materials

The dataset supporting the conclusion of this article is available from the corresponding author upon reasonable request.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Harran University. All subjects provided informed written consent documents in accordance with the Declaration of Helsinki before enrollment. Approval was obtained from the Ministry of Health for the use of data for the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

1 Department of Chest Disease, Mardin State Hospital , Mardin, Turkey

Declarations

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Tables

Table 1. Demographic Characteristics of Patients				
		HFNO (High Flow Nasal oxygen) (n=26 patients)	NRMS+NC (Non-Rebreathing Masks+Nasal Cannula) (n=28 patients)	P value
Gender	Women	7(26.9%)	11(39.3%)	0,45
	Men	19(73.1%)	17(60.7%)	
Comorbidity	Hypertension	16(61.5%)	16(57.1%)	0,23
	Diabetes Mellitus	3(11.5%)	7(25%)	0,35
	Coronary Artery Disease	3(11.5%)	2(7.1%)	0,42
	Chronic Obstructive Pulmonary Disease	1(3.8%)	4(14.3%)	0,34
	Asthma	0(0%)	2(7.1%)	0,59
	Congestive Heart Failure	2(7.7%)	0(0%)	0,54
	Chronic Renal Failure	1(3.8%)	1(3.8%)	0,74
Discharge status	Discharged	17(65.4%)	21(75%)	0.43
	Died	9(34.6%)	7(25%)	

Table 2. Clinical Characteristics of Patients				
		HFNO (High Flow Nasal Oxygen) (n=26 patients)	NRMS+NC (Non-Rebreathing Masks+Nasal Cannula) (n=28 patients)	*P* value
Age (year)		62.30+/-15.73	65.28+/-13.32	0.45
Gender	Women	7	11	0.33
	Men	19	17	
Saturation without oxygen at admission		61.34+/-9.82	60.14+/-8.49	0.63
ICU Length of Stay (Days)		10.19+/-6.29	8.70+/-5.20	0.35
Total Length of Stay (Days)		17.88+/-8.28	23.60+/-12.92	0.057
Patients Needing an Invasive Mechanical Ventilator		11	10	0.39
Comorbidity	Yes	17	22	0.28
	No	9	6	
Discharge status	Discharged	17	21	0.43
	Died	9	7	

Table 3. Comparison of Patients' Laboratory Parameters			
	HFNO (High Flow Nasal Oxygen) (n=26 patients)	NRMS+NC (Non-Rebreathing Masks+Nasal Cannula) (n=28 patients)	*P* value
WBCs (White Blood Cells)	10.87+/-5.36	12.18+/-5.02	0.36
Platelets	235.34+/-102.16	279.92+/-108.11	0.12
Lymphocytes	1.00+/-0.80	0.99+/-0.93	0.98
CRP(C-Reactive Protein)	105.23+/-90.30	72.05+/-57.99	0.11
Procalcitonin	2.11+/-3.77	1.00+/-2.41	0.20
D-dimer	2642.61+/-5557.11	2228.07+/-3197.38	0.74
Ferritin	1274.56+/-669.56	980.67+/-798.79	0.14
Urea	60.64+/-36.22	63.68+/-32.81	0.74
Creatinine	1.44+/-0.86	5.32+/-21.51	0.35