Turk J Intensive Care 2023;21:220-7
DOI: 10.4274/tybd.galenos.2023.09825

ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

Cem Erdoğan,
Bahadır Çiftçi,
Deniz Kızılaslan,
Erkan Cem Çelik,
Işılay Ayar,
Tamara Buruk Topgül,
Selçuk Alver,
Yavuz Demiraran

Sequential Application of Oxygen Therapy via High-flow Nasal Cannula and Non-invasive Ventilation in COVID-19 Patients with Acute Respiratory Failure in the Intensive Care Unit: A Prospective, Observational Study

Yoğun Bakım Ünitesinde Akut Solunum Yetmezliği Olan COVİD-19 Hastalarında Yüksek Akışlı Nazal Kanül ve İnvaziv Olmayan Ventilasyon Yoluyla Oksijen Tedavisinin Sıralı Uygulanması: Prospektif, Gözlemsel Bir Çalışma

Received/Geliş Tarihi : 12.01.2023
Accepted/Kabul Tarihi : 07.03.2023

Cem Erdoğan, Bahadır Çiftçi, Deniz Kızılaslan, Işılay Ayar, Tamara Buruk Topgül, Selçuk Alver, Yavuz Demiraran
İstanbul Medipol University Faculty of Medicine, Department of Anesthesiology and Reanimation, İstanbul, Turkey

Erkan Cem Çelik,
Atatürk University Faculty of Medicine, Department of Anesthesiology and Reanimation, Erzurum, Turkey

Assist. Prof. Cem Erdoğan, MD (✉),
İstanbul Medipol University Faculty of Medicine, Department of Anesthesiology and Reanimation, İstanbul, Turkey

E-mail : cerdogan@medipol.edu.tr
Phone : +90 505 266 25 91
ORCID ID : orcid.org/0000-0002-5715-8138

ABSTRACT *Objective:* Non-invasive mechanical ventilation (NIV) and high-flow nasal oxygen therapy (HFNO) are the most frequently used methods for treating hypoxemia in those diagnosed with coronavirus disease-2019 (COVID-19) in the intensive care unit (ICU). In this prospective study, we compared the effects of these two treatment modalities applied alternately in the same patient.
Materials and Methods: Standard oxygen therapy (SOT) was administered for 1 hour to patients hospitalized in the ICU with a diagnosis of acute hypoxemic respiratory failure (AHRF) and acute respiratory distress syndrome (ARDS) due to COVID-19. HFNO and NIV were applied alternately to patients who met the inclusion criteria, and we evaluated the effects of HFNO and NIV applied to the same patient.
Results: Thirty of forty-five patients admitted to the ICU for COVID-19 ARDS met the inclusion criteria for the study. According to the first and second arterial blood gas (ABG) values, the PaO_2/FiO_2 (P/F) ratio was significantly higher during NIV compared to both baseline and HFNO. In addition, the ROX index was significantly higher during NIV than HFNO, and SpO_2 in NIV increased significantly compared with the baseline value. In both methods, patient satisfaction according to the visual analog scale was better than that of SOT. Eighty percent (24/30) of the patients were orotracheally intubated; 13 patients were transferred to the ward (43.3%), 2 patients were discharged home (6.7%), and 15 patients died (50%).
Conclusion: Starting respiratory support with HFNO and/or NIV rather than SOT is more effective in improving oxygenation in patients with AHRF and ARDS due to COVID-19 and other causes. NIV is more effective than HFNO in increasing the SpO_2 and P/F ratio.
Keywords: COVID-19, intensive care units, non-invasive ventilation, respiratory distress syndrome, visual analog scales

ÖZ *Amaç:* Yoğun bakım ünitesinde (YBÜ) koronavirüs hastalığı-2019 (COVİD-19) tanısı alan hastalarda hipokseminin tedavisinde en sık kullanılan stratejiler yüksek akışlı nazal oksijenizasyon (HFNO) ve non-invaziv ventilasyon (NİV) stratejileridir. Bu prospektif çalışmada, aynı hastada dönüşümlü olarak uygulanan bu iki tedavi yönteminin etkilerini karşılaştırmayı amaçladık.
Gereç ve Yöntem: Akut hipoksemik solunum yetmezliği (AHSY) ve COVİD-19'a bağlı akut respiratuvar distress sendromu (ARDS) tanısı ile YBÜ'de yatan hastalara 1 saat standart oksijen tedavisi uygulandı. Dahil edilme kriterlerini karşılayan hastalara dönüşümlü olarak HFNO ve NİV uygulandı ve aynı hasta üzerinde HFNO ile NİV etkileri araştırıldı.
Bulgular: COVİD-19 ARDS nedeniyle YBÜ'ye kabul edilen kırk beş hastadan otuzu çalışmanın dahil edilme kriterlerini karşıladı. Birinci ve ikinci arter kan gazı değerlerine göre NİV sırasında PaO_2/FiO_2

(P/F) oranı hem başlangıca hem de HFNO'ya göre anlamlı olarak yüksekti. Ek olarak, ROX indeksi, NİV sırasında HFNO'dan önemli ölçüde daha yüksekti ve NİV'deki SpO_2 değeri başlangıç değerine kıyasla önemli ölçüde arttı. Her iki yöntemde de vizüel analog skalaya göre hasta memnuniyeti standart oksijen terapisine (SOT) göre daha iyiydi. Hastaların yüzde sekseni (24/30) orotrakeal entübe edildi; 13 hasta servise sevk edildi (%43,3), 2 hasta taburcu edildi (%6,7), 15 hasta öldü (%50).

Sonuç: COVİD-19 ve diğer nedenlere bağlı AHSY ve ARDS hastalarında solunum desteğine SOT yerine HFNO ve/veya NİV ile başlamak oksijenizasyonu iyileştirmede daha etkilidir. NİV, SpO_2 ve (PaO_2/ FiO_2) P/F oranını artırmada HFNO'dan daha etkilidir.

Anahtar Kelimeler: COVİD-19, yoğun bakım ünitesi, non-invazif ventilasyon, respiratuvar distress sendromu, vizuel analog skalası

Introduction

The coronavirus disease-2019 (COVID-19) is a mortal infection that triggers a new kind of severe acute respiratory syndrome (SARS). A mortality rate of 61% has been reported in those critically ill who have been identified with COVID-19 (1,2). The highest mortality rate was reported as 86% in mechanically ventilated patients (3). Progressive hypoxemia is the main problem in these patients, resulting from lung injury and associated multi-organ damage. Aggressive treatments, such as tracheal intubation and classic mechanical ventilation, which are used to treat lung injury, have been reported to be unhelpful and potentially damaging. Acute respiratory distress syndrome (ARDS) that develops in patients infected with COVID-19 is not typical and is estimated to have a different mechanism; therefore, it is emphasized that different strategies should be used for the treatment of ARDS in these patients (4,5).

Two main strategies used for these patients in the intensive care unit (ICU) are high-flow nasal oxygenation (HFNO) and non-invasive ventilation (NIV). HFNO is a frequently used method for the treatment of hypoxemia in adult patients with acute respiratory failure. It's principle based on administering humidified oxygen to the patient through a nasal cannula in the range between 1-70 L/min. Due to the limited number of mechanical ventilators in many ICUs at the beginning of the COVID-19 pandemic, HFNO was used for a lot COVID-19 patients and also found effective in retrospective analyses. Many studies have reported that HFNO therapy is more effective than conventional mask oxygen therapy (6,7). It is considered beneficial compared to NIV because it is easier to apply and comfortable for the patient.

Classical NIV comprises continuous positive airway pressure (CPAP) or bi-level positive airway pressure ventilation. It has been used as oxygen/ventilation therapy in SARS and H1N1 patients and at a rate of 70% for the treatment of hypoxemia in COVID-19 patients. However, mortality was high in the COVID-19 patients.

HFNO and NIV strategies are the most used strategies for the hypoxemia treatment in patients with a diagnosis of COVID-19 in the ICU. No study has yet compared these two methods in the treatment of COVID-19. In this prospective study, we want to compare the effectivity between these two treatment modalities applied alternately in the same patient. The primary aim was to evaluate the success of the treatment [oxygenation and PaO_2/FiO_2 (P/F ratio)] and to investigate the predictive role of the ROX index [(SpO_2/FiO_2)/ respiratory rate]. The secondary aim was to discharge the patients from the ICU to the ward or home.

Materials and Methods

Ethics approval was obtained from the İstanbul Medipol University Non-Invasive Clinical Research Ethics Committee for this prospective, observational study (decision no: 889, date: 10.12.2020). Permission was obtained for the study from the Ministry of Health of the Republic of Turkey (permission no: 2020-12-22T15_20_37). The clinical trial was registered at clinicaltrials.gov (NCT05137431). This study was conducted in the ICU of İstanbul Medipol University, an academic university hospital, between December 2021 and April 2022. Forty-five patients with COVID-19 ARDS were admitted to the ICU during the study period. Standard oxygen therapy (SOT, mask oxygen) was administered for 1 hour to the patients hospitalized in the ICU with a diagnosis of acute hypoxemic respiratory failure (AHRF) and ARDS due to COVID-19. HFNO and NIV were applied alternately to the patients who met the inclusion criteria, and we evaluated the effects of HFNO and NIV applied to the same patient. All participants provided informed consent.

Standard Oxygen Therapy

Oxygen was administered with a simple face mask in patients who needed oxygen of over 6 L/min. It was started with 5 L/min oxygen and increased to a maximum of 15 L/min after the FiO_2 reached 60% at most.

Study inclusion and exclusion criteria:

Inclusion Criteria

- Polymerase chain reaction (+),
- P/F ratio ≤300 mmHg (despite standard mask oxygen support for 1 hour at 15 L/min),
- Respiratory rate ≥24/min or signs of respiratory failure (intercostal retraction, nasal wing breathing),

Exclusion Criteria

- Chronic respiratory failure,
- Cardiogenic pulmonary edema,
- Aplasia,
- Glasgow coma scale ≤12,
- Hemodynamic instability (use of vasopressors),
- Emergency intubation requirement.

Implementation of NIV and HFNO

The patients who met the criteria received HFNO for 16 hours and NIV for 8 hours in 24 hours; they were treated alternately with 2 hours of HFNO and 1 hour of NIV.

HFNO: The HFNO device (Optiflow, Fisher & Paykel Healthcare, Auckland, New Zealand) contains an air-oxygen mixture. The current in the device was adjusted from 50 to 70 liters during the treatment. The patient's SpO_2 value was maintained at at least 92%. Arterial blood gas (ABG) was evaluated at 1 hour. The blender providing the correct adjustment of FiO_2 was set at between 0.21 and 1.0, and the delivery of the gas flow was provided by a heated humidifier (MR850, Fisher & Paykel Healthcare) at 70 L/min.

NIV: The patients who underwent NIV were placed in a semi-recumbent position. The tidal volume was adjusted to 6-8 mL/kg. The respiratory rate was adjusted to be <30/min. The patient's SpO_2 value was maintained at least 92%. The positive end-expiratory pressure value was set to at least 5 cmH_2O. ABG was evaluated at 1 hour. NIV was administered with a full face mask (Fisher & Paykel Healthcare) connected to a mechanical ventilator (Evita XL, Evita 4 or Evita 2 dura, Dräger, Lübeck, Germany) and a heated humidifier (MR850, Fisher & Paykel Healthcare). FiO_2 was set to keep SpO_2 at its lowest (6).

The patients whose HFNO and NIV application could be followed for at least two cycles (6 hours) were evaluated.

Data Collection

We used STROBE flow chart for our observational study (Figure 1). The patients' demographic characteristics, ARDS criteria, and severity scores were recorded prospectively.

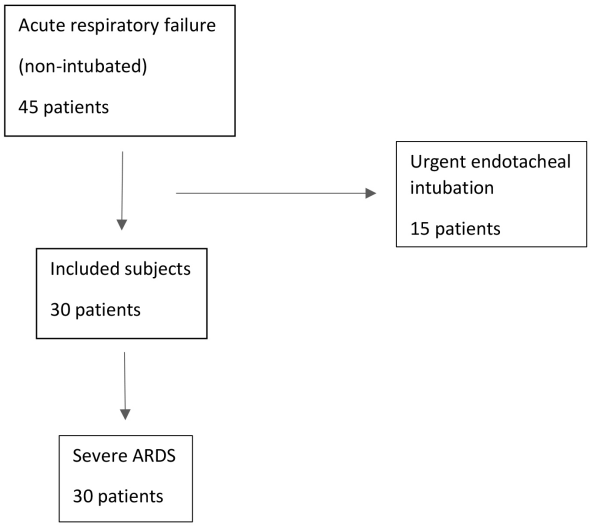

Figure 1. STROBE flow chart of the study
ARDS: Acute respiratory distress syndrome

The ARDS severity was assessed with the Berlin definition according to the oxygenation value in the first hour after treatment: mild (201≤ PaO_2/FiO_2 ≤300 mmHg), moderate (101≤ PaO_2/FiO_2 ≤200 mmHg), or severe (PaO_2/FiO_2 ≤100 mmHg) (8). The respiratory parameters, ventilator settings, tolerance, FiO_2, and blood gas parameters were recorded as baseline values when applying the face mask during spontaneous ventilation and in the first hour after the start of treatment. Tolerance was evaluated by visual analog scale (VAS) scoring (with a scoring system from 0 to10). All values were recorded 1 hour after the start of the second cycle of the HFNO and NIV sequences. NIV and HFNO application continued between NIV sessions until the respiratory distress resolved or the patient was intubated. C-reactive protein (CRP), D-dimer, and ferritin levels were recorded for all the patients, and the ROX index (the ratio of oxygen saturation measured by pulse oximetry/FiO_2 to the respiratory rate) was calculated.

The following criteria were used for endotracheal intubation: Loss of consciousness or psychomotor agitation hindering nursing care; persistent hypotension (defined by systolic arterial blood pressure >90 mmHg or mean arterial blood pressure <65 mmHg) despite fluid resuscitation or need for vasopressors; or two of the following criteria: evident worsening of respiratory distress, breathing frequency of >30 breaths/min, SpO_2 remaining below 80%

despite an FiO_2 of 1.0, or pH <7.30. NIV failure was defined as the need for endotracheal intubation.

Statistical Analysis

All data are expressed as a median with interquartile ranges (25th and 75th percentiles) or as a number with percentages. The data distribution was analyzed using the Kolmogorov-Smirnov test. Non-parametric tests were applied according to the result of the test. The qualitative data were compared using Pearson's chi-square test, and the quantitative data were compared by One-Way analysis of variance (the Friedman test). The Wilcoxon signed-rank test was applied for repeated measures. A p value >0.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS 20.0 software.

Results

Thirty of forty-five patients admitted to the ICU for COVID-19 ARDS met the inclusion criteria for the study. Fifteen patients were intubated urgently, so we excluded them. The characteristics and demographic data of the patients at admission are shown in Table 1. There was no statistical difference in terms of demographic characteristics.

Table 1. Demographic parameters of patients

Variables	Values
Age (age)	61.5 (51-66)
Weight (kg)	82 (76-90)
Height (cm)	169.5 (164-172)
Status (ward/discharge/exitus)	13 (43.3%)/2 (6.7%)/15 (50%)
Female/male	13/17 (43.3%/56.7%)
Intubation rate	24/30 (80%)

According to the first and second ABG values, the P/F ratio was significantly higher during NIV compared to both the baseline and HFNO. In addition, the ROX index was significantly higher during NIV than HFNO, and the SpO_2 in NIV increased significantly compared to the baseline value. The median P/F ratio of the patients was 74, and the median ROX index was 7.61. All the patients met the criteria for severe ARDS (Tables 2-4). In both methods, patient satisfaction according to the VAS was better than SOT. Moreover, a significant improvement in VAS was observed in the HFNO-1 and HFNO-2 measurements (Table 3).

No significant difference was observed in the patients in terms of the laboratory parameters (CRP, D-dimer, and ferritin) (Tables 2-4).

Eighty percent (24/30) of the patients were orotracheally intubated (OTE); 13 patients were transferred to the ward (43.3%), 2 patients were discharged home (6.7%), and 15 patients died (50%) (Table 1).

Discussion

In this study, the P/F ratio and SpO_2 were significantly higher during NIV compared to baseline and HFNO. The VAS score was better for HFNO and NIV-2 than O_2 therapy applied with a standard mask for SOT. It was thought that the increase in saturation and, consequently, the decrease in hypoxic agitation compared to the standard mask application may be the reason. The features of HFNO for patients that make it comfortable (eating, drinking water, and heated-humidified

Table 2. Evolution of arterial blood gases and biochemistry parameters in all patients during HFNO and NIV sessions

Variables	Baseline	HFNO-1	NIV-1	HFNO-2	NIV-2
SpO_2	91 (90-94)	90.5 (84-94)	95 (90-97)[a,b]	91 (86-95)	92 (89-97)[*a,b]
P/F	74 (60-97)	71 (60-119)	106 (72-158.5)[**a,b]	74 (63-117)	117.5 (86-176)[**a,b]
pH	7.43 (7.40-7.45)	7.46 (7.44-7.48)	7.46 (7.41- 7,48)	7.46 (7.41-7.48)	7.44 (7.41-7.47)
ROX	7.61 (5.25-9.07)	4.02 (3.56-6.34)	7.92 (5.27-9.39)[a,b]	5.15 (4.06-6.59)	6.69 (4.61-9.07)[**a,b]
$PaCO_2$	34.5 (31-37)	32.5 (30-35)	34 (32.1-35)	33 (31-38)	34 (31-37)
MRR	30 (22-30)	29 (24-32)	28 (23-30)	26 (22-30)	26.5 (24-30)[b]
VAS	3 (3-4)	3 (2-4)**	3 (2-4)	3 (2-4)**	3 (2-4)**
D-dimer	1063 (689-2089)	1105 (800-1780)	1195.5 (911-1974)[a]	1348 (624-2910)	1348 (636.4-2910)
CRP	80.15 (54.2-117.2)	101.5 (56.1-149)	76 (39.6-142)	77.1 (45-149)	86.5 (33-142)
Ferritin	980 (459-1970)	1005.5 (705-1660)	985 (705-1657)	1111 (606-1660)	1111 (606-1660)

HFNO: High-flow nasal oxygen therapy, NIV: non-invasive mechanical ventilation, P/F: PaO_2/FiO_2, MRR: minute respiratory rate,: VAS: visual analog scale, CRP: C-reactive protein
*p<0.001 versus baseline, **p<0.05 versus baseline, [a]p<0.05 versus HFNO-1, [b]p<0.05 versus HFNO-2

Table 3. Evaluation of arterial blood gases and biochemistry parameters in patients during HFNO sessions				
Variables/ HFNO	Baseline	HFNO-1	HFNO-2	p-value
SpO_2	91 (90-94)	90.5 (84-94)	91 (86-95)	0.974
P/F	74 (60-97)	71 (60-119)	74 (63-117)	0.610
pH	7.43 (7.40-7.45)	7.46 (7.44-7.48)	7.46 (7.41-7.48)	0.500
ROX	7.61 (5.25-9.07)	4.02 (3.56-6.34)	5.15 (4.06-6.59)	0.113
$PaCO_2$	34.5 (31-37)	32.5 (30-35)	33 (31-38)	0.561
MRR	30 (22-30)	29 (24-32)	26 (22-30)	0.547
VAS	3 (3-4)	3 (2-4)**	3 (2-4)**	0.02
D-dimer	1063 (689-2089)	1105 (800-1780)	1348 (624-2910)	0.900
CRP	80.15 (54.2-117.2)	101.5 (56.1-149)	77.1 (45-149)	0.411
Ferritin	980 (459-1970)	1005.5 (705-1660)	1111 (606-1660)	0.513

HFNO: High-flow nasal oxygen therapy, P/F: PaO_2/FiO_2, MRR: minute respiratory rate, VAS: visual analog scale, CRP: C-reactive protein
**p<0.05 versus baseline

Table 4. Evaluation of arterial blood gases and biochemistry parameters in patients during NIV sessions				
Variables/NIV	Baseline	NIV-1	NIV-2	p-value
SpO_2	91 (90-94)	95 (90-97)	92 (89-97)*	0.003
P/F	78 (60-97)	106 (72-158.5)**	117.5 (86-176)**	0.001
pH	7.42 (7.40-7.45)	7.46 (7.41-7.48)	7.44 (7.41-7.47)	0.176
ROX	7.61 (5.25-9.07)	7.92 (5.27-9.39)	6.69 (4.61-9.07)**	0.23
$PaCO_2$	34 (31-37)	34 (32.1-35)	34 (31-37)	0.695
MRR	30 (22-30)	28 (23-30)	26.5 (24-30)	0.361
VAS	3 (3-4)	3 (2-4)**	3 (2-4)	0.01
D-dimer	1146 (760-2089)	1195.5 (911-1974)	1348 (636.4-2910)	0.623
CRP	80.2 (67.1-117.2)	76 (39.6-142)	86.5 (33-142)	0.857
Ferritin	980 (542-1970)	985 (705-1657)	1111 (606-1660)	0.503

NIV: Non-invasive mechanical ventilation, P/F: PaO_2/FiO_2, MRR: minute respiratory rate, VAS: visual analog scale, CRP: C-reactive protein
*p<0.001 versus baseline, **p<0.05 versus baseline

air advantage) may have had a positive psychological effect. Similarly, Frat et al. (6) found that although HFNO showed few useful effects for treatment of hypoxemia and respiratory distress than NIV compared to SOT, HFNO was better tolerated and could be used in transition between NIV sessions without significant oxygenation impairment.

We found no significant difference in the intubation and mortality rates of the NIV and HFNO applications compared to studies that compared patients who underwent OTE after standard mask application. More prospective randomized controlled studies are needed on whether it contributes to the improvement of oxygenation in patients discharged without OTE. In a study focusing on ARDS patients receiving NIV as first-line therapy according to the Berlin ARDS classification, Thille et al. (9) reported an intubation rate of 61%. However, some patients in that study had a diagnosis of severe ARDS. In this study, the rate of intubation was 80% in all the patients with a diagnosis of severe ARDS, which can be attributed to the fact that all the patients had severe ARDS. Despite this, the 50% mortality rate appears to be similar to other clinical studies of deaths from COVID-19-related ARDS (1,2).

In line with this study, Zhu et al. (10) reported that HFNO is more effective in terms of oxygenation than SOT with a nasal cannula or oxygen face mask. In another study, the VAS showed that HFNO was easily tolerated in addition to its ease of application compared to NIV (11). Other studies have concluded that HFNO is recommended because of the

side effects (skin deterioration) associated with the use of NIV (11,12).

The ROX index, defined as the ratio of SpO_2/FiO_2 to the respiratory rate, was evaluated as an indicator of the need for intubation in the patients receiving NIV and HFNO therapy (13). In this study, a significant increase was found in the ROX index during NIV compared to HFNO, and the P/F ratio increased significantly in the NIV group compared to the HFNO application. The reason why the VAS score was higher for HFNO than for SOT may be the higher ROX index and P/F ratio of NIV as well as HFNO's ease of use.

Although it was not possible to evaluate the effect of HFNO and NIV on intubation, since they were applied in the same patient, the mortality and intubation rates were similar compared to the literature, although our patients had severe ARDS. In the study by Koga et al. (14), the risks of treatment failure and 30-day mortality were not significantly different between HFNO and NIV as first-line therapy in respiratory failure. Levy et al. (15) reported in their study that HFNO decreased the intubation rate, while NIV increased the intubation rate in AHSY patients (16). It has been suggested that HFNO should be used before NIV in critically ill COVID-19 patients (17).

In a study by Perkins et al. (18) to determine whether CPAP or HFNO improved clinical outcomes in patients with AHRF due to COVID-19 compared with SOT, the application of CPAP as the first strategy significantly increased the risk of tracheal intubation or mortality compared to SOT However, when HFNO was the first strategy, there was no significant difference with SOT.

A study found that the probability of NIV failure was higher in hypoxemic patients, and the intubation rate could reach 60% in randomly selected patients. Providing a high flow of heated and humidified oxygen, HFNO has been shown to improve oxygenation and comfort of patient and alleviate symptoms of illness. For this reason, intermittent HFNO applications in patients connected to NIV may be a way to maintain long-term NIV sessions while maintaining adequate oxygenation (6).

Ospina-Tascon et al. (7) found that the use of HFNO among severe COVID-19 patients significantly reduced the need for mechanical ventilation support and clinical recovery time compared to SOT. Although there was no significant difference between the rates of HFNO due to COVID-19, HFNO was associated with a lower rate of invasive mechanical ventilation (19). Another study concluded that HFNO was a useful treatment to avoid intubation in ARDS or as a bridge treatment and that mortality did not increase due to a delay in intubation (20).

In the study by Zucman et al. (21), 34% of the patients who presented with deep hypoxemia were successful with HFNO application and were discharged from the ICU, 63% required mechanical ventilation, and 3% died due to the patient's desire not to be intubated while receiving HFNO. The overall ICU mortality was 17%. The authors concluded that the ROX index, measured within the first 4 hours after the onset of HFNO, can be an easy-to-use predictor of early ventilation response (21). In our study, the mortality rate was 50%, and the intubation rate was 80%. The ROX index differed significantly between NIV-1 and NIV-2, but there was no significant difference in HFNO.

As stated by Oczkowski et al. (22) the guidelines published by the European Respiratory Society; It has been suggested to use HFNO instead of NIV in hypoxemic AHRF patients, and HFNO instead of SOT between NIVs in patients with AHRF. Our study also points to results consistent with the guideline (22).

He et al. (23), on the other hand, stated that the use of HFNO for COVID-19 patients was associated with a decrease in mortality and hospital stay at 28 days, and they observed a significant improvement in the P/F ratio at 24 hours. However, it was observed that there was no difference between HFNO and NIV in transition to invasive mechanical ventilation. In our study, although an improvement in the P/F ratio was observed in both strategies, our OTE rate was 80% (23).

The limitations of our study were the lack of a control group to evaluate the effects of a strategy combining HFNO and NIV on outcomes. In addition, because our patient group consisted of severe ARDS patients, the long-term effects of the ROX index could not be evaluated, since only two cycles could be completed in these patients.

Conclusion

Starting respiratory support with HFNO and/or NIV rather than SOT is more effective in improving oxygenation in patients with AHRF and ARDS due to COVID-19 and other causes. NIV is more effective than HFNO in increasing the SpO_2 and P/F ratio. In our study, the fact that the ROX index was high during NIV, which contributes positively to the P/F ratio and SpO_2, seems to be compatible with the literature

data in that it can be used in the evaluation of oxygenation. We conclude that it may be more beneficial to prefer HFNO, where patient compliance is better, to SOT as a transitional treatment in NIV applications.

Ethics

Ethics Committee Approval: Ethics approval was obtained from the İstanbul Medipol University Non-Invasive Clinical Research Ethics Committee for this prospective, observational study (decision no: 889, date: 10.12.2020).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: C.E., D.K., Concept: I.A., Y.D., Design: B.Ç., S.A., Data Collection and Process: D.K., E.C.Ç., T.B.T., Analysis or Interpretation: B.Ç., E.C.Ç., Y.D., Literature Search: I.A., T.B.T., Writing: C.E.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054-62.
2. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA 2020;323:1061-69.
3. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 2020;8:475-81.
4. Gattinoni L, Chiumello D, Caironi P, Busana M, Romitti F, Brazzi L, et al. COVID-19 pneumonia: different respiratory treatments for different phenotypes? Intensive Care Med 2020;46:1099-102.
5. Gattinoni L, Coppola S, Cressoni M, Busana M, Rossi S, Chiumello D. COVID-19 Does Not Lead to a "Typical" Acute Respiratory Distress Syndrome. Am J Respir Crit Care Med 2020;201:1299-300.
6. Frat JP, Brugiere B, Ragot S, Chatellier D, Veinstein A, Goudet V, et al. Sequential application of oxygen therapy via high-flow nasal cannula and noninvasive ventilation in acute respiratory failure: an observational pilot study. Respir Care 2015;60:170-8.
7. Ospina-Tascón GA, Calderón-Tapia LE, García AF, Zarama V, Gómez-Álvarez F, Álvarez-Saa T, et al. Effect of High-Flow Oxygen Therapy vs Conventional Oxygen Therapy on Invasive Mechanical Ventilation and Clinical Recovery in Patients With Severe COVID-19: A Randomized Clinical Trial. JAMA 2021;326:2161-71.
8. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA 2012;307:2526-33.
9. Thille AW, Contou D, Fragnoli C, Córdoba-Izquierdo A, Boissier F, Brun-Buisson C. Non-invasive ventilation for acute hypoxemic respiratory failure: intubation rate and risk factors. Crit Care 2013;17:R269.
10. Zhu Y, Yin H, Zhang R, Ye X, Wei J. High-flow nasal cannula oxygen therapy versus conventional oxygen therapy in patients after planned extubation: a systematic review and meta-analysis. Crit Care 2019;23:180.
11. Stephan F, Barrucand B, Petit P, Rezaiguia-Delclaux S, Medard A, Delannoy B, et al. High-Flow Nasal Oxygen vs Noninvasive Positive Airway Pressure in Hypoxemic Patients After Cardiothoracic Surgery: A Randomized Clinical Trial. JAMA 2015;313:2331-9.
12. Leone M, Einav S, Chiumello D, Constantin JM, De Robertis E, Abreu MG, et al. Noninvasive respiratory support in the hypoxaemic peri-operative/periprocedural patient: A joint ESA/ESICM guideline. Eur J Anaesthesiol 2020;37:265-79.
13. Roca O, Caralt B, Messika J, Samper M, Sztrymf B, Hernández G, et al. An Index Combining Respiratory Rate and Oxygenation to Predict Outcome of Nasal High-Flow Therapy. Am J Respir Crit Care Med 2019;199:1368-76.
14. Koga Y, Kaneda K, Fujii N, Tanaka R, Miyauchi T, Fujita M, et al. Comparison of high-flow nasal cannula oxygen therapy and non-invasive ventilation as first-line therapy in respiratory failure: a multicenter retrospective study. Acute Med Surg 2019;7:e461.
15. Levy SD, Alladina JW, Hibbert KA, Harris RS, Bajwa EK, Hess DR. High-flow oxygen therapy and other inhaled therapies in intensive care units. Lancet 2016;387:1867-78.
16. Huang HB, Peng JM, Weng L, Liu GY, Du B. High-flow oxygen therapy in immunocompromised patients with acute respiratory failure: A review and meta-analysis. J Crit Care 2018;43:300-5.
17. Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E. Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19). Crit Care Med 2020;48: 440-69.
18. Perkins GD, Ji C, Connolly BA, Couper K, Lall R, Baillie JK, et al. Effect of Noninvasive Respiratory Strategies on Intubation or Mortality Among Patients With Acute Hypoxemic Respiratory Failure and COVID-19: The RECOVERY-RS Randomized Clinical Trial. JAMA 2022;327:546-58.
19. Bonnet N, Martin O, Boubaya M, Levy V, Ebstein N, Karoubi P, et al. High flow nasal oxygen therapy to avoid invasive mechanical ventilation in SARS-CoV-2 pneumonia: a retrospective study. Ann Intensive Care 2021;11:37.
20. Panadero C, Abad-Fernández A, Rio-Ramirez MT, Acosta Gutierrez CM, Calderon-Alcala M, Lopez-Riolobos C, et al. High-flow nasal cannula for Acute Respiratory Distress Syndrome (ARDS) due to COVID-19. Multidiscip Respir Med 2020;15:693.
21. Zucman N, Mullaert J, Roux D, Roca O, Ricard JD; Contributors. Prediction of outcome of nasal high flow use during COVID-19-related acute hypoxemic respiratory failure. Intensive Care Med 2020;46:1924-26.
22. Oczkowski S, Ergan B, Bos L, Chatwin M, Ferrer M, Gregoretti C, et al. ERS clinical practice guidelines: high-flow nasal cannula in acute respiratory failure. Eur Respir J 2022;59:2101574.
23. He Y, Liu N, Zhuang X, Wang X, Ma W. High-flow nasal cannula versus noninvasive ventilation in patients with COVID-19: a systematic review and meta-analysis. Ther Adv Respir Dis 2022;16:17534666221087847.