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Araştırma/*Research Article*

The Comparison of Noninvasive Ventilation, High-Flow Oxygen Therapy and Conventional Oxygen Therapy for Weaning Failure in High-Risk Patients

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Yüksek Riskli Hastalarda Weaning Başarısızlığı Açısından Noninvaziv Ventilasyon, Yüksek Akışlı Oksijen Tedavisi ve Konvansiyonel Oksijen Tedavisinin Karşılaştırılması

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ABSTRACT

Objective: *The most common reason for intensive care unit admission is acute respiratory failure and after extubation mainly three methods are used to bring the PaO_2 level to a sufficient level: conventional oxygen therapy (COT), high flow oxygen therapy (HFO), and non-invasive ventilation (NIV). The aim of this study was to determine if NIV or HFO is beneficial in decreasing weaning failure in high-risk patient population (HRP) and compare these noninvasive methods.*
Methods: *This prospective, observational cohort study was conducted between March 2019 and March 2020 in a tertiary state hospital in Turkey. Our study included 3 main groups as COT, HFO, and NIV.*
Results: *During the study period, 71 patients were enrolled in this study and 24 patients were in the COT group, 22 HFO group, and 25 in the NIV group. The mean duration of mechanical ventilation assistance (MVA) before extubation was 5.8 days and the mean PaO_2 was highest in the HFO group 6 hours after extubation with a statistically significant difference ($p<0.001$). The HFO group had the highest PaO_2/FiO_2 immediately before and 6 hours after extubation. The reintubation rate was lowest in the HFO group and the other outcomes as total MVA duration, length of stay in ICU and hospital also differed between groups favoring the HFO group.*
Conclusion: *The results of our study suggest that NIV and HFO were beneficial in decreasing weaning failure and 30-day mortality rate among HRP compared to COT. When these noninvasive methods were compared, it was observed that HFO was preferable because of these advantages although the main characteristics of the groups were different.*

Keywords: *non-invasive ventilation, high flow oxygen therapy, conventional oxygen therapy, weaning failure, high-risk patients*

ÖZ

Amaç: *Yoğun bakım ünitesine yatışın en yaygın nedeni akut solunum yetmezliğidir ve ekstübasyondan sonra PaO2 düzeyini yeterli düzeye getirmek için başlıca üç yöntem kullanılır: konvansiyonel oksijen tedavisi (KOT), yüksek akışlı oksijen tedavisi (YAO) ve non-invaziv ventilasyon (NIV). Bu çalışmanın amacı, yüksek riskli hasta popülasyonunda NIV veya YAO'nun weaning başarısızlığını azaltmada yararlı olup olmadığını belirlemek ve bu noninvaziv yöntemleri karşılaştırmaktır.*
Yöntem: *Bu prospektif, gözlemsel kohort çalışma Mart 2019 ve Mart 2020 tarihleri arasında Türkiye'deki bir üçüncü basamak devlet hastanesinde gerçekleştirildi. Çalışmamız KOT, YAO ve NIV olmak üzere 3 ana grubu içermektedir.*
Bulgular: *Çalışma süresi boyunca, bu çalışmaya 71 hasta kaydedildi ve 24 hasta KOT grubuna, 22 YAO grubuna ve 25 hasta NIV grubundaydı. Ekstübasyon öncesi ortalama entübasyon süresi 5,8 gündü ve ortalama PaO_2 ekstübasyondan 6 saat sonra YAO grubunda en yüksekti ve fark istatistiksel olarak anlamlıydı. YAO grubu ekstübasyondan hemen önce ve ekstübasyondan 6 saat sonra en yüksek PaO_2/FiO_2 değerine sahipti. Yeniden entübasyon oranı YAO grubunda en düşüktü ve hastanede toplam kalış süresi gibi klinik sonuçlar da YAO grubunu destekler şekilde farklılık gösterdi.*
Sonuç: *Çalışmamızın sonuçları, NIV ve YAO'nin KOT'ye kıyasla yüksek riskli hastada weaning başarısızlığı ve ölüm oranını azaltmada faydalı olduğunu göstermektedir. Bu non-invaziv yöntemler karşılaştırıldığında, grupların temel özelliklerinin farklı olmasına rağmen, bu faydada YAO'nin tercih edilebilir olduğu görülmüştür.*

Anahtar kelimeler: *non-invaziv ventilasyon, yüksek akışlı oksijen tedavisi, konvansiyonel oksijen tedavisi, weaning başarısızlığı, yüksek riskli hasta*

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INTRODUCTION

The most common reason for intensive care unit (ICU) admission is acute respiratory failure (ARF) and most of the admitted patients need mechanical ventilation assistance (MVA) until the indication for MVA is eliminated [1]. After gradual discontinuation of MVA which was defined as weaning, oxygen therapy is utilized to resolve remaining deterioration in oxygen supply. Mainly three universal methods are used to bring the partial oxygen (PaO_2) pressure to a sufficient level: conventional oxygen therapy (COT), high- flow oxygen therapy (HFO), and noninvasive ventilation (NIV) [2,3].

Although in the literature, many criteria have been used to define the weaning failure and the high-risk patients (HRP) after extubation, the three most widely used and easily identified criteria for HRP are defined as being over 65 years of age, having a history of cardiac disease and a chronic respiratory disease [4]. Weaning failure might be defined as the requirement of reintubation and MVA within 72 hours after extubation while weaning failure is a known risk factor increasing morbidity and mortality especially in HRP [1,5].

The weaning process which starts at the time of intubation has always been a critical decision in the intensive care unit (ICU). Even in planned cases in which the patient successfully passes the spontaneous breathing test or the preparation test for weaning, an average of 15% of patients and 20-25% of high-risk patients may require reintubation [1,6]. To decrease weaning failure, NIV was proposed by some researchers either as a preventive or therapeutic strategy [7]. HFO is another option that offers delivery of heated, fully humidified high flow oxygen (up to 60 L/min) through a nasal cannula, which might reduce the risk of reintubation. It is claimed to be superior to NIV with its availability, patient comfort, secretion management, and cost [2].

Over the last two decades, NIV and later HFO have gained popularity in different clinical settings including weaning failure and they might increase end-expiratory lung volume and reduce work of breathing in principle but to what extent these benefits help to avoid the risk of weaning failure is unclear and unconvincing for some researchers especially in terms of high-risk patients [2,8,9]. The primary objective of this study was to prove if NIV or HFO is beneficial in decreasing weaning failure in high- risk patient population. The second aim was to determine the extent of this benefit, if any, and compare these noninvasive methods.

MATERIAL and METHOD

This prospective, observational cohort study was conducted between March 2019 and March 2020 in a tertiary state hospital in Turkey. Our study was approved by the local ethics committee (E1-19-029) and all patients or their relatives were informed and signed written informed consent. As our study had an observational design, the study participants did not interfere with the weaning process and if deemed it necessary, reintubation process. However, since these stages are routinely recorded in our intensive care practice, it was possible to make re-evaluations by reviewing the patients' files in case of any suspicion about compliance with the standard weaning criteria. Patients with suspected compliance with these standards or with insufficient data were excluded from the study. The required criteria complied with standard patient care and follow-up could be briefly summarized as follows:

a) The weaning stage and criteria: included the spontaneous breathing trial with awake patients who met the standard respiratory and clinical criteria for weaning after the daily evaluation of the patients whose indication for intubation weakened.
b) Spontaneous breathing trial (SBT): Patients whose clinical and respiratory parameters did not regress for 30-120 minutes with T-tube or low-pressure support were considered ready for weaning and extubated. Patients who failed SBT were taken to MV support and re-evaluated one day later.
c) Low-pressure support was defined as positive end-expiratory pressure (PEEP) of 5 mmHg and pressure support of 5 mmHg using either continuous airway positive pressure (CPAP) or SBT mode.

Study design

The intubated patients who needed mechanical ventilator support for more than 24 hours in ICU and

weaned after SBT or for whom extubation was planned were considered as candidates for the study. The patients who met at least one of the following criteria were considered as HRP and included in our study:

1) age > 65 years,
2) history of cardiological problems
3) history of respiratory problems

In this study, those who met one or more of the following criteria would be excluded from the study:

a) Individuals meeting the do-not-resuscitate criteria
b) Patients with tracheostomy
c) Individuals who were hypercapnic in spontaneous breathing or T-tube trials
d) Individuals who were uncontrolled extubated (self-extubated or accidentally extubated)
e) Cases with multi-weaning procedures/extubation episodes
f) Patients younger than 18 years
g) Patients with suspected compliance with standard criteria.

Randomization

Since our study had completely observational design, there was no possibility of randomization. However, the clinical care team-including the nurses and the doctors- who followed up the patient independently of the researchers, regularly changed in each shift and this situation provided a kind of randomization.

Variables

Dependent variables to be considered and evaluated in our study were as follows; demographic characteristics of the patients such as age and gender; history of cardiac or respiratory disease; Acute Physiology and Chronic Health Evaluation (APACHE) II scores assigned 24 hours after admission to ICU; the indication for intubation and duration of intubation; hemodynamic and respiratory parameters immediately before and 6 hours after extubation; need for endotracheal reintubation; duration of mechanical ventilation; length of intensive care and hospital stay, and 30-day mortality. Laboratory data and blood gas analysis were routinely requested by the primary clinician on a daily routine basis in our clinic. Our independent variables were the duration of the HFO or NIV to be applied and indications for their application (if any).

The specified parameters above were evaluated by the researchers at the end of each day with data retrieved from patients' files, doctor notes, nurse sheets, and hospital databases regularly until discharge from ICU. All data were recorded by researchers in Microsoft Excel (Microsoft Excel 2013, and Microsoft Corporation) sheets.

To avoid selection bias, as this was an observational study, we calculated the delta values of gasometric variables like PaO_2 and $PaCO_2$ and compared these delta values as well.

Delta value X=value of X 6 hours after extubation-value of X immediately before extubation

Interventions and groups

Our study included 3 main groups as COT, HFO, and NIV. Since the study was a purely observational study and the researchers did not interfere with patients' care, we did not choose or intervene in the oxygen therapy method. The conventional oxygen therapy group was supported with a blended air/oxygen mixture at a flow rate of less than 15 liters/minute (L/min) delivered either with a nasal cannula or standard face mask. HFO group was supported with a specific nasal cannula and the Optiflow Device System (850 system; Fisher and Paykel, New Zealand), and the gas flow rate was at a maximum of 60 L/min. Full facemask NIV (BiPAP Vision; Respironics Inc) was delivered in the NIV group.

In all groups, the target FiO_2 was decided by the primary clinician to maintain respiratory rate at less than 25 breaths/min, arterial oxygen saturation (SaO_2) higher than 92%, and a reasonable blood gas analysis. The same doctors and nurses (excluding the study researchers) continued to treat all the groups after the weaning stage using similar medical management modalities.

We calculated the sample size by using Statsoft Statistica v.10 (StatSoft, Inc., 2011; STATISTICA, data analysis software system, version 10) program. The determined case number was at least 20 for each group with 5% standard error and unilateral 95% CI analysis. After all data were collected, the statistical

evaluation was done using SPSS version 20.0 (SPSS Inc.; Chicago, IL, USA). In this evaluation, firstly, the normal distribution of the variables was tested by the One-Sample Kolmogorov- Smirnov test and then the suitability of parametric or non-parametric tests was decided. The continuous variables were expressed as mean±standard deviation (SD) and the categorical variables as total number (n) and frequency (%). Mann-Whitney U test or Student T-test and Pearson Correlation Test or Spearman Rho Test was used when appropriate, depending on whether the data are parametric or nonparametric in comparison of the groups. All statistical tests were 2-sided and p-value <0.05 was considered statistically significant.

RESULTS

During the study period of 12 months, 639 patients were admitted to our ICU. After exclusion of the unsuitable cases for the study,the remaining 71 patients were enrolled in this study. The study population was summarized in Figure 1. Twenty-four patients were included in the COT group, 22 in the HFO group, and 25 in the NIV group.

The mean age of the patient population including 37 (52.1%) male cases was 72±12.1 years, The baseline characteristics of patients' are summarized in Table 1. The mean APACHE 2 score was 22.2±8.2 which was the lowest in the HFO and highest in the COT group. The difference between groups was statisti-

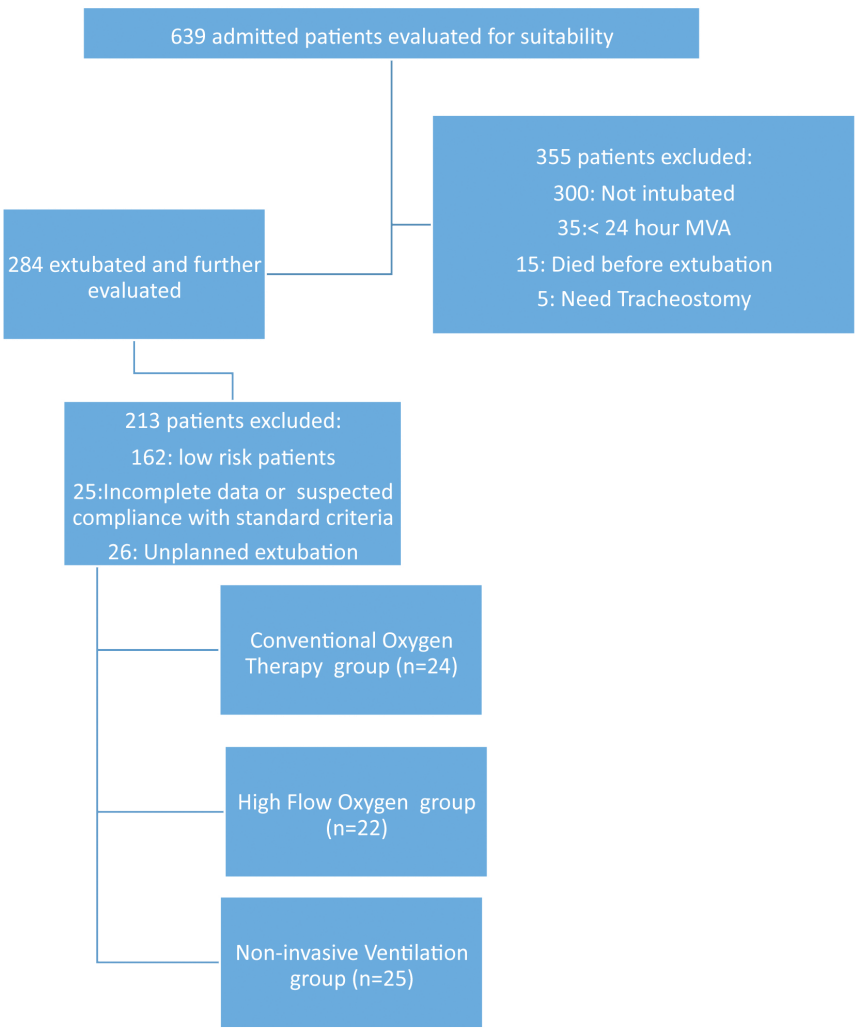

Figure 1. Flowchart of the study; 71 patients were included in this study after the exclusion of unsuitable patients.
MVA, mechanical ventilation assistance.

Table 1. Patients' baseline characteristics

Variable	Total patient (n=71)	COT group (n=24)	HFO group (n=22)	NIV group (n=25)	p
Age, years	72±12.1	69.4±11.6	72.4±15.3	74.1±8.9	0.549
Male gender, n (%)	37 (52.1%)	12 (50%)	16 (72.7%)	9 (36%)	0.314
APACHE II score	22.2±8.2	25.7±9.6	18.7±4.4	21.8±8.2	0.036
NIV preentubation,n(%)	5 (7%)	0	2 (9.1%)	3 (12%)	0.105
Cardiac Comorbidity, n(%)	34 (47.9%)	3 (12.5%)	12 (54.5%)	19 (76%)	<0.001
Respiratory Comorbidity, n(%)	53 (74.6%)	24 (100%)	17 (77.3%)	12 (48%)	<0.001
Over 65 years old, n(%)	57 (80.3%)	18 (75%)	16 (72.7%)	23 (92%)	0.134
Reason for intubation					0.711
ARF, n (%)	38 (53.5%)	15 (62.5%)	8 (36.4%)	15 (60%)	
Shock, n (%)	8 (11.3%)	0	4 (18.2%)	4 (16%)	
Cardiac arrest, n (%)	20 (28.2%)	6 (25%)	10 (45.5%)	4 (16%)	
Postoperative prolonged intubation, n (%)	5 (7%)	3 (12.5%)	0	2 (8%)	
Duration of MVA pre-intubation, days	5.8±4.8	4.8±1.7	6.82±7.0	5.80±4.3	0.972

Values are given as mean±standard deviation (SD) or as numbers and percentages.
COT, Conventional oxygen therapy; HFO, High flow oxygen; NIV, Non-invasive ventilation; APACHE II, Acute Physiology and Chronic Health Evaluation; ARF, Acute respiratory failure; MVA, mechanical ventilation assistance

Table 2. Hemodynamic and respiratory parameters- including gasometric variables-immediately before extubation and 6 hours after extubation.

Variable	Total patient (n=71)	COT group (n=24)	HFO group (n=22)	NIV group (n=25	p
PE PaO_2, mmHg	81.8±20.4	80.7±19.2	84.9±13.2	80.1±26.3	0.06
PE FiO_2, mmHg	32.2±5.2	34.3±4.7	30.2±5.8	31.8±4.4	0.024
PE PaO_2/FiO_2, mmHg	257.2±57.3	234.1±36.5	288.2±54.1	252.1±65.7	0.002
PE Arterial pH, units	7.43±0.1	7.41±0.05	7.46±0.06	7.42±0.07	0.198
PE PCO_2, mmHg	42.3±12.1	44.6±9.9	35.7±6	45.9±15.5	0.005
PE PCO_2 >45 mmHg	29 (40.8%)	15 (62.5%)	2 (9.1%)	12 (48%)	0.340
PE RR (breaths/min)	24.5±4.3	23±4.4	25.1±4.1	25.2±4.2	0.105
PE HR (beats/min)	108.7±12.7	106.4±12.8	106.4±13.9	112.8±10.6	0.087
AE PaO_2, mmHg	68.4±17.1	59.2±12.8	79.9±15.9	67.1±16.3	<0.001
AE FiO_2	32.9±4.4)	31.9±3.5	33.6±4.9	33.2±4.7	0.501
AE PaO_2/FiO_2, mmHg	212.3±62.8	189±49.9	242.5±63.8	207.8±64.5	0.011
AE PCO_2, mmHg	43.1±13.4	45.6±15.9	35.3±3.4	47.2±13.7	0.001
AE RR (breaths/min)	21.9±5.9	27.2±4.7	17.8±2.8	20.8±5.2	<0.001
AE HR (beats/min)	104.2±14.6	116.1±11.5	92.3±5.5	103.8±13.9	<0.001
Delta PaO_2	-7.7±58.6	-4.7±97.4	-5±10.4	-12.9±28.1	0.001
Delta PaO_2/FiO_2	-44.9±72	-45.1±66.9	-45.6±66	-44.2±83.8	0.748
Delta PCO_2	0.7±8.4	1 ±10.3	-0.4±5.6	1.3±8.4	0.695
Delta RR (breaths/min)	-2.5±6.1	4.1±3.2	-7.3±3.3	-4.4±4.5	<0.001
Delta HR (beats/min)	-4.5±14.3	9.6±7.1	-14.1±10.9	-9±11.9	<0.001

Values are given as mean±standard deviation (SD) or as numbers and percentages.
COT, Conventional oxygen therapy; HFO, High flow oxygen; NIV, Non-invasive ventilation; PE, immediately before extubation; AE, 6 hours after extubation; PaO_2, partial pressure of oxygen in arterial blood; FiO_2, the fraction of inspired oxygen; PaO_2/FiO_2, the ratio of the partial pressure of oxygen in arterial blood to the fraction of inspired oxygen; $PaCO_2$, the partial pressure of carbon dioxide in arterial blood; RR, respiratory rate; HR, heart rate.

cally significant (p=0.036). Cardiac comorbidity was more frequent in the NIV and respiratory comorbidity in the COT group and the difference between groups was statistically significant in terms of past medical history (p=<0.001). Only 5 patients needed NIV support before intubation and there was no statistically significant difference between groups (p=0.134).

The main reasons for intubation were acute respiratory failure (n=38, 53.5%) and cardiac arrest (n=20, 28.2%), and the groups did not differ according to

indication for intubation. The mean duration of MVA before extubation was 5.8±4.8 days and the difference was not statistically significant between groups (p=0.972). Hemodynamic and respiratory parameters-including gasometric variables-immediately before, and 6 hours after extubation were compared between groups (Table 2). The mean PaO_2 immediately before extubation was 81.8 mmHg (±20.4) and the difference was not significant between groups while PaO_2 was highest in the HFO group 6 hours after extubation (79.9±15.9 mmHg); and the intergroup difference was statistically significant (p=<0.001). The FiO_2 variable immediately before extubation was highest in the COT group (34.3±4.7) with a statistically significant intergroup difference (p=0.02). Meanwhile, it was highest in the HFO group 6 hours after extubation (33.6±4.9) without any statistically significant difference. The HFO group had the highest PaO_2/FiO_2 Ratio (P/F Ratio) immediately before (288.2±54.1) and 6 hours after extubation (242.5±63.8) with a statistically significant intergroup difference (p=0.002 and p=0.011 respectively).

This discrepancy is shown in Figure 2. $PaCO_2$ level immediately before and 6 hours after extubation was lowest in the HFO group and the intergroup difference was statistically significant (35.7±6 mmHg and 35.3±3.4 mm Hg; p=0.005 and 0.001, respectively). The delta values which are summarized in Table 2 told us another story and delta PaO_2 was highest in NIV while the delta PF ratio between groups did not differ statistically. Delta CO_2 value was similar between groups while delta RR and HR values were in favor of the HFO group.

The heart and respiratory rates immediately before extubation were comparable between groups (p=0.105 and p=0.087 respectively). Yet, both the respiratory and heart rates were lowest in the HFO group 6 hours after extubation 17.8±2.8 breaths/min and 92.3±5.5 heart rate/min and intergroup difference was statistically significant (p=<0.001). In Figure 3, the respiratory rates are compared between groups.

The reintubation rate within 72 hours and 7 days later was lowest in the HFO group with a statistically significant intergroup difference (p=0.027 and <0.001 respectively) (Table 3). The other outcomes as total MVA duration, length of stay (LOS) in ICU and hospital also differed between groups favoring the HFO group (p=<0.001, p=0.031 and p=0.012). The 30-day mortality rate was also lowest in the HFO group yet the intergroup difference was not statistically significant (p=0.063).

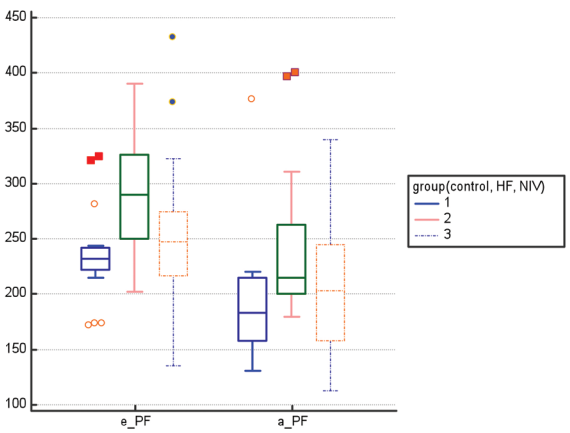

Figure 2. The comparison of groups according to the P/F ratio variable immediately before extubation and 6 hours after extubation. Group 1 representing the COT- control- group, group 2 representing the HF group, and group 3 representing the NIV group.
COT, Conventional oxygen therapy; HF, High flow oxygen; NIV, Non-invasive ventilation; e_PF, the ratio of the partial pressure of oxygen in arterial blood to the fraction of inspired oxygen immediately before extubation; a_PF, the ratio of the partial pressure of oxygen in arterial blood to the fraction of inspired oxygen 6 hours after extubation.

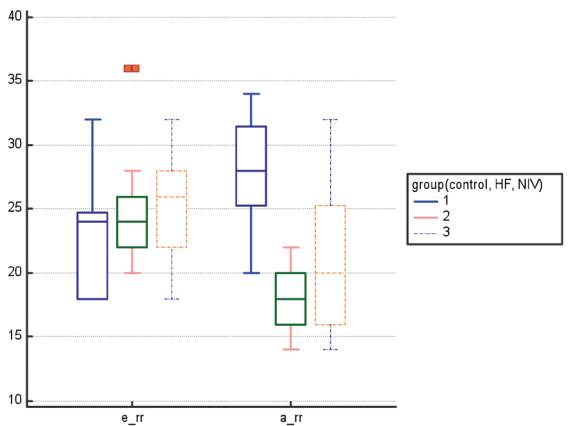

Figure 3. The comparison of groups according to the respiratory rate variable immediately before extubation and 6 hours after extubation Group 1 representing the COT- control- group, group 2 representing the HF group, and group 3 representing the NIV group.
COT, Conventional oxygen therapy; HF, High flow oxygen; NIV, Non-invasive ventilation; e_rr, respiratory rate immediately before extubation; a_rr, respiratory rate 6 hours after extubation.

Table 3. Clinical outcomes.

Variable	Total patient (n=71)	COT (n=24)	HFO group (n=22)	NIV group (n=25)	p
Total duration of MVA, days	16.5±15.3	24.8±17.3	8.23±8.8	15.7±13.9	<0.001
LOS ICU (days)	25.3±17.1	30.4±17.4	18.4±14.7	26.6±17.2	0.031
LOS hospital (days)	30.8±16.8	36±16.7	23.9±14.1	31.9 ±17.6	0.012
Reentubation in 72 hrs	23 (32.4%)	15 (62.5%)	0	8 (32%)	0.027
Reentubation in 7 days	38 (53.5%)	24 (100%)	2 (9.1%)	12 (48%)	<0.001
30-day mortality	26 (36.6%)	15 (62.5%)	2 (9.1%)	9 (36%)	0.063
Need for NIV or HFO > 48 hrs	20 (28.2%)	0	2 (9.1%)	18 (72%)	<0.001

Values are given as mean±standard deviation (SD) or as numbers and percentages.
COT, Conventional oxygen therapy; HFO, High flow oxygen; NIV, Non-invasive ventilation; MVA, mechanical ventilation assistance; LOS, length of stay; ICU, intensive care unit

DISCUSSION

The weaning process starts just after endotracheal intubation and discontinuation of MVA is the main fulcrum of ICU practice yet not all weaning attempts always succeed. The weaning failure (WF) rate was observed as high as 29% and related to mortality as an independent risk factor [10]. First NIV then HFO was increasingly used either as a therapeutic or preventive strategy after weaning to prevent WF and mortality. NIV was claimed to be beneficial to decrease WF, pneumonia, and LOS in ICU in postsurgical [11], immunocompromised and acute-on-chronic respiratory failure patients [7,12]. Hence, Maitra et al. [7] queried the previous meta-analyses which supported the usefulness of NIV in weaning failure in the early period and claimed that these meta-analyses included trials in which only one-third of the study population were high-risk patients and this factor underpowered the studies. In a previous meta-analysis, Krishna et al. [13] showed that NIV was related to a lower reintubation rate in the prophylactic group (p=0.04) while this relation was not detected in the therapeutic group (p=0.31).

A meta-analysis of two heterogenous populations (-comprising critically ill patients and post-surgical patients-) arrived at a different conclusion. Xu et al.[14] favored HFO on reintubation whereas Zhu et al. did not reveal any benefit with HFO [15]. In a study by Maggiore et al. [3], a lower reintubation rate with HFO was accomplished similar to our study (3.8 vs 9.1). In a recent study, the benefit of HFO in the reintubation rate, gasometric variables and patient comfort was detected in low-risk patients compared to COT but the effectiveness of HFO in HRP was not clear [16]. In their study Hernandez et al. [2] searched the effectiveness of HFO and NIV in HRP in a multicenter randomized clinical trial and found the reintubation rate as 19% in NIV patients and 22.8% in the HFO group and concluded that HFO was comparable to NIV at preventing reintubation. Similarly, in our study, it was clearly presented that HFO and NIV had a beneficial effect on 30-day mortality and reintubation rates. Especially, the HFO group had the best clinical outcomes in this study with shorter LOS in ICU, and in hospital, lower reintubation , and 30-day mortality rates. However, the mean APACHE II score was also the lowest in the HFO group and only 2 patients (9.1%) in this group had CO_2 >45 mmHg immediately before extubation. This situation raised a question mark in minds about selection bias while we, as study researchers, did not interfere with the chosen method after extubation. Our study was designed in an observational manner not as a randomized clinical trial and the difference according to APACHE II scores and hypercarbia variables between groups were noticed after statistical evaluation was performed.

The most critical drawback on routine usage of NIV was the delay in reintubation and increment in mortality rates [17,18] and Kang et al. [19] claimed that HFO might reprieve intubation and lead to increased mortality rate. We did not observe any increment in mortality rate, on the contrary, both NIV and HFO had a beneficial effect on decreasing mortality rates. The selection of HRP instead of the general population could be the reason for this discrepancy. In our

study, we evaluated HRP as a subset of patients at high-risk for reintubation which was proposed by Thille et al. [4] as easily identifiable criteria and these patients were older than 65 years and/or had an underlying cardiac or respiratory disease.

In a Cochrane database, the decrease in mortality rate was found as 46% in COPD patients [20]. This decrement in mortality and intubation rates reflected itself in guidelines and the official European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines recommended the utilization of NIV to achieve decrease in COPD patients [21]. In our study, respiratory comorbidity in past medical history was seen in the COT group (100%) predominantly, and 30-day mortality and reintubation rates were higher in this group. We did not search for a cause and effect relationship hence we could not specify a result for the relationships between these variables. In another meta-analysis, COT, HFO, and NIV groups were compared with each other [22]. In this meta-analysis, HFO and NIV were found superior to COT in terms of reintubation rate and NIV and HFO had similar treatment benefits. The reason for that discrepancy was explained with the insufficiency of COT to guarantee satisfactory gas exchange compared to NIV or HFO therapy and NIV was proposed to prevent reintubation and to decrease mortality rate after planned weaning as a prophylactic approach. In our study, the HFO group had the lowest reintubation and 30-day mortality rates in contrast to the Zhou et al. [9] study in which NIV was found superior to HFO regarding survival benefit but not reintubation rates. This difference was explained with higher positive airway pressure and greater improvement in cardiac performance provided by the NIV technique.

Theoretically HFO had advantages over NIV as decreased risk of adverse effects like mouth dryness, leaks and pressure sores, easier clearance of secretions, and enhanced patient comfort [19]. Tan et al. [23] emphasized this advantage with better tolerance and higher comfort than NIV besides similar WF among COPD patients after extubation. We did not investigate this aspect while the need for NIV or HFO more than 48 hours later was higher in the NIV group (72% vs 9.1%).

CONCLUSION

The results of our study suggest that NIV and HFO were beneficial in decreasing weaning failure and 30-day mortality rates among HRP compared to COT. When these noninvasive methods were compared, it was observed that HFO was preferable thanks to these advantages, although the main characteristics of the groups were different.

Limitations

The main limitation of our study is ite being a unicenter trial performed with small number of patients. The strict inclusion criteria of this study might be the reason for this limitation. A total of 639 patients were evaluated for suitability and only 71 of them were included in the study. The second limitation becomes obvious after the statistical evaluation of the study. Higher APACHE scores and higher incidence rates of respiratory comorbidities in the COT group have emerged as a major limitation. The lack of randomization is the third limitation while the clinical care team-including the nurses and the doctors- who followed up the patients independently of the researchers, regularly changed in each shift and this situation provided a kind of randomization.

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