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RESEARCH ARTICLE

USE OF HIGH-FLOW NASAL CANNULA IN PATIENTS WITH COVID-19: A RETROSPECTIVE STUDY

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Abstract

Background: During COVID-19 pandemia, the healthcare systems all over the world had to confront many different and complicated issues. One of them was the way to support the patients' respiratory system. Generally, the HFNC therapy was applied in the past for respiratory support, but we did not have studies to establish its efficiency. Therefore, with the recent study, despite the small number of patients, an effort was made to apply the HFNC therapy so as to avoid intubation and invasive mechanical ventilation.

Methods: This current study is a retrospective. Patients' medical data admitted in the Covid – 19 ward from Agios Pavlos General hospital in Thessaloniki from October 25, 2020 to May 25, 2021 were reviewed. General clinical outcomes, the success of HFNC therapy, and related respiratory support methods were evaluated.

Results: The present study included 39 patients (27 men and 12 women), whose mean age was 64,5±10,3 years old, 44% of the population had a clear medical history, and 56,4% had some comorbidities. After applying HFNC therapy, 66,7% withdrew successfully, and 33,3% were intubated. The mean time of HFNC therapy is 3,3±2,4 days, while the mean total length of hospitalization was 18,3±10,9.

Conclusions: This current study describes the application of HFNC during the COVID-19 pandemia, and the conclusion is that the use of HFNC is an effective way to treat COVID-19 infected patients but under close monitoring. It had been shown that the application of HFNC can reduce the rate of intubation and mortality. Nevertheless, the conclusions of this particular study cannot be generalized.

Keywords: COVID-19, high-flow nasal cannula, oxygen therapy, respiratory support, Acute Respiratory Failure (ARF).

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INTRODUCTION

According to European Centre for Disease Prevention and Control (ECDC), since December 31, 2019, and as of week 2021-39, 68,691,602 cases of COVID-19 have been reported from Europe. From these cases, the number of deaths is 1,318,779 deaths.[1] The primary spectrum of this infection is broad, and it includes asymptomatic clinical view, mild upper respiratory tract infection with fever, cough, and more severe symptoms such as pneumonia with acute respiratory failure (ARF), characterized by chest imaging lesions.[2,3] In most cases, the ARF was the most common reason for admission to intensive care units (ICUs), and the mortality rate was high for the patients with severe COVID-19 infection.[4,5]

A report from Lombardi, Italy, mentions, that of 1591 Covid-19 critically ill patients, 99% of them supported with supplemental oxygen, and 88% of them (1150 patients) needed invasive mechanical ventilation (IMV).[5,6]

High-flow nasal cannula (HFNC) belongs to non-invasive ventilation (NIV) system, and the clinicians can administrate air-oxygen blends from 30L – 60L/min and a titratable fraction of oxygen as high as 100%. HFNC therapy is a new type of oxygen support, and it provides heated and humified oxygen to relieve the nasal cavity.[2] HFNC therapy improves oxygenation, and reduces the possibility for invasive or non-invasive mechanical ventilation.[2] The HFNC strategy is that oxygen blend is administrated to patients with $Sp0_2$ _<92% and the respiratory rate (RR) ≥25 times/min.[2,5,7]

HFNC therapy has not been applied to COVID-19 patients for a long time. Even though some studies have already shown that this therapy is safe and effective in patients with ARF.[2,8,9] The HFNC has been tested in one large randomized control trial, in which were compared the effectiveness of conventional oxygen therapy, non-invasive ventilation combined with HFNC, and HFNC alone in hypoxemic ARF. This study showed that the HFNC alone reduced the need for invasive mechanical ventilation (IMV) in the most critically ill patients (PaO_2/FiO_2≤200mm Hg). Also, this subgroup of patients had a higher 90-day survival rate.[10] Therefore, the application of HFNC in ARF is accepted, and, nowadays, in the pandemic of COVID-19, HFNC is applied to critically ill patients with COVID-19. Also, some other studies have demonstrated that the HFNC oxygen therapy reduced the need for IMV compared to other forms of NIV. [11,12]

Although HFNC reduces the need for IMV, in some cases, it may delay the initiation of IMV, and therefore, this situation worsens the patients' outcome.[13] Also, concerning the use of HFNC, it has been shown that HFNC is associated with a similar rate of reintubation in case of post-extubation respiratory failure.[2]

In addition to these concerns, some studies are against the application of HFNC because of fear of aerosolization of the COVID-19 virus, and therefore, this situation would increase the transmission to healthcare providers.[14-16]

In this study, we retrospectively analyzed the use of HFNC in patients with COVID-19 in our 4 COVID-19 wards of our hospital.

METHODS

Study design and patients

This was a retrospective study of 39 patients were admitted to "Agios Pavlos" Hospital in Thessaloniki, Greece, for COVID-19 infection from October 25, 2020 to May 25, 2021. COVID-19 was diagnosed according to diagnosis and clinical classification criteria and treatment plan of SaRS-CoV-2 pneumonia, launched by the National Institutions of Health.[17]

Initially, all patients were admitted to one of the 4 COVID-19 respiratory wards. All patients' data were extracted from clinical records. The retrospective study was approved by the Ethics committee and administrative council of the hospital. Exclusion criteria were oxygen therapy with HFNC as withdrawal therapy in ICU and hospitalization for less than 48 hours.

Study variables

Data included demographics (sex, age), comorbidities, admission day after the onset of symptoms, and admission laboratory data included complete blood count with ferritin, C reactive protein (CRP), D-Dimer, fibrinogen, Oxygen Saturation Index, and blood platelets. The patients' condition was classified according to Total Severity Score (TSS).[17] Also, we collected data for oxygen saturation and oxygen-saturation index (SpO_2/FiO_2). Additionally, we collected data for the use of the HFNC (day of therapy application and the total number of the days when the patients used this therapy) and the outcomes of the application of

HFNC and specifically, for the Length of Stay (Los), the patient's survival and the 29 days outcome. Successful HFNC treatment was defined as HFNC withdrawal with improved oxygenation, no need for NIV, and/or IMV discharge alive. On the other hand, HFNC failure was defined as the need for NIV or IMV and/or death while on HFNC support.

Statistical analysis

In this retrospective study, we summarized the patients' baseline characteristics using percentages for categorical variables and medians and interquartile ranges for continuous variables. Multivariate analysis was performed using logistic regression analysis to identify independent predictive factors for HFNC therapy success or failure. Factors with a p-value less than 0.10 in the univariable analyses were included in the multivariate model. The significance level was defined as $p<0.05$. All statistical analyses were performed using SPSS 19.0.

RESULTS

The sample of the study consisted of 39 patients. Half of them (50%) had moderate stage of COVID-19 on the admission date, and the other half of the sample was admitted to the hospital with severe COVID-19, according to NIH clinical spectrum of COVID-19 classification.[17]

In this sample, there was a higher prevalence of males (69.2%). The mean age of the patients was 64.6±10.3 years old. The characteristics of patients are shown in Table 1. 44% of the patients had no medical history, and 56,4% had some comorbidities. The main comorbidities were heart failure, cancer, hypertension, and diabetes (Fig.1). The median PaO_2/FiO_2 ratio of patients was 323.3±63.1. At admission, the patients had very high serum ferritin levels (846.7±571.4ng/ml). Additionally, patients had high values of D-Dimers (0.6±0.5mg/L), fibrinogen levels (568.2±125.2ml/dl), CRP (8.8±5.1), and one of three patients had thrombocytopenia (platelets>140000/ml) (Fig.2). The characteristics of patients are shown in Table 1.

The patients were admitted to the hospital approximately 5.56±2.21 days after the symptoms' onset. The mean application day of HFNC was the 3(third)±2.2 day of hospitalization. The mean length of HFNC use was 3.3±2.4 days, while the mean total Los was 18.3±10.9 days.

Outcomes of HFNC application

Regarding the patients' needs for respiratory support during hospitalization, 13 (33.3%) patients required mechanical ventilation, while 26 (66.7%) patients withdrew from HFNC therapy because their condition was improved gradually.

Concerning the outcome of the application of HFNC on day 29 of admission, the results were encouraging for the majority of the patients. In all, 28 (71.8%) patients were discharged successfully, 3 (7.7%) patients were admitted to ICU, and 8 (20.5%) patients died.

According to multivariable analysis, the advanced age of patients on HFNC therapy was related to increased danger of intubation or death in comparison with younger patients (69.9±10.1 vs. 62±9,5) (table 2). Also, the patients who were in danger of intubation or death had higher percentages of all stages of thrombocytopenia in relation to patients who withdrew (mild:76.9% vs. 11,5%, moderate: 53.8% vs. 11,5%, severe: 15.4% vs. 0%). Additionally, the ferritin level was significantly higher in the group of high risk of intubation or death in relation to the withdrawal group (1117.5±783.1 vs. 711.3±380.4). The respiratory ratio was significantly lower in the high-risk group in relation to the lower risk group (283.2±35.2 vs. 343.3±64.8). Finally, the high-risk group patients were ill significantly more days before the day of hospital admission than the other group (8.2±0.9 vs. 4.2±1.2).

DISCUSSION

This current, retrospective study was composed to evaluate the efficacy of HFNC therapy in COVID-19 patients who were admitted to 4 COVID-19 wards of "Agios Pavlos" hospital in Thessaloniki, Greece. Our study's results showed that HFNC therapy was an effective treatment for these patients. Almost 67% of them withdrew from HFNC and only 33% were intubated and were admitted to ICU.

Concerning early identification of the COVID-19 patients' IMV need predictors, World Health Organization (WHO) recommends that the COVID-19 patients, who are under HFNC therapy, must be monitored very closely, in order for the personnel to adjust the oxygen timely the oxygen therapy.[29] The indicators

that have been reported to be useful concerning the oxygen need monitoring in patients with HFNC are Oxygen Saturation Index(SpO_2/FiO_2) and Respiratory rate-oxygenation index(ROX index: SpO_2/FiO_2*RR).[30,31]

Also, some studies highlighted that the mortality of COVID-19 increases as the number of comorbidities increases.[4,9,32] Our study agrees with these results. In addition to these findings, our study found that the laboratory findings, ferritin, D-Dimer levels, fibrinogen, C reactive protein (CRP) were increased. Also, some other studies found their laboratory findings increased, especially on the severe and very severe infected patients.[4,33-35] In our study, patients who were in danger of intubation or death had higher percentages of all stages of thrombocytopenia in relation to patients, who withdrew (mild:76.9% vs. 11,5%, moderate: 53.8% vs. 11,5%, severe: 15.4% vs. 0%)This indication agrees with some other studies, which concluded that some patients may have signs of hypercoagulability and high risk of venous and arterial thrombosis of small and large vessels.[2,18-28] Finally, the high-risk group patients were ill significantly more days before the day of hospital admission than the other group (8.2±0.9 vs. 4.2±1.2). Some studies have shown that delayed admission is related to a high risk of intubation or death.[2]

Limitations

This study has some significant limitations. First of all, this was a retrospective study. Secondly, the number of patients was extremely small (*n=39*), but this was all patients who met the criteria to participate in this study. Our goal was to provide a picture of using the HFNC therapy to treat COVID-19 patients. For this reason, the conclusions of this particular study cannot be generalized.

CONCLUSION

This study describes the application of HFNC during the COVID-19 pandemic, and the conclusion is that the use of HFNC is an effective way to treat COVID-19 infected patients but under close monitoring. It has been shown that the application of HFNC can reduce the rate of intubation and mortality.

Despite the fact, that the healthcare professionals applied the HFNC therapy for respiratory support, during the COVID-19 pandemic, we tried to apply HFNC therapy to COVID-19 patients, in order to investigate its efficacy. Although our sample was small and the results cannot be generalized, we concluded that the HFNC therapy had encouraging results for COVID-19 patients' respiratory support.

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ANNEX

Table 1. Characteristics of patients with moderate and severe COVID-19 treated with HFNC.

Characteristics	Minimum	Maximum	Mean	Std. Deviation
Age	40	86	64.6	10.3
CRP at admission (mg/L; normal range<3)	3.2	23.2	8.8	5.1
Ferritin at admission (ng/ml; normal range 12-300)	112	2538	846.7	571.4
TSS classification	3	22	11.6	3.8
Classification at admission day	3	4	3.6	0.5
PaO_2/FiO_2 ratio	240	579	323.3	63.1
Application day of HFNC	1	11	2.9	2.2
Length of HFNC use (days)	1	13	3.3	2.4
Length of hospital stay (days)	6	66	18.3	10.9
Length of illness before admission (days)	3	10	5.6	2.2

Figure 1. Sample's medical history.

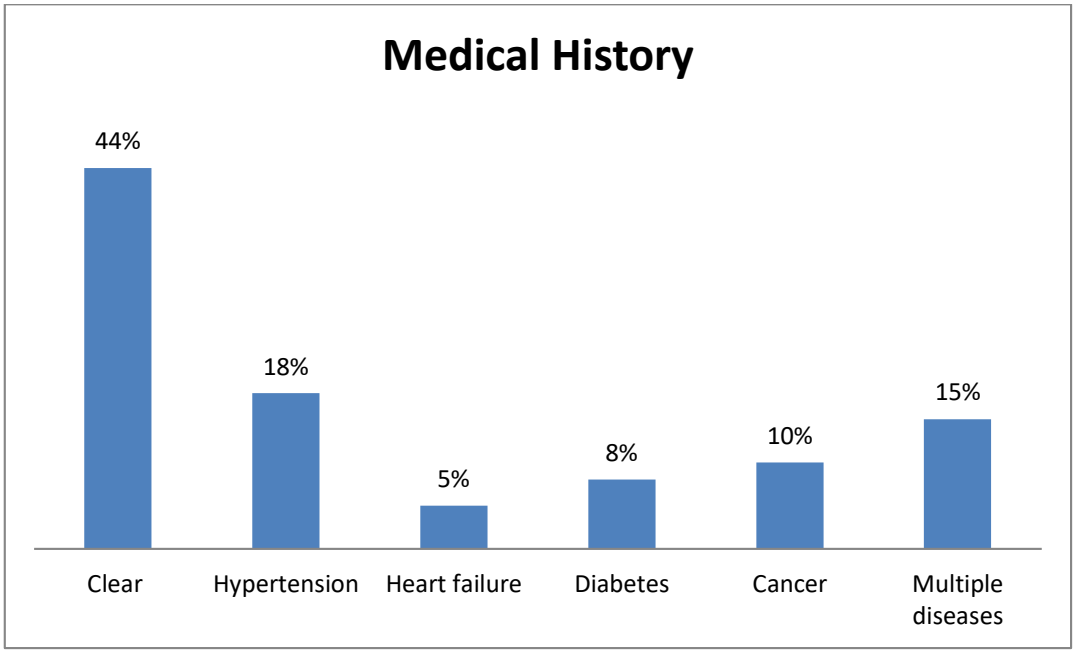

Figure 2. Percentage of thrombocytopenia on the patients with HFNC.

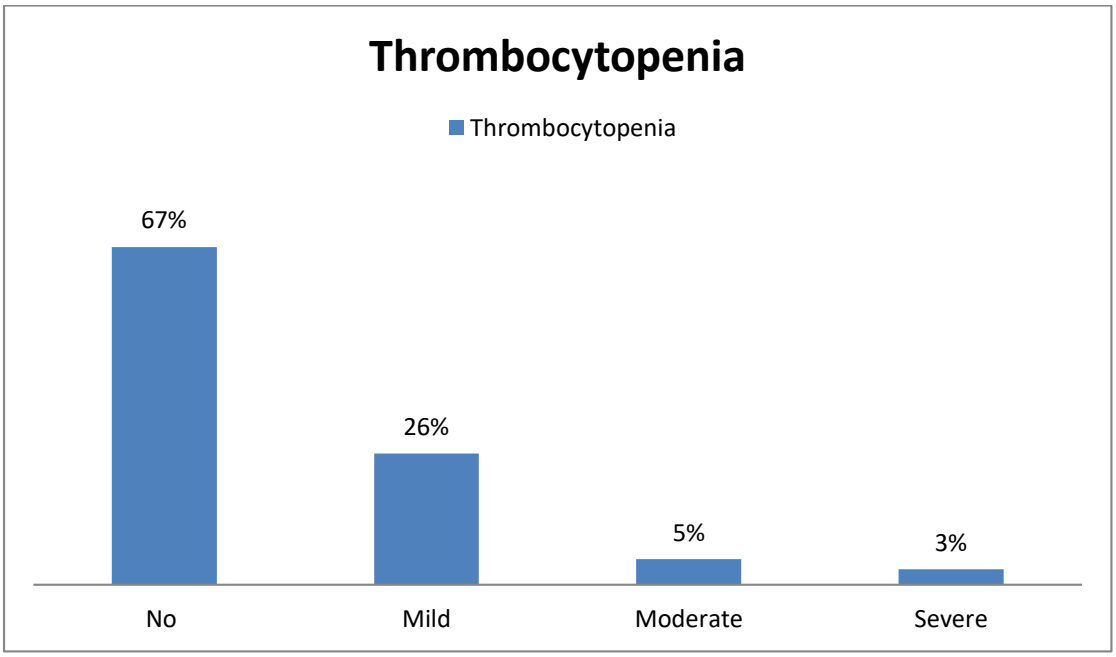

Table 2. Multivariate analysis of predictive factors for successful HFNC.

Variables	Withdrawal	Intubation or death	p-value
Age, years	62±9.5	69.9±10.1	0.028
Thrombocytopenia	11.5%	76.9%	0.002
Mild	11.5%	53.8%	
Moderate	0	15.4%	
Severe	0	7.7%	
Ferritin	711.3±380.4	1117.5±783.1	0.034
TSS Classification	10.3±3.4	14.2±3.4	0.002
Classification day of admission	3.3±0.5	4	0.001
Respiratory ratio	343.3±64.8	283.2±35.2	0.001
LOS	15.2±5.9	24.6±15.5	0.009
Days of illness before admission	4.2±1.2	8.2±0.9	0.001

LOS length of stay, *TSS* total severity score in radiological imaging