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Conventional Oxygen Therapy Versus High Velocity Nasal cannula in patients with acute pulmonary edema

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Abstract:

Background: Acute pulmonary edema (APE) is one of the main diagnoses for dyspnea patients in emergency departments (ER). High-velocity nasal cannula (HVNC) might be considered as an alternative support for early management of APE in the ER. **Objectives:** to compare the effectiveness of HVNC therapy for those with APE to that of conventional oxygen therapy (COT). **Methodology:** This study was a randomized controlled trial with 60 APE patients admitted to the critical care and chest units at Beni-Suef University Hospital. We randomly assigned patients to Group A, who received COT. Group B received HVNC. All patients received a full history and evaluation, a chest X-ray, and a chest CT scan. A complete blood count (CBC), coagulation profile, renal function tests, and assessments of serum sodium, potassium, and arterial blood gas (ABG) were included in laboratory examinations. We conducted these tests at admission and again six hours later. **Results:** We linked the use of HVNC to a significant drop in respiratory rate. Both groups' PO_2 levels increased while PCO_2 decreased. The HVNC intervention was more effective in increasing PO_2 and decreasing PCO_2 levels than the COT. There was a trend in the HVNC group toward less reliance on mechanical ventilation (MV) as compared to COT. The length of time patients spent in the ICU dropped significantly for those receiving HVNC. **Conclusion:** In patients with APE, HVNC significantly improves ABG, ICU stay duration, and MV frequency compared to COT.

Keywords: High velocity nasal cannula, Pulmonary edema, Conventional oxygen therapy, Mechanical Ventilation

1. Introduction:

Patients seeking emergency department admission for dyspnea often get the diagnosis of APE. About 40% of patients with severe pulmonary embolism (PE) also have respiratory failure and hypercapnia. Hypercapnia has been associated with changes in cognitive function and the development of central apnea. Hypercapnia increases the need for intubation in patients and has been associated with a higher risk of mortality during hospitalization [1].

Treatment for acute respiratory failure due to acute pulmonary edema typically involves restoring normal tissue oxygen levels and treating the underlying causes. In the emergency room, doctors often treat patients with dyspnea with oxygen using a nasal cannula or a face mask. Patients and doctors commonly use these methods due to their convenience and familiarity. However, studies suggest that standard therapy alone may not provide enough oxygen to the tissues in certain individuals suffering from acute respiratory failure [2].

We use various pieces of equipment to improve physiological parameters and reduce symptoms. We may use continuous positive airway pressure (CPAP) or noninvasive positive pressure ventilation (NIPPV) to improve treatment outcomes. Dyspneic patients whose respiration rates are more than 20 breaths per minute [2] are the target population for these therapies, which attempt to reduce hypercapnia and acidosis and alleviate respiratory distress.

High-flow oxygen therapy (HFOT) is a NIMV approach that has seen a surge in popularity in recent years among critically ill patients. The aforementioned action helps warm and moisten the mixture of oxygen-rich air and ambient air. We use a nasal cannula to provide a high flow of medication or air. The HFOT system has several benefits, one of which is its ability to provide positive pressure and keep the FiO2 level constant. It enables high flow rates, enhances patient comfort, and successfully clears the anatomic dead space. As a result, the use of HFOT among people with terminal illnesses has grown significantly [3].

High-flow nasal cannulas, of which high-velocity nasal insufflation is a type, focus on getting rid of as much dead space as possible to improve ventilation by taking carbon dioxide out of the tidal volume. In addition to the advantages of HFNC, this method has its own distinct set of advantages. For this purpose, we use a nasal cannula with a modest internal diameter (typically 2.7 mm for adults). This cannula produces a high velocity flow, approximately 360% higher than the cannula with a wider diameter used in earlier studies. Adults widely acknowledge that high-velocity nasal insufflation requires a flow rate of 25 to 35 L/min to efficiently remove the extra-thoracic anatomic reservoir during the inter-breath interval [4]. This is based on both flow experiments and clinical observations.

High-velocity nasal insufflation, if administered for an hour, may benefit hypercapnic individuals who report to the emergency room with respiratory failure due to severe pulmonary edema, according to recent studies. Several measures of respiratory function, including PaCO2, pH, breathing rate, and signs of increased labor of breathing, all improved as a result of the therapy. High-velocity nasal insufflation may be considered an alternative first aid method for treating acute pulmonary edema in an emergency room [1]. The goal of this study was to compare the efficacy of a high-velocity nasal cannula to conventional oxygen therapy in patients with pulmonary congestion.

2. Patients and methods:

2.1. Study design and participants:

Patients with APE admitted to the ICU are the focus of the current randomized comparative controlled trial. Beni-Suef University's Critical Care and Chest Departments conducted the research between March 2022 and January 2023. The study included a total of 60 patients, assigning 30 to Group A for COT and 30 to Group B for HFNC. The following inclusion characteristics must be present in the participants: Tachypnea is defined as a respiratory rate greater than 24 breaths per minute. SPO_2 is 88% or lower. Bilateral rales are diagnostic of PE. Fine crackles may be heard bilaterally at the lung bases during the inspiratory phase; if the edema worsens, they may spread to the lung apices. We took both the lateral and postero-anterior views of a chest X-ray, which revealed congestion in the lungs. There were two types of pulmonary edema: cardiovascular and non-cardiogenic.

Exclusion criteria: age less than 18; Glasgow Coma Scale (GCS) score less than 13. Blood pressure below 90/60 indicates hemodynamic instability, Pregnancy, Patients who require immediate endotracheal intubation. There are several contraindications to the use of Hi-VNI, including patients who are unable to protect their airway and those who have sustained injuries to the nasal pathway. Severe respiratory or cardiovascular instability, as well as impending arrest, are considered contraindications to the use of Hi-VNI. Abnormalities in the upper airway, such as choanal atresia, cleft palate, or tracheoesophageal fistula, may be present. The study also included cases of burns to the face or chest [5, 6]. Two groups participated in the study.

2.2. Methodology:

All study participants completed the following measures during the data collection: We obtained written informed consent from the patients and first-degree relative agreement for their inclusion in the study. We collected a comprehensive medical history and personal data from the patients and their close relatives. We subjected all patients to a comprehensive clinical examination, which included general, chest, and cardiology exams. We conducted investigations such as CBC, NA, K, Kidney function, Coagulation profile, and ABG on admission and 6 hours after admission. We also performed a chest X-ray on admission and 24 hours after admission, additional imaging based on clinical judgment (C.T. chest), and echocardiography.

2.3. Intervention:-

Patient with mild to moderate hypoxemia were divided randomly into two groups: COT or HFNC.

2.3.1. Large-bore bi-nasal prongs continuously applied HFNC at a flow rate of up to 40 L/mmin. For adults, high-velocity nasal insufflation needs a flow of 25 to 35 L/min to completely empty the extra-thoracic anatomic reservoir between breaths. Using thermo-humidified nasal high-flow oxygen is a way to get rid of as much carbon dioxide as possible from the "dead space" between breaths, while also getting the other benefits of a high-flow nasal cannula. Adult patients typically use a small-bore nasal cannula with an inside width of 2.7 mm for this purpose. This cannula creates a high-speed flow that is about 360% stronger than the bigger cannula that was used in earlier studies. Based on flow studies and clinical practice, we adjusted the FiO_2 to maintain the oxygen saturation level (measured by pulse oximetry) between 92% and 95%. We maintained this amount during the patient's stay in the ICU or during the use of assisted breathing. First, the flow rate was 20 L/min. Depending on the patient's needs, it could change to 5 to 40 L/min. The oxygen level started at 60% and could go anywhere from 21% to 100%

depending on the patient's condition at 37. We used these specific factors to start the study. We then conducted follow-up tests for an hour, six hours, and the entire patient's stay in the ICU. We changed the settings based on the ABG analysis, the measure of breathing effort, and the tracking of oxygen levels [7].

2.3.2. The patient received COT throughout their stay in the ICU, which included the use of modalities such as nasal cannulas or nonrebreather masks. MV was also used when necessary. We initiated COT using a nasal cannula at a flow rate of 5 liters per minute and adjusted the flow rate based on the patient's oxygen saturation levels. We started the study with these specific parameters and conducted follow-up assessments 1 hour after admission, 6 hours after admission, and throughout the patient's stay in the intensive care unit. We adjusted the settings based on the values obtained from arterial blood gas analysis, breathing effort, and oxygen saturation. COT involves the use of low (below 5 L/min) to moderate flows (below or equal to 15 L/min) [6].

2.4. Study outcomes:

2.4.1. The primary outcome measures included RR assessment at admission, after 6 hours, and throughout the patient's stay in the ICU. We evaluated the ABG levels upon admission, after 6 hours, and throughout the ICU stay.

2.4.2. The ICU monitored the patients throughout their entire stay, which included secondary outcome. We measured the SPO2 levels at the time of admission, six hours later, throughout the patient's stay in the ICU, the need for MV, and the death rate.

2.5. Statistical analysis:

Data collection, coding, and input into SPSS version 25 followed. We assessed categorical variables using descriptive statistics like frequency and percentage. We evaluated numerical variables, especially the mean and SD, using descriptive statistics. We used the independent sample t-test to compare the two groups. We can analyze categorical data from both samples using either the Chi-Square test or the Fisher Exact test. When analyzing data, statisticians often use the mixed model, which takes into account both fixed and random factors. We used ANOVA to compare the effect of HFNC on patient outcomes with conventional care. This evaluation included an analysis of pre- and post-intervention timing and group differences. The purpose of the study was to evaluate the effectiveness of HFNC in improving patient outcomes. P-values less than 0.05 were considered statistically significant.

3. Results:

In table (1); Group (A):19 patients (63.3%) were males and 11 (36.7%) were females. Group (B):20 patients (66.7%) were males and 10 (33.3%) were females. In group A, a mean age and standard deviation of (50.3±15.9), however in group B a mean age and standard deviation of (50.4±14.6). There was no statistically significant difference between conventional and HFNC groups regarding their age and sex (P-value>0.05). There was a number of comorbidities and risk factors related to the patients involved in both groups in group A ,4 (13.3%) of patients had chest disease while 3 (10%) of patients had chest disease in group B, 22 patients (73.3%) were hypertensive in group (A) while in group B there were 19 patients (63.3%) , in group A there was 11 diabetic patient (36.7%) while in group B, 10 patients (33.3%), in group A, 8 patients (26.7%) were smokers while in group B, 9 patients (30%) , in group A , 20 patients (66.7%) had chronic kidney disease while in group B15 (50%) . In group A11 (36.7%) had heart failure while in group B10 (33.3%). there was no statistically significant difference between conventional and Hi-VNI groups regarding their distribution comorbidities (P-value>0.05). there was no statistically significant difference between conventional and Hi-VNI groups regarding their CBC, sodium, potassium, urea and creatinine levels (P-value>0.05).

Table (1) Baseline characteristics clinical and laboratory data of the studied patients:

Items	Group (A)	Group (B)	P-value
Age (mean±SD)	50.3±15.9	50.4±14.6	0.875
Sex			0.787
Males	19(63.3%)	20(66.7%)	
Females	11(36.7%)	10(33.3%)	
Comorbidities			
HTN	22(73.3%)	19(63.3%)	0.405
DM	11(36.7%)	10(33.3%)	0.787
Chest disease	4(13.3%)	3(10.0%)	>0.999

CKD	20(66.7%)	15(50.0%)	0.190
HF	11(36.7%)	10(33.3%)	0.787
Smoking	8(26.7%)	9(30.0%)	>0.999
Basal laboratory findings			
HB (g/dL)	10.1±1.8	10.5±2.1	0.454
TLC X 10^3	12.5±5.0	13.2±4.9	0.602
PLT X 10^3	251.1±73.6	230.9±94.9	0.362
Na (mEq/L)	137.6±4.7	138.2±4.5	0.601
K (mEq/L)	4.4±0.7	4.2±0.8	0.144
Urea(mg/dL)	92.0±69.1	74.5±51.3	0.271
Create (mg/dL)	3.4±2.3	2.7±2.0	0.264

HTN: hypertension, DM: Diabetes mellitus, CKD: chronic kidney disease, HF: Heart failure, HB: Hemoglobin, TLC: Total leucocytic count, PLT: Platelets, Na: sodium, K: Potassium,*P-value is significant; (P-value≤0.05)

In table (2): there was a statistically significant of HFNC in decreasing RR. Oxygen saturation showed that there was no statistically significant between both groups. In the 1st hour of intervention, regarding group A the parameters of ABG were of mean value ± SD (PH 7.35±0.06, PCO2 37.7±5.5, PO2 95.1 ±11.6, HCo3 19.6. ±3.8), while in group B the parameters were of mean value ± SD (PH 7.36±0.04, PCo2 36.9±4.2, PO2 96.6 ±8.2, $Hco_3$19.3±3.9) In the 6th hour of intervention regarding group A the parameters of ABG were of mean value ± SD (PH 7.36±0.05, PCo2 35.4±7, PO2 127.5±31.1, Hco_3 21.4±4.1) , while in group B the parameters of ABG were of mean value ± SD (PH 7.38±0.05 , Pco2 28.6±4.6, PO2 141.2±19.1, Hco_3 20.5±4.1). There was a statistically significant difference before and after in the PCO2 in both groups, there is a significant effect of the Hi-VNI superior to the traditional management in decreasing the PCO2**.** There was a statistically significant increase in the PO2 before and after in both groups, there is a significant effect of the Hi-VNI superior to the traditional management in increasing the PO2**.** There is no effect of the Hi-VNI superior to the traditional management in increasing the HCO3**.**

Table (2): Post interventional clinical and Laboratory data:

	Group (A)	Group (B)	P-value
Respiratory rate (breath /minute)			
Before	33.9±3.3	34.8±3.5	0.316
After	27.9±3.5	24.9±3.0	0.001*
P-value before vs after	<0.001*	<0.001*	
SPO_2			
Before	82.5±2.9	81.2±2.95	0.174
After	91.9±2.2	94.6±3.7	0.602
P-value before vs after	<0.001*	<0.001*	
PH			
Before	7.35±0.06	7.36±0.04	0.171
After	7.36±0.05	7.38±0.05	0.115
P-value before vs after	0.217	0.068	
PCO_2			
Before	37.7±5.5	36.9±4.2	0.484
After	35.4±7	28.6±4.6	<0.001*
P-value before vs after	0.031*	<0.001*	
PO_2			
Before	95.1±11.6	96.6±8.2	0.584
After	127.5±31.1	141.2±19.1	0.045*
P-value before vs after	<0.001*	<0.001*	
HCO_3			
Before	19.6±3.8	19.3±3.9	0.780
After	21.4±4.1	20.5±4.1	0.409
P-value before vs after	0.008*	0.021*	0.780

**P-value is significant;(P-value≤0.05)*

In table (3): There was insignificant difference between the studied groups regarding the need to mechanical ventilation (P-value>0.05). There is no statistically significance but need of mechanical ventilation decreased in Hi-VNI groups. There was no statistically significant difference between the studied groups regarding the mortality proportion (P-value>0.05). There was a significant decrease of the ICU length of stay in the Hi-VNI group (P-value<0.05).

Table (3): Comparison between groups regarding study outcomes:

Items	Group (A)	Group (B)	P-value
Need to MV			0.100
No	17(56.7%)	23(76.7%)	
Yes	13(43.3%)	7(23.3%)	
Mortality			0.448
Survived	25(83.3%)	27(90.0%)	
Died	5(16.7%)	3(10.0%)	
ICU LOS	12.3±5.1	8.7±3.3	0.002*

*MV: Mechanical ventilation, ICU: Intensive care unit, LOS: Length of stay,*P-value is significant; (P-value≤0.05).*

4. Discussion:

The rapid onset of respiratory failure is a hallmark of the pathological condition known as APE, which, if ignored, may lead to cardiorespiratory collapse in a matter of hours or even minutes. Prompt intervention can prevent this catastrophic outcome. Hemodynamic pulmonary congestion and increased capillary pressures define ACPE. Diuretics, NIVs, and vasodilators are the mainstays of treatment for ACPE [8].

The goal of high-velocity nasal insufflation, a type of high-flow nasal cannula treatment, is to maximize the efficiency of carbon dioxide removal from the tidal space between breaths. This method also has benefits like increasing oxygen humidity, better clearance of mucus and cilia, controlling the percentage of inspired oxygen, creating positive expiratory pressure, recruiting alveoli, making breathing easier, and making the patient more comfortable. We use a small-bore nasal cannula to generate a high-velocity flow that is 360% greater than that of the larger-bore cannula [9].

The purpose of this research was to compare the effectiveness of high-velocity nasal cannula therapy for pulmonary congestion to that of more traditional oxygen therapy. A block-randomized comparative controlled trial at Beni-Suef University Hospital's critical care and chest departments studied sixty patients with acute pulmonary edema. The study took place from March 2022 to January 2023. The research divided the patients into two groups. Group A consisted of 30 patients treated with conventional oxygen therapy, whereas Group B got a high-velocity nasal cannula for the same number of patients.

Our study found that the average age (mean, SD) of the participants in group A was 5015.9, whereas the average age of the participants in group B was 5014.6. When comparing the ages of participants in groups A and B; there was no discernible difference (P > 0.05).

Pratik Doshi et al. [10] conducted a multicenter study on 204 patients, finding that the HVNI group had a mean age of 63.4 years (SD = 13.6), whereas the conventional group had a mean age of 63.3 years (SD = 14.8). There was no discernible difference between the ages of the two groups.

Our study found that there was no statistically significant difference (P-value > 0.05) between group (A) and group (B) in the number of these medically important co-morbidities in the patients that were studied. Sener et al. [11] conducted research in Turkey and found no statistically significant difference between the HVNI group and the usual oxygen treatment group on comorbid illnesses (p = 0.099), gender (p = 0.492), and age (p = 0.441).

Our research showed that there was no statistically significant difference between groups (A) and (B) in terms of CBC, sodium, potassium, urea, and creatinine levels at baseline (P-value > 0.05), which has implications for the two groups. Similarly, Sener et al. [11] observed no differences in pretreatment laboratory results between the HVNI and the conventional oxygen therapy groups (p > 0.820).

Our data showed a statistically significant difference between the HVNI group and the group getting conventional oxygen therapy with respect to respiratory rate. Makdee et al. [12] looked at 231 people who went to the emergency room in Thailand, thinking they had cardiogenic pulmonary edema. Compared to traditional oxygen treatment, HVNI was associated with significantly lower mean respiratory rates at 60 minutes post-intervention.

Saturation with oxygen increased during therapeutic testing in both groups, according to our research (P 0.001). When we implemented HVNI, the SPO2 values in the HVNI group reached 94.63.7, whereas they only reached 91.92.2 with conventional oxygen treatment, indicating a significantly superior effectiveness in improving oxygen saturation in the HVNI group. Makdee et al. [12] found no statistically significant difference in oxygen saturation levels between the two groups; hence, these results contradict their findings. We measured oxygen saturation at the 60-minute mark, and found that the standard oxygen therapy group averaged 98.7% (SD 1.5), while the HVNI group averaged 99.2% (SD 1.2), indicating the superiority of HVNI. Sener et al. [11] demonstrated that HVNI increases oxygen saturation. When comparing HVNI to standard oxygen therapy, however, the research found no statistically significant differences.

Our research showed no statistically significant difference in pH levels between the two groups when evaluating arterial blood gases between the first and sixth hours of therapeutic treatments. Our data also shows that HVNI treatment had no discernible effect beyond that of standard care in terms of pH modification (p-value = 0.115). Pratik Doshi et al.'s research [10], which found substantial similarity between the pH levels in the high-velocity nasal insufflation group and the regular oxygen therapy group through blood gas tests, is consistent with this result. In addition, the research found that all of the measured characteristics improved with time.

Our analysis of PCO2 measurements from both groups showed a statistically significant difference (P 0.001). The HVNI method was much more effective than the usual therapy in lowering PCO2. Adhikari P et al. [13] demonstrated similar results, revealing a significant difference in ABG parameters between the HVNI group and the usual treatment group at both the baseline and post-60-minute PCO2 levels. Ko DR and colleagues [14] showed that high-velocity nasal insufflation had a more positive long-term effect on the partial pressure of carbon dioxide (PCO2) compared to conventional oxygen therapy.

Using PO2 measurements, we found that both groups had a statistically significant increase in PO2 during the therapy assessments. The HVNI group also had a statistically significant increase in PO2 compared to the conventional oxygen treatment group (P 0.001). This research's findings are consistent with those of a previous study that compared conventional oxygen therapy to HVNI in a group of 69 patients with heart failure and pulmonary edema who presented to the emergency room. We took arterial blood gas measurements again 30 and 60 minutes after the first time point. Overall, the research demonstrated superior performance of HVNI treatment over standard care in all examined metrics. We observed significant differences in both PO2 and SpO2 values.

Our study found no statistically significant difference between the two groups in terms of increasing HCO3 levels after treatment with HVNI or conventional therapy (p-value = 0.409). The emergency room at Montpellier University Hospital was the site of prospective, observational, and comparative research by Marjanovic et al. [15]. Thirty-two people with a diagnosis of acute cardiogenic pulmonary edema were the focus of the investigation. The results showed that after 6 hours of treatment, there was no statistically significant difference between HVNI and standard care with regard to arterial blood gases, particularly HCO3 levels (p = 0.98).

There was no statistically significant difference between the two groups in terms of the demand for mechanical ventilation, according to our analysis (P value > 0.05). While 43.3% of patients in the standard oxygen therapy group needed mechanical ventilation, a trend showed a reduced requirement for artificial breathing in the HVNI group. Doshi et al. [10] did a similar study using a randomized controlled trial that was prospective, multicenter, and included 204 patients from five locations in the southern United States. According to this research, HVNI and traditional oxygen treatment had similar rates of intubation and the requirement for mechanical ventilation. In contrast, HVNI showed better results in preventing the need for intubation. HVNI patients had a lower rate of adverse events (7%) compared to the usual oxygen therapy population (13%).

We found no statistically significant difference in death rates (P value > 0.05) between the groups we analyzed. Consistent with the findings of a meta-analysis of randomized clinical trials evaluated by Bruno L. et al. [16], When comparing high-velocity nasal insufflation to standard oxygen therapy, the researchers found no statistically significant difference in the mortality rate.

Our study found that the HVNI group had significantly shorter ICU stays when we compared the amount of time spent in the ICU across the study groups. The difference was statistically significant ($P \geq 0.05$). Sener et al. [11] demonstrated in a prospective observational study that HVNI significantly reduced the hospital stays of patients with acute pulmonary edema compared to those treated with standard oxygen therapy. Conclusions HVNI has the potential to shorten stays in the emergency department and the intensive care unit, according to the study's authors.

Sener et al. [11] also analyzed 112 individuals with APE in a prospective observational study. Standard oxygen treatment was associated with a considerably longer ICU admission than HVNI, with a p-value of 0.040.

5. Conclusions:

HVNC has been shown to have a significant effect on arterial blood gases monitoring by improving oxygen saturation and decreasing CO_2 levels more effectively than with regular oxygen therapy alone. Research has demonstrated that HVNC treatment significantly reduces intensive care unit hospitalizations for individuals with APE. Studies have also demonstrated that HVNC treatment decreases the frequency of MV. However, the mortality rate does not change much.

6. References:

1. Nicolas Marjanovic, Alexandre Flacher, Loı¨c Drouet, et al: High-Flow Nasal Cannula in Early Emergency Department Management of Acute Hypercapnic Respiratory Failure Due to Cardiogenic Pulmonary Edema. Respir Care 2020;65(9):1241–1249.
2. Dong Ryul Ko, Jinho Beom, Hye Sun Lee, et al: Benefits of High-Flow Nasal Cannula Therapy for Acute Pulmonary Edema in Patients with Heart Failure in the Emergency Department: A Prospective Multi-Center Randomized Controlled Trial. J. Clin. Med. 2020, 9, 1937.
3. Kemal Şener, Mustafa Çalış, Zikret Köseoğlu, et al: Comparison of high-flow oxygen treatment and standard oxygen treatment in patients with hypertensive pulmonary edema. Anatol J Cardiol 2020; 24: 260-266.
4. Panel Pratik Doshi, Jessica S. Whittle, Michael Bublewicz, et al: High-Velocity Nasal Insufflation in the

Treatment of Respiratory Failure: A Randomized Clinical Trial. Annals of Emergency Medicine, Volume 72, Issue 1, 2018, 73-83.

5. Sarkar M, Madabhavi I, Niranjan N and Dogra M. Auscultation of the respiratory system.. Annals of thoracic medicine.(2014) ; 10 (3): p.158.
6. 54- Edward M, Maged SM and Michael JM. Clinical anesthesiology. 4th edition, 2005.
7. Doshi P, Whittle JS, Bublewicz M, et al. High-Velocity Nasal Insufflation in the Treatment of Respiratory Failure: A Randomized Clinical Trial. Ann Emerg Med. 2018;72(1):73-83 e75.
8. Alberto Domínguez-Rodríguez, Coral Suero-Mendez, Guillermo Burillo-Putze, et al: Midazolam versus morphine in acute cardiogenic pulmonary oedema: results of a multicentre, open-label, randomized controlled trial. European Journal of Heart Failure (2022) 24, 1953–1962.
9. Miller TL, Saberi B and Saberi S. Computational fluid dynamics modeling of extra thoracic airway flush: evaluation of high flow nasal cannula design elements. J Pulmon Respir Med. 2016; 6:376.
10. Pratik Doshi, Jessica S. Whittle, Michael Bublewicz, et al: High-Velocity Nasal Insufflation in the Treatment of Respiratory Failure: A Randomized Clinical Trial. Ann Emerg Med. 2017; 12:1-11.
11. Şener K, Çalış M, Köseoğlu Z, et al: Comparison of high-flow oxygen treatment and standard oxygen treatment in patients with hypertensive pulmonary edema. Anatol J Cardiol. 2020, 24:260-266.
12. Onlak Makdee, Apichaya Monsomboon, Usapan Surabenjawong, et al: High-Flow Nasal Cannula Versus Conventional Oxygen Therapy in Emergency Department Patients with Cardiogenic Pulmonary Edema: A Randomized Controlled Trial. Ann Emerg Med. 2017;70:465-472.
13. Adhikari P, Bhattarai S, Gupta A, et al: Physiological Effects of High-Flow Nasal Cannula Therapy and Its Use in Acute Cardiogenic Pulmonary Edema. Cureus (2021)13(2): e13372.
14. Ko DR, Beom J, Lee HS, You JS and Chung HS, Chung SP: Benefits of high-flow nasal cannula therapy for acute pulmonary edema in patients with heart failure in the emergency department: a prospective multi-center randomized controlled trial. J Clin Med. 2020, 21:1937.
15. Nicolas Marjanovic, Alexandre Flacher, Loı¨c Drouet, et al: High-Flow Nasal Cannula in Early

Emergency Department Management of Acute Hypercapnic Respiratory Failure Due to Cardiogenic Pulmonary Edema. Respir Care 2020;65(9):1241–1249.

16. Bruno L. Ferreyro, Federico Angriman, Laveena Munshi, et al: Association of Noninvasive Oxygenation Strategies with All-Cause Mortality in Adults With Acute Hypoxemic Respiratory Failure A Systematic Review and Meta-analysis. JAMA. 2020; 324(1):57-67.