Comparison of high-flow oxygen treatment and standard oxygen treatment in patients with hypertensive pulmonary edema

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Abstract

Objective: The aim compares the blood gases, vital signs, mechanical ventilation requirement, and length of hospitalization in patients with hypertensive pulmonary edema treated with standard oxygen therapy (SOT) and high-flow oxygen therapy (HFOT).

Methods: This prospective observational study was conducted in patients with tachypneic, hypoxemic, hypertensive pulmonary edema. The patients' 0^{th}, 1^{st}, and 2^{nd} hour blood gas results; 0^{th}, 1^{st}, and 2^{nd} hour vital signs; requirement of endotracheal intubation, length of hospitalization, and the prognosis were recorded on the study form.

Results: A total of 112 patients were included in this study, of whom 50 underwent SOT and 62 received HFOT. The initial blood gas analysis revealed significantly lower levels of pH, PaO_2, and SpO_2 and significantly higher levels of $PaCO_2$ in the HFOT group. Patients in the HFOT group had significantly higher respiratory rate and pulse rate and significantly lower SpO_2 values. The recovery of vital signs was significantly better in the HFOT group ($p<0.05$). Similarly, follow-up results of arterial blood gas analysis were better in the HFOT group ($p<0.05$). Both length of stay in the emergency department ($p<0.05$) and length of intensive care unit hospitalization s significantly shorter in the HFOT group ($p<0.05$).

Conclusion: HFOT can be much more effective in patients with hypertensive pulmonary edema than SOT as it shortens the length of stay both in the emergency service and in the intensive care unit. HFOT also provides better results in terms of blood gas analysis, heart rate, and respiratory rate in the follow-up period. *(Anatol J Cardiol 2020; 24: 260-6)*

Keywords: emergency department, hypertensive pulmonary edema, high-flow oxygen treatment, lactate

Introduction

Heart failure (HF) is a worldwide important problem because of its high prevalence, being 0.3%–2% in the general population and reaching up to 3%–5% in people aged 65 years and 25% in those aged >75 years (1-3).

The rates of mortality and morbidity are seriously high in patients with HF. The mortality rates for 10 and 15 years are approximately 40% and 56%, respectively. In cases of severe HF, the annual mortality rate is 40%–70% (4). Moreover, one-third of patients with HF aged >65 years return to the emergency department (ED) within 3 months and half of them return in 6 months (5, 6).

Early recognition and treatment of decompensated HF (DHF) in the ED is important for preventing morbidity, prolonged stay in the ED room, prolonged hospitalization, and mortality.

There are several treatment options such as mask oxygen treatment, standard nasal cannula oxygen treatment (SOT), noninvasive mechanical ventilation (NIMV), and invasive mechanical ventilation (IMV) for patients with DHF. SOT is advantageous because of its easy application; however, it cannot provide high flow and positive pressure. Higher than 6 L/min with SOT causes dryness in the respiratory tract. In addition, incompatibility of the patients to the NIMV technique and aspiration risk, limitation of talking, and prevention of feeding can be accepted as disadvantages of this method. Invasive procedures such as endotracheal intubation may cause other complications (7).

Recently, high-flow oxygen therapy (HFOT), an NIMV method, has been widely used in critically ill patients. This treatment moistens and heats the combination of air and oxygen. It is administered with high flow via a nasal cannula. HFOT has superior properties such as providing a positive pressure and a constant FiO_2, sweeping the anatomic dead space, providing high flow, and offering much more comfort to the patients. Thus, HFOT has

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become popular in critically ill patients. However, acute respiratory failure ratio is increasing each day, and this situation results in much more crowded EDs, empty bed problems in intensive care units (ICUs), and unfortunately prolonged stay in the ED. Because of these problems, the use of NIMV techniques, including HFOT, has become valuable (8).

In the present study, our aim was to compare the blood gases, vital signs, mechanical ventilation requirement, length of stay in the ED, and length of hospitalization in patients with hypertensive pulmonary edema treated with SOT and HFOT.

Methods

This prospective observational study was performed in patients with hypertensive pulmonary edema aged >18 years between January 1, 2019 and October 31, 2019 after obtaining approval from the Ethics Committee (No: 2020-457). Patient consent form was signed by each patient. Patients were divided into two groups according to the treatment method. The first group was treated with HFOT and the second group was treated with SOT. We recorded the 0^{th}, 1^{st}, and 2^{nd} hour blood gas parameters (pH, PaO_2, $PaCO_2$, SaO_2, etc.); vital signs such as mean blood pressure (MBP), heart rate (HR), respiratory rate (RR), SpO_2, and fever; requirement of intubation; hospitalization place (clinic/ICU); length of stay in the ED, length of hospitalization; and the outcome (discharged/dead) for the two groups.

Our study groups also received standard pulmonary edema treatment in addition to SOT/HFOT. Patients were administered 0.5–1 mg/kg loop diuretic and 5–10 mg/min glyceryl trinitrate according to their clinical status. An additional dose was administered if required.

Blood gas analyses of the patients were performed via a Radiometer ABL90 flex (Radiometer, Copenhagen, Denmark) device. Standard wall-fixed oxygen (1–6 lt/dk) was used for SOT and titrated via a flowmeter. For HFOT, Vapotherm, Precision Flow (Exeter, USA) device was used. To the HFOT group, 100% FiO_2 and 40 L/min oxygen were administered. The flow value and the FiO_2 level were rearranged according to the 1^{st} hour blood gas results. We provided endotracheal intubation decision for the following:

- Persistent or worsening hypoxemia
- Worsening tachypnea
- Worsening $PaCO_2$ despite optimal O_2 treatment
- Weakness in respiratory muscles
- Loss of safety in airway
- Worsening mental status

The primary outcome of this study was change in blood gas results in both the HFOT and SOT groups. The secondary outcomes were requirement of IMV, number of hospitalization days, and mortality.

Patients who underwent other NIMV techniques, hemodynamically unstable patients, those diagnosed with acute coronary syndrome, those with a low Glasgow Coma Scale score (≤12), patients with rapid serial intubation, and nontolerable patients were excluded from the study (Fig. 1).

Statistical analyses

Statistical comparisons were performed using the statistical software package SPSS 23.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov–Smirnov test was used for normal distribution. Normally distributed variables were analyzed using the unpaired t-test. Non-normally distributed variables were evaluated using the Mann–Whitney U test. Categorical variables are expressed in frequencies and percentages. The chi-square test was used to compare categorical variables. Paired t-test was used for continuous variables. Differences between the initial (0^{th}) and 2^{nd} hour pH and lactate values were evaluated using paired samples t-test. Definitive statistics were expressed as mean±standard deviation (SD) and median (interquartile range, IQR). A p value <0.05 was considered as statistically significant.

Results

We included 112 patients with HF with a mean age of 71.85±10.02 years (range: 49–97 years). There were 57 (50.9%) male patients. Patients with more than two comorbid chronic diseases constituted 78.6% of the study population. In total, 91

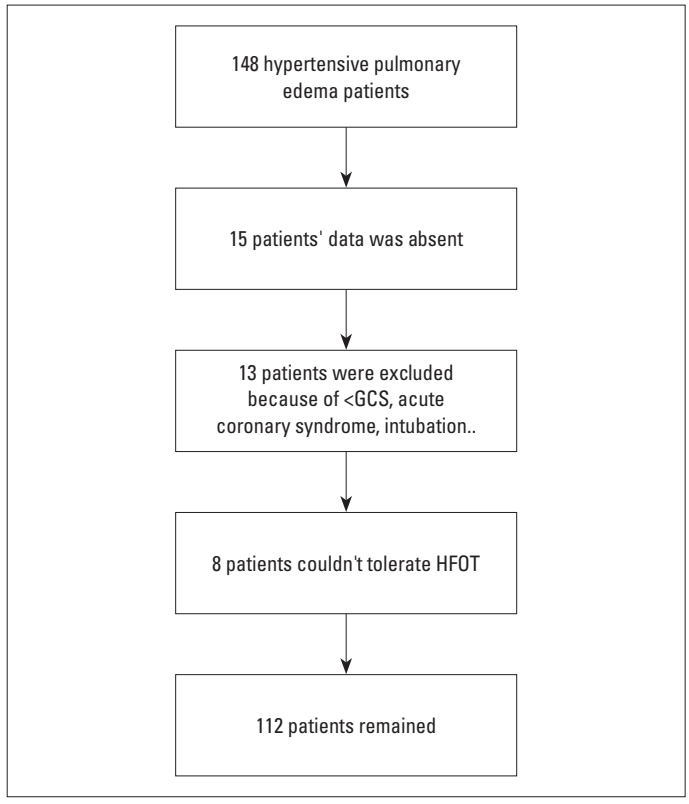

Figure 1. Exclusion flow chart of the patients

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patients (81.3%) had hypertension, 80 (71.4%) had coronary artery disease, and 54 (48.2%) had diabetes mellitus.

HFOT was administered to 62 (55.4%) patients, and SOT was administered to 50 (44.6%) patients.

In both groups, the initial 0th, 1st, and 2nd hour pH, PaO_2, HCO_3, SaO_2, and base deficit levels were lower and $PaCO_2$ and lactate levels were higher. Similarly, the 0th, 1st, and 2nd hour HR, MBP, and RR values were high and SpO_2 levels were low in both groups (Table 1).

A total of 98 (88.5%) patients were hospitalized, including 58 (59.2%) patients in the ICU and 40 (40.8%) in the clinic.

During hospitalization, 109 (97.3%) patients survived and 3 (2.7%) died. Endotracheal intubation was not required in 96.4% (n=108) of the patients.

There were no significant differences between the two groups in terms of gender (p=0.492), comorbid diseases (p=0.099), and age (p=0.441).

There were no differences between the groups in terms of their laboratory results as follows: pH 1st hour (p=0.707), 2nd hour (p=0.820); $PaCO_2$ 1st hour (p=0.354), 2nd hour (p=0.194); HCO_3 0th hour (p=0.111), 1st hour (p=0.988), and 2nd hour (p=0.842); lactate 0th hour (p=0.093), 1st hour (p=0.249), and 2nd hour (p=0.081); base

Table 1. Laboratory results of the HFOT and SOT groups

	Treatment method		t	*P*
	HFOT (n=62) Mean±SD	**SOT (n=50) Mean±SD**		
pH				
0th hour	7.23±0.08	7.30±0.09	-4.143	**<0.001**
1st hour	7.32±0.06	7.33±0.09	-0.377	0.707
2nd hour	7.36±0.04	7.37±0.07	-0.228	0.820
PO_2 (mm Hg)				
0th hour	58.19±6.05	63.54±9.28	-3.671	**<0.001**
1st hour	163.62±75.84	80.24±21.86	7.521	**<0.001**
2nd hour	143.93±44.89	93.70±32.75	6.616	**<0.001**
$PaCO_2$ (mm Hg)				
0th hour	54.64±12.01	48.14±13.32	2.712	**0.008**
1st hour	45.48±9.83	43.66±10.87	0.931	0.354
2nd hour	42.32±8.12	40.20±9.01	1.308	0.194
HCO_3 (mmol/L)				
0th hour	20.60±3.88	21.80±4.01	- 1.606	0.111
1st hour	22.58±3.54	22.59±3.99	-0.015	0.988
2nd hour	23.61±3.13	23.48±3.66	0.200	0.842
SpO_2 (%)				
0th hour	81.67±5.60	86.04±6.43	-3.837	**<0.001**
1st hour	97.31±2.80	92.20±4.70	7.42	**<0.001**
2nd hour	97.84±1.95	95.10±2.54	6.453	**<0.001**
Lactate (mmol/L)				
0th hour	27.93±17.05	22.16±18.94	1.695	0.093
1st hour	16.80±10.83	20.18±19.50	-1.159	0.249
2nd hour	12.87±7.45	15.90±10.69	-1.762	0.081
Base deficit (mmol/L)				
0th hour	-3.47±5.24	-1.94±6.02	-1.444	0.152
1st hour	-1.59±4.90	-1.60±5.63	0.011	0.991
2nd hour	-0.52±4.35	-0.54±5.06	0.027	0.979

Values are presented as mean±SD and analyzed by independent samples t-test
HFOT - high-flow oxygen therapy; SOT - standard oxygen therapy

deficit level 0th hour (p=0.152), 1st hour (p=0.991), and 2nd hour (p=0.979) (Table 1).

The 0th hour pH and PaO_2 levels were significantly higher in the SOT group than the 0th pH and SPO_2 levels in the HFOT group (Table 1, Fig. 2).

The initial 0th hour HR was higher in the HFOT group (p=0.001) (Table 1). Regarding other vital signs, there were no significant differences between the groups in the following values: HR (/min) 1st hour (p=0.728), 2nd hour (p=0.370); systolic pressure (mm Hg) 0th hour (p=0.747), 1st hour (p=0.232), and 2nd hour (p=0.058); diastolic pressure (mm Hg) 0th hour (p=0.533), 1st hour (p=0.135), and 2nd hour (p=0.371); and MBP (mm Hg) 0th hour (p=0.766), 1st hour (p=0.107), and 2nd hour (p=0.106) (Table 2). The 0th hour RR was statistically higher in the HFOT group (p<0.001). The 1st and 2nd hour RR values were significantly higher in the SOT group (1st

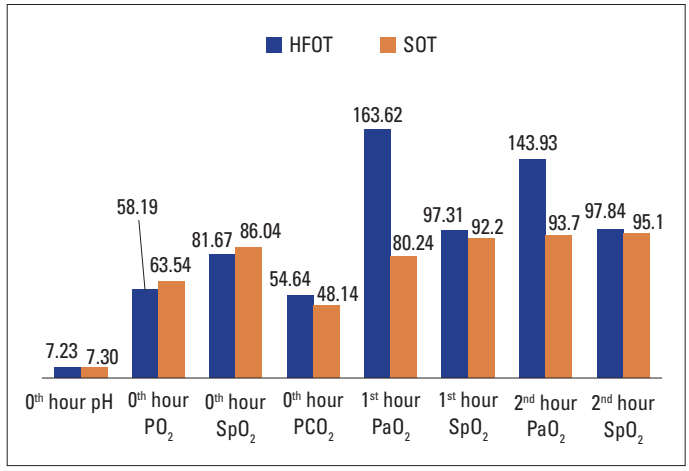

Figure 2. Blood gas analyses diagram of HFOT and SOT groups

Table 2. Vital signs at 0th, 1st, and 2nd hour of the groups

	Treatment method		t	*P*
	HFOT (n=62) Mean±SD	SOT (n=50) Mean±SD		
Pulse (/min)				
0th hour	115.04±20.88	102.18±20.46	3.271	**<0.001**
1st hour	94.62±15.97	95.86±21.31	-0.349	0.728
2nd hour	87.91±15.21	90.70±17.47	-0.900	0.370
Systolic T.A (mm Hg)				
0th hour	182.90±23.35	181.40±25.71	0.324	0.747
1st hour	147.74±17.12	152.20±22.15	-1.201	0.232
2nd hour	130.64±14.47	137.0±20.52	-1.918	0.058
Diastolic T.A (mm Hg)				
0th hour	101.61±11.76	100.20±12.03	0.625	0.533
1st hour	84.83±9.70	87.80±11.11	-1.504	0.135
2nd hour	77.2±9.08	78.80±8.95	-0.899	0.371
MBP (mm Hg)				
0th hour	127.74±14.42	126.92±14.62	0.298	0.766
1st hour	105.59±10.97	109.38±13.66	-1.626	0.107
2nd hour	94.64±9.29	97.86±11.58	-1.629	0.106
Respiratory rate (/min)				
0th hour	33.59±4.82	28.24±5.26	5.604	**<0.001**
1st hour	23.46±4.11	26.58±5.37	-3.471	**<0.001**
2nd hour	20.17±2.71	24.06±4.54	-5.607	**<0.001**
SpO_2 (%)				
0th hour	82.24±5.62	86.58±5.70	-4.034	**<0.001**
1st hour	97.41±2.83	92.72±4.51	6.715	**<0.001**
2nd hour	98.64±1.69	95.94±2.27	7.207	**<0.001**

Values are presented as mean±SD and analyzed by independent samples t-test
HFOT - high-flow oxygen therapy; SOT - standard oxygen therapy; MBP - mean blood pressure; T.A - tension arterial

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hour p=0.001, 2nd hour p<0.001). Finger SpO_2 at the 0th hour was higher in the SOT group (p<0.001). This value was higher in the HFOT group at the 1st and 2nd hour (p<0.001) (Table 2).

There were no significant differences between the groups in the primary outcome (p=0.440), admission place (clinic/ICU) (p=0.492), mortality (p=0.419), and intubation requirement (p=0.233) (Table 3).

The duration of hospitalization in service was longer in the SOT group but not statistically significant (p=0.622). However, the length of ICU hospitalization was significantly higher in the SOT group (p=0.040, Table 4).

The mean ejection fraction values were 41.40%±9.32% (range: 20%–60%) in the HFOT group and 42.14%±10.34% (range: 20%–60%) in the SOT group, with no significant difference between the groups (p=0.693). The mean length of stay in the ED was longer in the SOT group [233±79.64 min (range: 120–520 min)] than in the HFOT group [178.79±67.70 min (range: 20–480 min)] (p<0.001).

The 2nd hour pH level was higher than the 0th hour pH level in the HFOT groups (p<0.001). Similarly, the 2nd hour pH level was higher than the 0th hour pH level in the SOT group (p<0.001) (Table 5). The 0th hour lactate levels were higher than the 2nd hour lactate levels in both groups (HFOT group p<0.001, SOT group p=0.001) (Table 5).

Discussion

Hypertensive pulmonary edema is one of the serious life-threatening emergency conditions. HFOT, a noninvasive method, has several advantages because of its positive pressure property in clinical use in these patients. The amount of oxygen administered may increase up to 100% and provides a constant FiO_2 support and diminishes the dead space in lungs (9-11). To our knowledge, the use of HFOT in patients with hypertensive pulmonary edema has not been well defined in the literature. In

Table 3. Differences between groups according to admission, mortality, intubation status, and outcome

	Treatment method			
	HFOT n (%)	SOT n (%)	"χ^2"	*P*
Outcome				
Discharge (n=14)	7 (11.3)	7 (14.0)	0.186	0.440
Stay in hospital (n=98)	55 (88.7)	43 (86.0)		
Admission				
Intensive care unit (n=58)	32 (58.2)	26 (60.5)	0.052	0.492
Service (n=40)	23 (41.8)	17 (39.5)		
Mortality				
Died (n=3)	1 (1.6)	2 (4.0)	0.605	0.419
Alive (n=109)	61 (98.4)	48 (96.0)		
Intubation requirement				
+ (n=108)	61 (98.4)	47 (94.0)	1.547	0.233
– (n=4)	1 (1.6)	3 (6.0)		

Values are presented as number % and analyzed by the Mann–Whitney U test.
n: median; HFOT - high-flow oxygen therapy; SOT - standard oxygen therapy; IQR - interquartile range

Table 4. Differences between groups according to hospitalization time and outcome

	HFOT Mean±SD	SOT Mean±SD	U/t	*P*
Number of days in intensive care unit (n=63)	2.45±1.72	5.11±7.44	U: 332.5	**0.040**
Number of days in clinic (n=61)	4.55±4.54	5.11±4.02	U: 401.0	0.622
Total hospitalization day (n=97)	4.55±4.11	6.23±6.55	t: -1.538	0.127

Values are presented as mean±SD and analyzed by independent samples t-test
HFOT - high-flow oxygen therapy; SOT - standard oxygen therapy

Table 5. Differences between groups according to lactate levels

	0th hour pH Mean±SD	2nd hour pH Mean±SD	*P*
HFOT	7.23±0.08	7.36±0.04	**<0.001**
Standard oxygen treatment	7.30±0.09	7.37±0.07	**<0.001**
	0th hour lactate	**2nd hour lactate**	***P***
HFOT	27.93±17.05	12.87±7.45	**<0.001**
Standard oxygen treatment	22.16±18.94	15.90±10.69	**<0.001**

Values are presented as mean±SD and analyzed by independent samples t-test
HFOT - high-flow oxygen therapy

the present study, we determined better blood gas results with HFOT in patients with hypertensive pulmonary edema.

Recently, Carratala et al. (12) reported that HFOT may be effective in patients with cardiogenic pulmonary edema, but they administered HFOT to those patients who had still been hypoxemic through the 24-hour oxygen treatment. After HFOT, they performed blood gas analysis that revealed that hypoxemia, tachypnea, and dyspnea resolved with HFOT. In addition, they suggested that HFOT is a much more useful and comfortable method. Similar to our results, the PO_2 and SpO_2 levels were better after HFOT. An important aspect was that none of our patients were denied HFOT because of discomfort.

In another study, 20 patients with acute respiratory distress admitted to the ICU received HFOT and SOT. Better results for PO_2 and SpO_2 were observed with HFOT than with SOT. HFOT resulted in decreased RR, lower mouth dryness, and much more comfort (13). Sztrymf et al. (14) reported similar results in 20 patients with pneumonia-induced acute respiratory distress. They observed better results in respiratory functions and oxygenation parameters with HFOT.

We observed that HFOT decreased the HR much more effectively than SOT. Similar to our results, HR and RR were decreased significantly with HFOT compared with SOT in the study of Carratala et al. (12). The difference in HR at the beginning improved at the 1st and 2nd hour in our study.

Other NIMV techniques, including continuous airway pressure (CPAP) and bilevel positive airway pressure (BPAP), are well-known methods for patients with hypoxemic. CPAP is the primary choice in hypoxemic respiratory failure, and BPAP is used for hypercarbic patients, but discomfort and compatibility of patients are the disadvantages. The mechanism is similar to that of HFOT in terms of a high positive pressure (15). HFOT is a new method for treating respiratory failure and not widely used in critically ill patients in the EDs. NIMV may decrease the venous return and it must be used much more carefully in preload dependent patients (16).

With HFOT, the airway pressure increases by 1.16 cm H_2O for each rise of 10 L/min flow. This pressure increases postexpiratory pulmonary volume, pressure in the alveoles, and decreases the RR (17).

Mauri et al. (18) reported that HFOT diminished the respiratory load of patients by affecting the central nervous system. According to their data, high FiO_2 provides better oxygenation and comfort because of moisturized air, optimal tidal volume because of positive pressure, and decrease in CO_2 levels and hypoxemia resolves (18).

According to the literature, HFOT is generally explored for patients with acute respiratory distress and supportive results have been suggested (19). In an animal model experiment comparing HFOT and CPAP, a significant decrement in CO_2 levels with HFOT was observed, and HFOT was suggested as an alternative for CPAP (20). In a randomized controlled prospective study, Makdee et al. (21) enrolled 128 patients with pulmonary edema and compared HFOT and SOT for determining the number of patients in terms of RR. It was observed that HFOT decreased the RR much more effectively at the 60th min of treatment. That study also suggested no significant difference between the groups according to the length of stay in the ED, number of hospitalization days, requirement of endotracheal intubation, and mortality (21). In our study, we determined shortened ED stay and shorter hospitalization period in the HFOT group.

In an ICU-based retrospective study, the clinicians compared early and late intubated patients after unsuccessful HFOT. They observed that late intubated patients had higher mortality rates, low success in extubation process, and difficulty in separating from the ventilator (22).

Lactate and base deficit levels have not been well defined in HFOT. In our study, the 2nd hour lactate levels were significantly lower in the HFOT group. This finding reveals that effective tissue and cell oxygenation was provided by HFOT.

Conclusion

HFOT in patients with hypertensive pulmonary edema demonstrated better improvement in terms of pH, PaO_2, SpO_2, fingertip SpO_2, $PaCO_2$, HR, and RR. It also shortened the length of stay in the ED and ICU. HFOT can be suggested as an effective method for patients with hypertensive pulmonary edema com-

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pared with SOT. Owing to the lack of literature, there is a need for prospective, comprehensive studies to further evaluate the efficacy of HFOT in patients with hypertensive pulmonary edema.

Study limitations

The study was conducted based on data from a single center and the number of patients was limited. Another limitation is that the length of stay of the patients in the emergency clinic sometimes had to be extended based on the bed availability in the services. A final limitation is that the blood gas values of those patients who were brought to the emergency clinic by ambulances were influenced by the nasal oxygen treatment that they received on the way.

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