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## **Comparative study between high flow nasal cannula, high velocity nasal insufflation and noninvasive ventilation in management of acute respiratory failure**

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**Abstract**---Background: Evidence supporting the benefits of High velocity nasal insufflation (HVNI) and High flow nasal cannula (HFNC) in management of Acute respiratory failure in adults beside Non invasive ventilation (NIV) has been proved. The work aim was to evaluate the advantages, efficacy and the hazards of HVNI/HFNC in comparison to those of NIV with acute hypoxemic and hypercapnic respiratory failure. Patients and methods: A prospective analytical study of 60 patients with ARF were randomized to receive either non-invasive positive pressure ventilation (NIV) using an oronasal mask 30/60(50%), high-velocity nasal insufflation (HVNI) 17/60(28.3%), or High-flow nasal cannula (HFNC) 13/60(21.7%). Precision Flow® Hi-VNI Packaging (Vapotherm Inc., USA) as HVNI device which delivered air flows between 35 and 60 L/min. Temperature was set at 34°C or 37°C, whereas FiO<sub>2</sub> was controlled to gain arterial oxygen saturation (SpO<sub>2</sub>) above 92% (that made PEEP from 1.7 to 5). I-Breathe HF60 TM - BioBusiness as HFNC device which delivered air flows up to 60 L/m to rise the O<sub>2</sub> saturation above 92% (that made PEEP from 1.7 to 7.7) and the chamber of humidification was set at 37°C. NIV (Machine Model Vivo 2 and Dräger Evita® Infinity® V500 ventilator), the Bipap mode was set at 10-15 cmH<sub>2</sub>O IPAP, 4-7 cmH<sub>2</sub>O EPAP, while CPAP mode, the pressure was set at 10-15 cmH<sub>2</sub>O. Monitoring clinical symptoms, vital signs (HR, RR), ABGs, SpO<sub>2</sub>/FiO<sub>2</sub> to respiratory rate

(RR), outcomes, and complication was done initially, 2 and 48 hours after initiation of treatment. Results: On progression of PH, PaCO<sub>2</sub>, PaO<sub>2</sub>, and SaO<sub>2</sub> in serial recordings, the efficacy of HFNC, HVNI, and NIV was comparable. However, NIV has the priority in patients with COPD and hypercapnic ARF in comparison to HFNC. Between the three categories, there was no statistically significant difference in the failure rate ( $p=0.286$ ), mortality ( $p=0.278$ ), or length of hospital stay. Patients felt more tolerable with HFNC/HVNI, which also offered better oral intake and communication. One HFNC device cost more than home NIV but was almost as expensive as a ventilator for NIV. Conclusions: HFNC/HVNI was a valuable and comfortable intervention in adults with ARF. NIV was superior and available treatment option for patients with hypercapnic respiratory failure if it compared to HFNC.

**Keywords**---high-flow nasal cannula, high velocity nasal insufflation, non invasive ventilation, acute respiratory failure.

## Introduction

A respiratory backup devices used in treatment of acute respiratory failure (ARF) are the conventional oxygen therapy (COT), and noninvasive ventilation (NIV), high-flow nasal cannula (HFNC) and high velocity nasal insufflation (HVNI)<sup>[1]</sup>. Different HFNC settings were used. The appropriate titration in accordance with tolerability resulted in a flow estimate of 35 to 60 L/min. Depending on the patient's comfortability, the temperature was set at either 34 or 37 degrees Celsius, and FiO<sub>2</sub> was managed to achieve arterial oxygen saturation (SpO<sub>2</sub>) of 92%.<sup>[1]</sup>

Improvements in oxygenation, alveolar recruitment, warmth and humidification, clearing of secretion, minimizing of dead space, and decrease in work of breathing are advantages of HFNC<sup>[1]</sup> that stop the deterioration of lung mechanics and avoid endotracheal intubation. These advantages are a major argument in favor of using HFNC to decrease the need for invasive and noninvasive positive-pressure breathing, free up time for an efficient treatment of the underlying illness, and lower mortality from ventilator-related complications.<sup>[2-3]</sup> While HFNC is more reasonable and comfortable than COT and NIV, it may not be as effective at reducing work of breathing in ARF as NIV. Long-term failure of either HFNC or NIV therapies may necessitate late intubation and increase hospital mortality<sup>[4-5]</sup>. One HFNC component, such as its interface, circuit, or humidity, may be as expensive as an NIV ventilator. NIV should be recommended in COPD patients with acute hypercapnic acidotic respiratory failure (pH 7.35), including those who need endotracheal intubation and mechanical ventilation, according to the official ERS/ATS recommendations<sup>[6]</sup>.

NIV use may be restricted despite its broad potential for use if a patient has complications to the interface or positive pressure. NIV necessitates the use of a tight-fitting mask or helmet, the application of high pressures to a patient who is awake, the risk of skin damage following prolonged use, the development of

gastric insufflation and an increased risk of aspiration, the potential for patient-ventilator asynchrony, and restrictions on both secretion control and dietary intake. Invasive mechanical breathing is frequently necessary for patients who cannot tolerate NIV<sup>[6]</sup>. Despite the fact that most HFNC research focuses on patients with acute hypoxemic respiratory failure. HFNC can improve ventilation by increasing mean airway pressure and flushing out dead space, all while making the patient feel more comfortable and tolerable <sup>[2-6]</sup>.

In contrast, HVNI can provide the same amounts of oxygen at flow rates as high as 40 L/min due to an improved velocity brought on by a lower flow with more kinetic energy in the delivered gas. Because it uses a smaller bore nasal cannula that closes about 50% of the surface area of the nostrils compared to its competitors who use large bore HFNC, it may be able to provide ventilatory support in addition to oxygenation support for patients with acute hypercapnic respiratory failure. It can completely purge extrathoracic dead space at flow rates of 35 liters/min. It has also advantage of better humidification and provides gas conditioning as it has triple-lumen heated water jacketed delivery tubing substitute for heated wire circuits. That maintains temperature and humidity all the way to the patient <sup>[6]</sup>.

### **Patients and Methods**

This prospective comparative study was carried out on 60 patients, with clinical criteria of ARF (Both type 1 and type 2 ARF) an arterial  $PO_2 < 60$  mm Hg and/or an arterial  $PCO_2 > 50$  mm Hg <sup>[7] [8]</sup> who were admitted to Chest Department Menoufia university hospital and Kafr El Sheikh Chest hospital, Egypt. After receiving approval from the Local Ethical Committee Faculty of Medicine, Menoufia University, the study was conducted from April 2021 to March 2022. All patients provided written, fully informed consent. Factors such as suspected drug overdose, end-stage cancer, cerebrovascular accident, recent myocardial infarction hemodynamic instability, cardiac or respiratory arrest at presentation, and the requirement for urgent intubation were used as exclusion criteria. All patients were divided into two equal groups, group A, which contained 30 ARF patients who were given HFNC and Hi-VNI, and group B, which contained 30 ARF patients who were given NIV.

All patients underwent history taking, clinical examination, investigations (complete blood count (CBC), arterial blood gases (ABG), PCR if we suspected they were covid 19 carriers, random blood sugar, erythrocyte sedimentation rate (ESR), liver and renal function tests, C-reactive protein), electrocardiography (ECG), (chest X-ray and chest computerized tomography (CT)).

Group A: The patients were divided into two groups, A1 (17 patients on HVNI) and A2 (13 patients on HFNC), group A1 used a Precision Flow® Hi-VNI Packaging (Vapotherm Inc., USA). This device delivered air flows stated from 10 up to 40 L/min to raise the O<sub>2</sub> saturation above 92% (making PEEP from 1.7 to 5) and humidification chamber was set at 37°C and may be lowered if necessary. Group B2 used air flows between 10 and 50 and 60 L/m that were provided by the I Breathe HF60 TM - Bio Business to increase the O<sub>2</sub> saturation over 92% (creating PEEP between 1.7 and 7.7). Their vital signs, ABGs on room air, after 2 hours after

putting on the application then every 6 hours and the ROX index (which equal the ratio of  $SpO_2/FiO_2$  to respiratory rate (RR)) which were observed after the first 12 hours of treatment to determine whether or not the treatment was successful.<sup>[7]</sup> . According to ROX index if in the green zone, continue on HFNC, 2 – 3 consecutive records in orange zones, shift to NIV and if at any time in red zone, intubate <sup>[7]</sup>. The patients who had type 2 respiratory failure were only put on Hi-VNI <sup>[7]</sup> .

Group B: Placed on NIV (Machine Model Vivo 2 and Dräger Evita® Infinity® V500 ventilator), For Bipap mode the initial IPAP was set at 10 cmH<sub>2</sub>O and increased to at least 15 cmH<sub>2</sub>O if pH was less than 7.25, and the EPAP was set at the lowest setting available in the used machine at 4 cmH<sub>2</sub>O, that help to avoid CO<sub>2</sub> rebreathing through exhalation port and may be increased to maximum level of 7 cmH<sub>2</sub>O in COPD depending on PaCO<sub>2</sub>. Supplemental oxygen was given through a mask to keep oxygen saturation above or equal to 92%. During the first trial, IPAP was increased by 1 cmH<sub>2</sub>O / 30 min or higher according to the patient tolerance, While in CPAP mode the pressure was set at 10 cmH<sub>2</sub>O and increased to at least 15 if SaO<sub>2</sub> was still below 92%. The head of the bed was raised to 45, an oronasal mask was well fitted to the patient head with straps that was well applied, then quite reassurance was offered to the patients.

The common complications in our study were nasal bridge irritations and ulcerations, dry mouth or nose, nasal congestion, hypotension, and rising PaCO<sub>2</sub>. Changing the mask kind, humidifier, or nasal decongestants, or adjusting the strap tension, IPAP reduction, and FiO<sub>2</sub> minimization were the optimal solutions of these troubles. Patients were followed up for improvement and treatment failure through monitoring vital signs, ABGs on room air, after 2 hours after putting on the application then every 6 hours and HACOR score (Heart rate, Acidosis, Conscious level, PaO<sub>2</sub>/FiO<sub>2</sub>, Respiratory rate) after 2 hours of treatment <sup>[6]</sup>.

Treatment failure was defined as: switch to NIV or IMV or death during HFNC/HVNI application or switch to IMV or death during NIV application. Impending respiratory arrest, severe respiratory distress with pH less than 7.15 and (GCS < 8), persistent hypotension (defined as systolic arterial blood pressure of 90 mm Hg or mean arterial blood pressure of 65 mm Hg) despite fluid resuscitation or the need for vasopressors, breathing more than 40 times per minute, and abundant secretion were the criteria used for endotracheal intubation. <sup>[7]</sup> .

### **Statistical Analysis**

Using SPSS version 27 for Windows® (IBM SPSS Inc, Chicago, IL, USA), the collected data were coded, processed, and analyzed. The Shapiro-Wilk test was employed to determine whether the data distribution was normal. Quantitative parametric data were given as mean SD (standard deviation), whereas non-parametric and parametric data were compared using the student t-test and Mann-Whitney U test, respectively. Chi-Square testing was used to compare qualitative data that was provided as frequencies and percentages. It was statistically significant at P 0.05.

## Results

The age difference between the cases in the three groups was statistically significant ( $p=0.030$ ). With no statistically significant difference between the other subgroups, the mean age was statistically substantially greater in the cases receiving NIV compared to the cases receiving HVNI. The distribution of gender ( $p=0.128$ ) and smoking prevalence ( $p=0.182$ ) between the three subgroups did not differ statistically significantly from one another. With the exception of COPD ( $p=0.007$ ), there was no statistically significant difference between the associated comorbidities. Comparing the NIV group to the HFNC group, the prevalence of COPD was statistically considerably greater in the NIV group. Table 1

Table 1: Comparison of the demographic data and comorbidities in the study groups

		Group A (HFNO) (N = 30)		Group B (NIV) (N=30)	P value
		Group A1 (HVNI) (N=17)	Group A2 (HFNC) (N=13)		
Age (Years)		53.71± 14.61	64.62 ± 12.39	63.83 ± 12.84	0.030* P1= 0.074 P2= 0.039* P3= 0.983
Sex	Male	5 (29.4%)	8 (61.5%)	17 (56.7%)	0.128
	Female	12 (70.6%)	5 (38.5%)	31 (43.3%)	
Smoking	Non-smoker	13 (76.5%)	6 (46.2 %)	16 (53.3%)	0.182
	Smoker	4 (23.5%)	7 (53.8 %)	14 (46.7%)	
DM		7 (41.2 %)	2 (15.4 %)	12 (40 %)	0.245
HTN		5 (29.4 %)	8 (61.5 %)	14 (46.7%)	0.208
IHD		1 (5.9 %)	2 (15.4 %)	4 (13.3 %)	0.686
Cardiomyopathy		0 (0 %)	0 (0 %)	4 (13.3%)	0.117
Hypothyroidism		2 (11.8 %)	0 (0 %)	1 (3.3%)	0.287
Liver cirrhosis		0 (0 %)	0 (0%)	2 (6.7%)	0.355
Pulmonary hypertension		0 (0 %)	0 (0%)	2 (6.7%)	0.355
Rheumatoid arthritis		1 (5.9 %)	0 (0 %)	0 (0%)	0.276
CKD		0 (0 %)	0 (0%)	1 (3.3%)	0.601
Bronchial asthma		1 (5.9 %)	0 (0 %)	0 (0%)	0.276
Bronchiectasis		0 (0 %)	0 (0 %)	1 (3.3%)	0.601
COPD		2 (11.8 %)	1 (7.7 %)	12 (40 %)	0.007* P1=0.722 P2= 0.054 P3= 0.015*
Emphysema		1 (5.9 %)	0 (0 %)	0 (0%)	0.276
OSA		0 (0 %)	0 (0 %)	3 (10%)	0.152
ILD		5 (29.4 %)	2 (15.4 %)	3 (10%)	0.158

Continuous data are presented as the mean, standard deviation, or number (%); DM stands for diabetes mellitus; HTN for hypertension; IHD for ischemic heart disease; and CKD for chronic kidney disease. Obstructive sleep apnea is also known as interstitial lung disease (ILD). Probability, or P. P1: Significance between Group A1(HVNI) and Group A2(HFNC), P2: Significance between Group A1(HVNI) and Group B(NIV), and P3: Significance between Group A2(HFNC) and Group B(NIV)..

In terms of the prevalence of pneumonia, there was a statistically significant difference between the three categories ( $p=0.022$ ), with the prevalence of pneumonia being statistically significantly higher in the HFNC group than the NIV group. The prevalence of COPD exacerbations was statistically significantly different among the three groups ( $p=0.044$ ), with the NIV group's prevalence being statistically significantly greater than the HFNC group's... Table 2

Table 2: Comparison of causes of ARF in the study groups

	Group A (HFNO) (N = 30)		Group B (NIV) (N=30)	P value
	Group A1 (HVNI) (N=17)	Group A2 (HFNC) (N=13)		
Covid 19	7 (41.2%)	8 (61.5 %)	15 (50 %)	0.543
Non-Covid				
Pneumonia	4 (23.5%)	4 (30.8%)	3 (10%)	0.022* P1=0.186 P2= 0.094 P3= 0.028*
Bronchiectasis exacerbation	0 (0 %)	0 (0 %)	1 (3.3%)	0.601
COPD exacerbation	1 (5.9 %)	0 (0 %)	6 (20%)	0.044* P1=0.664 P2= 0.320 P3= 0.050*
ILD exacerbation	3 (17.6%)	1 (3.3 %)	1 (3.3%)	0.068
Cardiogenic Pulmonary edema	0 (0 %)	0 (0 %)	4 (13.3%)	0.154
Rt pneumothorax	1 (5.9 %)	0 (0 %)	0 (0 %)	0.276
Traumatic left hemopneumothorax	1 (5.9 %)	0 (0 %)	0 (0 %)	0.276

P: probability. Categorical data expressed as Number (%). MC: Monte-Carlo. \*: Statistically significant ( $p \leq 0.05$ ). P1: Significance between Group A1(HVNI) and Group A2(HFNC), P2: Significance between Group A1 (HVNI) and Group B(NIV), P3: Significance between Group A2(HFNC) and Group B (NIV).

Between the three groups, There was no statistically significant difference in the kind of RF between the two study groups ( $p=0.042$ ). For either the  $FiO_2\%$  or the  $PO_2/FiO_2$ , there was no statistically significant difference between the three groups ( $p=0.051$  and  $p=0.089$ , respectively). The oxygen flow rate between the HFNC and HVNI groups did not differ statistically significantly ( $p=0.194$ ). The

incidence of improvement, requirement ( $p=0.268$ ), mortality ( $p=0.278$ ). For invasive mechanical breathing, there was no statistically significant difference between the two groups ( $p=0.717$ ) or length of hospital stay were not significantly different across the three groups. Table 3. Figure 1

Table 3: Comparison of the type of RF,  $FiO_2$  and  $PO_2/FiO_2$  in the study groups and flow in group A

	Group A (HFNO) (N = 30)		Group B (NIV) (N=30)	P value
	Group A1 (HVNI) (N=17)	Group A2 (HFNC) (N=13)		
Type of RF				
Type I RF	10 (58.8%)	13 (100%)	20 (66.7 %)	0.042* P1= 0.015* P2= 0.712 P3= 0.033*
Type II RF	7 (41.2%)	0 (0%)	10 (33.3%)	
$FiO_2\%$	46.47 ± 7.02	47.31 ± 8.81	56.27± 18.97	0.051
$PO_2/FiO_2$	226.71 ± 28.51	223.31 ± 20.42	206.20± 39.06	0.089
Flow L/M	29.18 ± 9.03	25.38 ± 5.58	-	0.194
Improvement				
Not improved	11 (64.7%)	5 (38.5%)	13 (40%)	0.268
Improved	6 (35.3%)	8 (61.5%)	17 (60 %)	
Need invasive ventilation				
No	12 (70.6%)	9 (69.2%)	18 (60%)	0.717
Yes	5 (29.4%)	4 (30.8%)	12 (40 %)	
Death				
Survived	15 (88.2%)	13 (100 %)	29 (96.7%)	0.287
Died	2 (11.8%)	0 (0 %)	1 (3.3 %)	
Hospital stay	6 (2-9)	5 (3-10)	6 (2-12)	0.692

Data are presented as frequency (%) or mean ± SD. \*: Statistically significant ( $p \leq 0.05$ ). P1: Significance between Group A1(HVNI) and Group A2(HFNC), P2: Significance between Group A1(HVNI) and Group B(NIV), P3: Significance between Group A2(HFNC) and Group B(NIV).

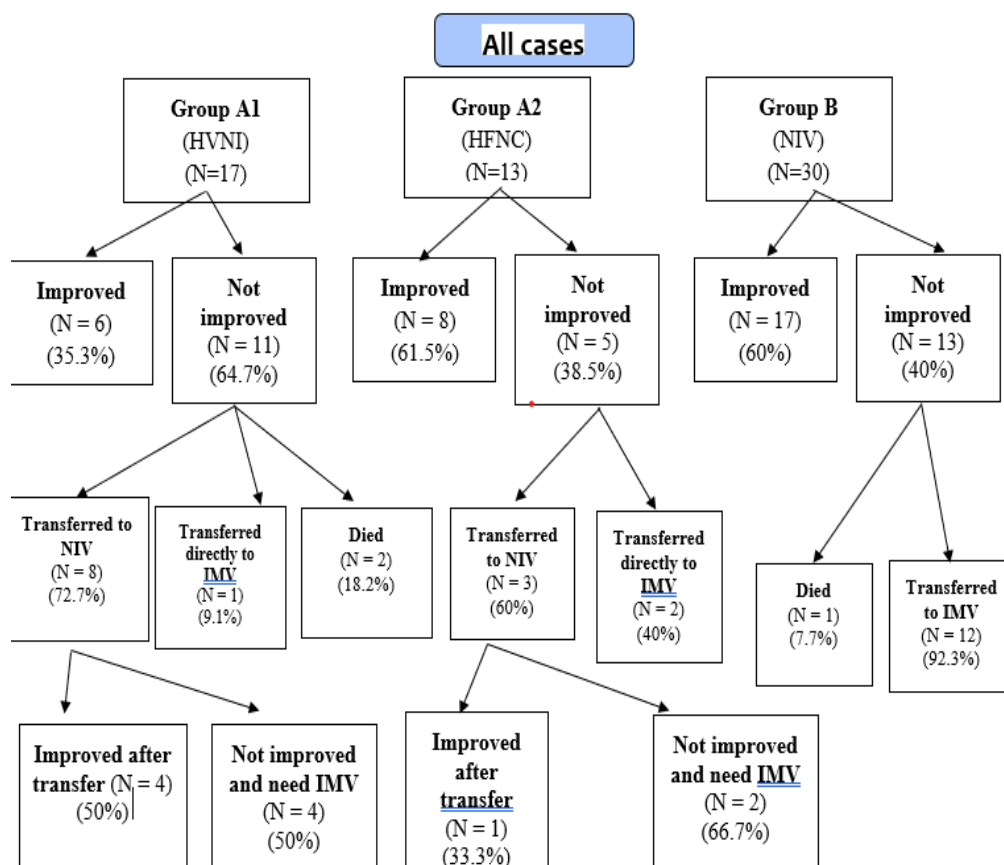


Figure 1: Flow chart of the patients

Regarding PH there was no statistically significant difference between the three study. In the cases within the HVNI and NIV groups, there was no statistically significant difference at different durations. In the HFNC group, there was a statistically significant decrease after 2 hours compared to the PH at room air. Figure 2(a).

PCO<sub>2</sub> at room air, after two hours, or after 48 hours did not statistically substantially differ between the three study groups. When compared to room air, the number of HVNI incidents increased statistically significantly after two hours. After 48 hours, there was a statistically significant increase in the NIV occurrences when compared to the PCO<sub>2</sub> at 2 hours. The HFNC group and the NIV group did not vary statistically significantly at any of the time points. Figure 2(b) At room air, but not at 2 hours or 48 hours, there was a statistically significant difference in PO<sub>2</sub> and SO<sub>2</sub> across the three research groups. There was a statistically significant rise in PO<sub>2</sub> compared to room air in the cases belonging to the HVNI, HFNC, and NIV groups after 2 hours and after 48 hours, but there was no statistically significant difference between 2 hours and 48 hours. Diagram 2(c). In comparison to room air, there was a statistically significant rise in SO<sub>2</sub> occurrences in the HVNI after 48 hours. At no point did the HVNI and NIV groups differ statistically substantially. When comparing the HFNC



and NIV group to room air after two hours and after 48 hours, there was a statistically significant increase. At all of the durations, there was no statistically significant difference. Image 2(d) There was no statistically significant difference for HCO<sub>3</sub> between the three research groups at room air, after two hours, or after 48 hours. Figure 2(e)

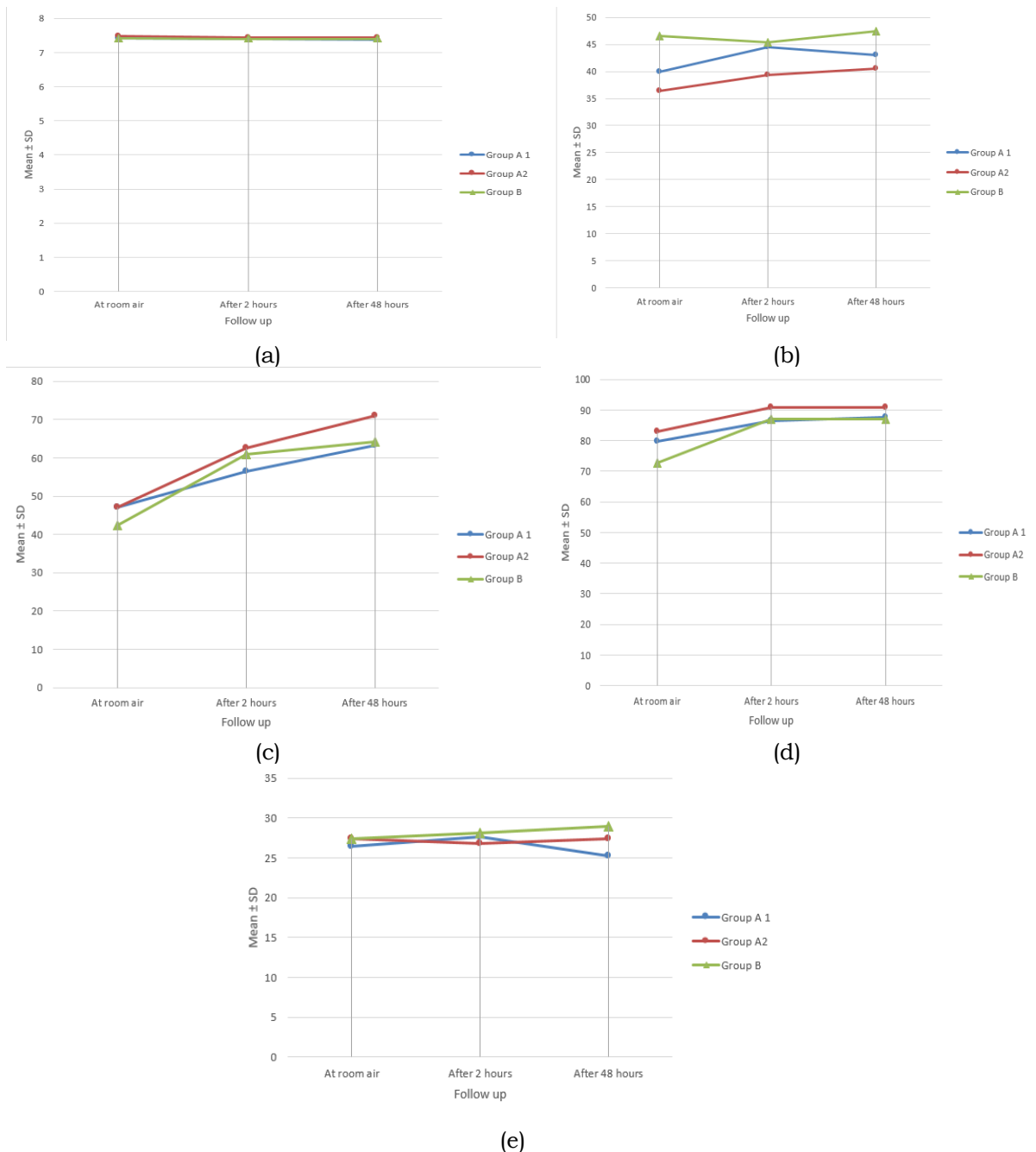


Figure 2: Comparison of ABG, (a): pH (b): PCO<sub>2</sub> (c): PO<sub>2</sub> (d): SO<sub>2</sub> (e): HCO<sub>3</sub> in the study groups along the study period

At room air or after two hours, there was no statistically significant difference in the RR across the three research groups. The RR for each trial group was statistically lower at 2 hours than it was at room air. At room air there was a statistically significant difference in the HR between the three research groups but not after two hours. There was no statistically significant difference between the RR at 2 hours and the room air in any of the research groups. After 12 hours, there was no statistically significant difference between the ROX index in the HVNI and HFNC groups ( $p= 0.184$ ). After two hours, the mean HACOR score ranged from 1 to 9, and in this table, it was  $4.57 \pm 2.66$ . Table 4

Table 4: Comparison of vital signs in the study groups along the first two periods, Rox index after 12 hours in group A and HACOR score after 2 hours in group B

	Group A (HFNO) (N = 30)		Group B (NIV) (N=30)	P value
	Group A1 (HVNI) (N=17)	Group A2 (HFNC) (N=13)		
RR				
Room air	30.76±6.84	33.38±5.45	30.20±5.66	0.276
After 2 hr	27.35±5.13	29±6.38	27.93±5.81	0.738
Interclass significance	P4< 0.001*	P4= 0.003*	P4= 0.002*	
HR				
Room air	90.06±6.08	79.15±15.69	91.79±7.89	0.001* P1= 0.010* P2= 0.829 P3= 0.001*
After 2 hr	90.41±4.68	87.38±6.34	91.63±7.58	0.164
Interclass significance	P4 = 0.701	P4 = 0.065	P4 = 0.731	
Rox index after 12 hr	4.18±1.52	4.99±1.74	-	0.184
HACOR score after 2 hr	-		4.57 ± 2.66	-

Data are presented as mean  $\pm$  SD. P: probability. \*: statistically significant ( $p < 0.05$ ). P1: Significance between Group A1(HVNI) and Group A2(HFNC), P2: Significance between Group A1(HVNI) and Group B(NIV), P3: Significance between Group A2(HFNC) and Group B(NIV), P4: Significance between value at room air and after 2 hours.

For eye irritation ( $p=0.12$ ), anxiety or claustrophobia ( $p=0.12$ ), or local facial nasal breakdown ( $p=0.06$ ) did not differ from one another statistically. There was a statistically significant difference regarding oral intake and the inability to communicate ( $p=0.001$ ). Price ranges for HVNI and HFNC are 25000 to 250000 L E or \$ 7625 [10] and for NIV are 15000 to 500000 L E, respectively.. Table 5

Table 5: Comparison of complications Prices range of HVNI, HFNC and NIV

Complications	Group A (HFNO) (N=30)		Group B (NIV) (N=30)	Test of significance (X <sup>2</sup> )	P-value
	Group A1 (HVNI) (N=17)	Group A2 (HFNC) (N=13)			
Local facial \nasal breakdown	0 (0.0)	0 (0.0)	5 (16.7)	5.45	0.06 P1 = ---- P2= 0.07 P3 = 0.12
Anxiety or claustrophobia	0 (0.0)	0 (0.0)	4 (13.3)	4.29	0.12 P1 = ---- P2= 0.12 P3 = 0.17
Eye irritation	0 (0.0)	0 (0.0)	4 (13.3)	4.29	P1 = ---- P2= 0.12 P3 = 0.17
Inability to Communicate and oral intake	0 (0.0)	0 (0.0)	30 (100)	60.0	<0.001 P1 = ---- P2<0.001 P3<0.001
Prices range	From 25000 to 250000 L E*		From 15000 to 500000 L E**		

X<sup>2</sup> = Chi squared test , P1: Significance between Group A1(HVNI) and Group A2(HFNC) , P2: Significance between Group A1(HVNI) and Group B(NIV), P3: Significance between Group A2(HFNC) and Group B(NIV).

\* 25000 LE for I-Breathe HF60 TM – BioBusiness ,250000 LE for Vapotherm Inc., USA [8]

\*\*15000LE for Cpap ,45000 LE for Machine Model Vivo 2, 500000 LE for Dräger Evita® Infinity® V500 ventilator

## Discussion

In addition to conventional oxygen therapy COT, the respiratory supporting and backup devices HFNC, HVNI, and NIV are employed in the management of acute respiratory failure. Through positive pressure, NIV enhances gas exchange and decreases inspiratory effort. Both HFNC and HVNI have active humidification systems that can provide FiO<sub>2</sub> at rates of up to 60 l/m for HFNC and up to 40 l/m for HVNI. They offer anatomical dead space clearance and (PEEP) [9] . Our study included 60 cases with ARF who were classified into two equal groups; group A (patients who were placed on (HFNO) and group B (patients were placed on (NIV)). The group A was divided into two subgroups; group A1 (17 patients who

received HFNI) and group A2 (13 patients who received HFNC). There was no statistically significant difference in our results between the three categories according to the gender and smoking state. The most associated systemic comorbidities in the three study groups were hypertension followed by diabetes mellitus and IHD.

This agreed with da Silva Costa et al. [10] who showed that the most represented comorbidities in the categories were HTN, DM, COPD, dyslipidemia, cardiac diseases and cancer. There was no difference between the NIV and HFNC groups. Regarding the cause of ARF in our results, COVID-19 was the most common cause for respiratory failure in the three categories representing 41.2%, 61.5% and 50% in the HVNI, HFNC and NIV groups respectively. Pneumonia had a statistically significantly higher prevalence in the HFNC group ( $p=0.022$ ). While, COPD exacerbation had a statistically significantly higher prevalence in the NIV group ( $p=0.044$ ). This came in accordance with Agmy et al. [11] and his colleagues who included 100 patients with ARF were randomly joined to HFNC and NIV groups. The authors reported that pneumonia was the predominant cause of ARF (41%), followed by acute exacerbation of ILD (40%).

There was no statistically significant difference in this study in the incidence of improvement between the three categories ( $p=0.268$ ). Although there was a greater degree of improvement in the HFNC and NIV groups compared to the HVNI group, the lack of a statistically significant difference is mostly due to the small sample size. In contrast to Koga et al. [1], that reports that the HFNC group's rate of treatment failure was higher than that of the NIV group ( $P = 0.001$ ). The justification could be based on the findings of Koga et al. [1], who showed that the treatment failure in the HFNC group was due to a weak PEEP impact. The incidence of IMV requirement was higher in the NIV group in the current study (40%) compared to the HFNC and HVNI groups, despite there being no statistically significant difference ( $p=0.717$ ). This was supported by Agmy et al.'s findings [11], which showed that the NIV group was more likely to move to mechanical breathing ( $p=0.001$ ). Worsening hypoxemia and increasing respiratory distress were the most prevalent causes of the need for mechanical ventilation. Elagamy et al.'s results [12] indicating patients assigned to HFNC had a lower rate of intubation than those receiving NIV were supported by the findings that were observed.

In our findings, there was no statistically significant difference in the rate of mortality between the three subgroups ( $p=0.278$ ). In the NIV group, there was only one death (3.3%) compared to two (11.8%) in the HVNI group. This agreed with Hao et al. [13] who found no statistically significant difference in the incidence of death between HFNC and NIV. This was opposed by Agmy et al.'s findings [11] which showed that the NIV group had significantly higher in-hospital mortality ( $P=0.001$ ). Regarding the duration of hospital stay in the current study, there was no statistically significant difference between the three study categories ( $p=0.736$ ). The median (range) of duration of hospital admission was 6 days (2-9), 5 days (3-10) and 6 days (2-12) in the HVNI, HFNC and NIV categories respectively. This agreed with Ovtcharenko et al. [14] who found that duration of hospital in HFNC did not vary in comparison to NIV (MD - 0.82 days, 95% CI - 1.83-0.20, I<sup>2</sup>=0%, high certainty).

At room air, after two hours, or after 48 hours, there was no statistically significant difference in the PH between our three study groups. In different times, there was no statistically significant change in the PH in the the HVNI category. After two hours, the PH in the HFNC group was statistically significantly lower than the PH in the room air group. The PH did not statistically differ significantly between the various times. Because of the small sample size, there was no statistically significant difference between the PH at various time points in the NIV groups. PH did not statistically significantly alter during the course of the various durations, as reported by Hao et al. [13], which is consistent with our findings. both in the HFNC group as well as the NIV group.

Between the three categories in the current study at room air, following two hours, or following 48 hours there was statistically significant difference. Following two hours, the PCO<sub>2</sub> in the HVNI showed elevation in comparison to PCO<sub>2</sub> in the room air. The PCO<sub>2</sub> in the different times didn't statistically alter. The PCO<sub>2</sub> at different times didn't vary in the HFNC category. In the NIV category, the PCO<sub>2</sub> at 48 hours showed elevation in contrast with the PCO<sub>2</sub> at 2 hours. The PCO<sub>2</sub> in the different times didn't show statistically significant difference, since 20 patients in the NIV group had hypocapnia and 10 had hypercapnia. Hao et al's [13] which is consistent with our findings, showed that there was no statistically significant difference in PCO<sub>2</sub> between the two groups (HFNC and NIV) at room air, following 2 hours, or following 24 hours. While with Plotnikow et al. [15] [19] who found that the PaCO<sub>2</sub> diminished from 57 to 52 mmHg (p esteem < 0.001), this improvement was kept up for the main day and up until HVNI was stopped.

Between the three groups, there was statistically significant difference in PO<sub>2</sub> at room air, however at 2 hours and 48 hours. The PO<sub>2</sub> in the HVNI group showed significantly elevation following 2 hours and following 48 hours when contrasted with the PO<sub>2</sub> at room air. There was no statistically significant difference in the PO<sub>2</sub> between 2 hours and 48 hours. The HFNC group show significantly elevation in PO<sub>2</sub> following 2 hours and following 48 hours in contrast with the PO<sub>2</sub> at room air. There was no statistically significant difference in the PO<sub>2</sub> between 2 hours and 48 hours. Following two hours and following 48 hours, the PO<sub>2</sub> in the NIV cases PO<sub>2</sub> was elevated when contrasted with the PO<sub>2</sub> at room air. There was no statistically significant difference in the PO<sub>2</sub> between 2 hours and 48 hours.

As consistent with our findings according to Mohamed et al. [16], the statistically significant difference between PaO<sub>2</sub>/FiO<sub>2</sub> at the beginning and the end (P-value 0.001) in both categories showed that oxygenation had improved. PaO<sub>2</sub> and the PaO<sub>2</sub>/FiO<sub>2</sub> ratio between the two categories were significantly different at the end of the research (P 0.05), however the NIV group had experienced a higher improvement in oxygenation.

Although the three research categories had varying SO<sub>2</sub> concentrations in the room air, there was no statistically significant difference after 2 hours or after 48 hours. After 48 hours, the SO<sub>2</sub> in the HVNI cases statistically significantly increased in comparison to the SO<sub>2</sub> at room air. The SO<sub>2</sub> did not vary statistically significantly over time. There was a statistically significant increase in the HFNC group's SO<sub>2</sub> after 2 hours and after 48 hours when compared to the SO<sub>2</sub> at room air. There was no statistically significant variation in the SO<sub>2</sub> over time. After two

hours and after 48 hours, the  $SO_2$  in the cases within the NIV statistically increased when compared to the  $SO_2$  at room air. There was no statistically significant variation in the  $SO_2$  between 2 hours and 48 hours. According to a study by Doshi et al. [17] reported that while  $SaO_2$  increased over time, there was no difference between the HVNI and NIPPV groups.

All study groups in the current findings had statistically lower RRs at 2 hours than they did at room air. At room air or after two hours, there was no statistically significant difference between the three groups. At room air, but not after two hours, there was a statistically significant difference in the HR between the three research categories. There was no statistically significant difference between the RR at 2 hours and the room air in any of the research categories. The room air vital sign parameters in the study by Agmy et al. [11] on vital signs did not significantly differ between the two categories. All metrics revealed a substantial difference between the two categories after the intervention's first 48 hours. Additionally, at 1-2 hours, 12 hours, or 24 hours after starting NIV therapy.

The ROX index after 12 hours did not statistically significantly vary between the HVNI and HFNC categories in the current study ( $p= 0.184$ ). In the HVNI group, it was  $4.18 \pm 1.52$  while in the HFNC group, it was  $4.99 \pm 1.74$ . Our findings were supported by Chandel et al.'s [18] discovery that the Rox index was 4.7 (3.4-6.2) 12 hours after HFNC. In our findings, the mean HACOR score after two hours ranged from 1 to 9, or  $4.57 \pm 2.66$ . In line with our findings, Hao et al. [13] showed that the mean HACOR score at baseline, after two hours, and after twenty-four hours was 4, 2, and 2. Local facial \nasal breakdown, anxiety or claustrophobia, eye irritation and oral intake were more common in NIV than HVNI or HFNC. This came in accordance to Cortegiani et al [19] who found that HFNC was better than NIV in comfort, improving dyspnea and RR. According to the cost, it was found that home NIV equipments are less costly and affordable than HVNI and HFNC equipments while hospital ventilator are more costly but better in infection control than home NIV.

Our study's data, when compared to other studies' data, support the idea that HVNI is not inferior to NIV in treating patients with type 2 RF, but HVNI has advantages because it is more pleasant and tolerable. This came in accordance to Doshi et al. [17] found that HVNI showed an elevation in PH and to a similar degree over time when compared to NIPPV. Plotnikow et al. [15] found that the  $PaCO_2$  reduced from 57 to 52 mmHg ( $p$  value  $< 0.001$ ), this improvement was kept up for the first day and up until HVNI was discontinued.

Additionally, the results demonstrate that HFNC performs well in type 1RF since it enables high flow rates of up to 60 L/m to raise  $FiO_2$  to 100%. Vargas et al. [20] demonstrated a considerable improvement in  $PaO_2/FiO_2$  with HFNC, but it was obviously greater with CPAP ( $P .01$ ), which is consistent with our results. Our study found a connection between the kind of ventilation, mortality, and improvement. Patients with ARF who are exposed to IMV and hospital death may not have overall improvement as a result of the momentary improvement in oxygenation. Peng et al. [21], who obtained the same results as our data indicated that HFNC and NIV did not differ in mortality on a subcategory of the helmet or CPAP group.

In contrast to what we found, Mohamed et al.<sup>[16]</sup> revealed that although employing a HFNC is advantageous for enhancing oxygenation, NIV was superior to HFNC.

### Conclusions

HFNC/HVNI was a valuable and comfortable intervention in adults with ARF. NIV was prior to use of HFNC in patients with hypercapnic respiratory failure with reasonable cost and availability.

### Limitations

The small sample size. Also, the short duration of follow up. Together, these limitations could decrease the power of the obtained results.

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