EARLY WEANING FROM MECHANICAL VENTILATION USING HFNO vs CONVENTIONAL METHOD IN HYPOXEMIC RESPIRATORY FAILURE: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

Thesis

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In partial fulfilment of the requirement for the degree of

DOCTORATE OF MEDICINE (D.M)

Critical Care Medicine

Dr. Hareesh Ayyawar

July, 2020

AIIMS, Jodhpur

CERTIFICATE

This is to certify that the thesis titled **'Early weaning from mechanical ventilation using HFNO vs Conventional method in hypoxemic respiratory failure: A prospective randomized controlled trial'** is a bonafide work of **Dr Hareesh Ayyawar**, carried out under our guidance and supervision, in the Department of Anaesthesiology and critical care, All India Institute of Medical Sciences, Jodhpur.

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Dr Hareesh Ayyawar

<u>Dedicated to</u>

My parents, (Late) Dharmapuri Ayyawar &

Shashikala Ayyawar

My Uncle, Ramesh Ayyawar
&
My Wife Dr Nikhita Ayyawar

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ABBREVIATIONS

ABG:	Arterial blood gases
ARDS:	Acute respiratory distress syndrome
BP:	Blood pressure
CI:	Confidence interval
ECG:	Electrocardiogram
FiO2:	Fraction of inspired oxygen
HFNO:	High flow nasal oxygenation
HR:	Heart rate
ICU:	Intensive care unit
IMV:	Invasive mechanical ventilation
NIV:	Non-invasive ventilation
NRBM:	Non-rebreathing mask
PEEP:	Positive end expiratory pressure
PaO2:	Partial pressure of oxygen in arterial blood
PaCO2:	Partial pressure of carbon dioxide in blood
P/F Ratio:	PaO2/FiO2 ratio
RR:	Rate of respiration per minute
RSBI:	Rapid shallow breathing index
SBT:	Spontaneous breathing trial
SPO2:	Percentage of oxygen saturation
VAP:	Ventilator associated pneumonia

SUMMARY

Objectives: Invasive mechanical ventilation (IMV) is a lifesaving therapy but prolonged ventilation is associated with increase in mortality and morbidity. Application of non-invasive ventilation after early extubation have been studied extensively in hypoxemic as well as hypercapnic respiratory failure but there is no data available so far on the use of high-flow nasal oxygenation (HFNO) as a mean to facilitate the process of early weaning and extubation from IMV in hypoxemic respiratory failure patients.

This study was aimed to assess the feasibility of early extubation followed by immediate HFNO compared with conventional weaning in patients with hypoxemic respiratory failure.

Methods: The present randomized, controlled, open-label trial analysed 80 adult patients (40 in each group) requiring IMV for more than 48hrs for hypoxemic respiratory failure. When the treating clinician decided that the patient is ready to be weaned based on clinical and rapid shallow breathing index (RSBI) criteria, the patient was given spontaneous breathing trial (SBT). In the Conventional group, SBT was given on achieving PaO2/FiO2 ratio of ≥ 200, while in HFNO group, it was given on achieving PaO2/FiO2 ratio of ≥ 150 with PEEP of ≤8. All patients were extubated after successful SBT and put on oxygen supplementation. Patients in the HFNO group received O2 through HFNO at 60 litres flow & 100% FiO2 and titrated to maintain SPO2 of ≥94% and RR ≤30. In the conventional group, patients received oxygen via venturi mask with flow titration to maintain SPO2 of ≥94%. In case of failed extubation based on clinical parameters and unacceptable ABG assessed by treating clinician, the patients were reintubated again and noted as weaning failure (if

reintubated within 48hrs of extubation) and continued further mechanical ventilation and weaning based on conventional method. All the pts were monitored for the signs of respiratory distress throughout the ICU stay.

Primary objective of this study was to compare weaning failure (defined by need of reintubation within 48hrs of extubation) and secondary objectives were to compare total invasive mechanical ventilation days, incidence of ventilator associated pneumonia (VAP), ICU length of stay, invasive mechanical ventilation free days, days of sedation requirement & all-cause mortality during ICU stay.

Results: Among 40 patients in each group, 5 (12.5%) patients experienced weaning failure in the HFNO group and 10 patients (25%) in the conventional group (p=0.252). No statistically significant difference was found in total invasive mechanical ventilation days, VAP incidence, total ICU length of stay, days of sedation requirement and all-cause mortality between the two groups. The median (IQR) invasive mechanical ventilation free days were significantly reduced in HFNO group [5 (4-6)] compared with conventional weaning [4 (2.25-6.75)] (p=0.033). Reintubation after 48hrs of extubation was needed in 1 patient (2.5%) in the HFNO group and 3 patients (7.5%) in the conventional group (P=0.615).

Conclusion: Among hypoxemic respiratory failure patients, early extubation on HFNO is a potential alternative to conventional method of weaning. Early weaning on HFNO significantly reduces the IMV free days.

INTRODUCTION

Invasive mechanical ventilation (IMV) requirement is one of the main reasons for intensive care unit (ICU) admissions. Invasive mechanical ventilation is a lifesaving therapy but prolonged ventilation is associated with increase in mortality and morbidity.[1,2] Successful and early weaning from invasive mechanical ventilation is important to improve outcomes in critically ill patients in intensive care.[1]

High Flow Nasal Oxygenation (HFNO) is an increasingly used therapy that allows high flows and fractions of inspired oxygen (FiO2) at a more physiological level of temperature and humidity. Nowadays, it is increasingly used in the intensive care and emergency medicine settings to manage patients with acute hypoxemic respiratory failure as well as to optimize pre-oxygenation prior to intubation in patients with mild-to-moderate hypoxemia.

The mechanisms by which HFNO acts include small pliable nasal prongs which increases comfort of the patient, warming and humidification of secretions which facilitates expectoration, washout of nasopharyngeal dead space that improves efficiency of ventilation, high flow rates that helps in reliable delivery of FiO2 and a small continuous positive airway pressure effect.

Prior application of HFNO have been extensively studied by comparing with conventional oxygen therapy and non-invasive ventilation (NIV) in preventing invasive mechanical ventilation in hypoxemic respiratory failure patients.[3-7]

HFNO application also have been studied in post extubation respiratory failure and high-risk patients compared with conventional oxygen therapy and NIV.[8-12]

The effect of high-flow nasal oxygen therapy among extubated patients at low risk for reintubation compared with conventional oxygen therapy also showed good results in reducing the risk of reintubation.[9]

Application of non-invasive ventilation after early extubation have been studied in hypoxemic as well as hypercapnic respiratory failure.[13,14] However, currently there is no data on the use of high-flow nasal oxygenation (HFNO) to facilitate the process of early weaning and extubation from IMV compared to conventional method in hypoxemic respiratory failure patients.

This study was aimed to assess the feasibility of early extubation followed by immediate HFNO, compared with conventional weaning in patients with resolving hypoxemic respiratory failure. We hypothesized that early weaning and extubation from invasive mechanical ventilation using HFNO is feasible and a better alternative to conventional method.

REVIEW OF LITERATURE

Invasive mechanical ventilation is one of the main indications for intensive care unit admissions. Even though it is a lifesaving therapy, prolonged IMV is associated with significant morbidity and mortality.[1,2] Therefore, minimizing the duration of IMV is an important consideration for clinicians who care for critically ill patients, and early weaning from IMV should be considered. A recent meta-analysis revealed that in most trials, protocol-based weaning has been shown to reduce duration of IMV, weaning, and ICU length of stay[15]. However, approximately 15% of patients receiving IMV require a prolonged process of weaning and experience higher mortality.[16] To improve outcomes in critically ill patients in intensive care early and successful weaning from invasive mechanical ventilation is very crucial.[1]

High-flow nasal oxygenation (HFNO) is an oxygen support device recently developed as an alternative to conventional oxygen therapy. HFNO consists of an air/oxygen blender connected through an active heated humidifier to the nasalcannula. It allows adjustment of the fraction of inspired oxygen (FiO2) independent of the flow rate and the gas mixture. HFNO is associated with several physiological benefits and many studies have shown improvement in comfort and overall outcomesin various clinical settings. Indeed, HFNO has been shown to be potentially useful and efficient in immunocompromised patients[3], hypoxemic acute respiratory failure[4], for preoxygenation[17] or during bronchoscopy.[18]

Frat JP et al[4] conducted a multi-centre, open-label randomized trial in 310 hypoxemic failure patients with PaO2/FiO2 ratio of <300 and compared different methods of oxygen therapy prior to intubation. The intubation rate was 38% in the HFNO group, 47% in the conventional oxygen therapy group, and 50% in the non-

invasive-ventilation group (P=0.18). The number of ventilator-free days at day 28 was significantly higher in the HFNO group (24±8 days), vs. 22±10 days in the standard-oxygen group and 19±12 days in the non-invasive-ventilation group. The hazard ratio for death at 90 days was 2.01 (95% confidence interval [CI], 1.01 to 3.99) with standard oxygen versus high-flow oxygen (P=0.046) and 2.50 (95% CI, 1.31 to 4.78) with non-invasive ventilation versus high-flow oxygen (P=0.006).

Schwabbauer N et al[7] conducted a randomized trial to compare the short-term effects of oxygen therapy via High flow nasal oxygenation (HFNO) on functional and subjective respiratory parameters in patients with acute hypoxic respiratory failure in comparison to non-invasive ventilation (NIV) and standard treatment via a Venturi mask. In the final evaluation of overall discomfort on a 10-point scale, patients gave the best ratings to HFNO 2.3 ± 1.4, followed by Venturi mask 3.2 ± 1.7 (ns vs. HFNO) and NIV 4.5 ± 1.7 ($p < 0.01$ vs. HFNO and $p < 0.05$ vs Venturi mask). Finally concluded that in hypoxic respiratory failure HFNO offers a good balance between oxygenation and comfort compared to NIV and Venturi mask and seems to be well tolerated by patients.

HFNO therapy has been studied extensively in post extubation low risk[9] and high risk[11] groups of hypoxemic respiratory failure, and found good results. Hernandez G et al[9] conducted a multicentre randomized trial in 527 adult critical patients to determine whether HFNO is superior to conventional oxygen therapy for preventing reintubation in mechanically ventilated patients at low risk for reintubation. Results showed that reintubation within 72 hours was less common in the high-flow group (13 patients [4.9%] vs 32 [12.2%] in the conventional group; absolute difference, 7.2% [95% CI, 2.5% to 12.2%]; P = .004). Post extubation

respiratory failure was less common in the high-flow group (22/264 patients [8.3%] vs 38/263 [14.4%] in the conventional group; absolute difference, 6.1% [95% CI, 0.7% to 11.6%]; P = .03). Time to reintubation was not significantly different between groups (19 hours [interquartile range, 12-28] in the high-flow group vs 15 hours [interquartile range, 9-31] in the conventional group.

Same investigator Hernandez G et al[11] conducted another multicentre randomized clinical trial in a high-risk group and Patients were randomized to undergo either high-flow conditioned oxygen therapy or NIV for 24 hours after extubation. Results showed that among high-risk adults who have undergone extubation, high-flow conditioned oxygen therapy was not inferior to NIV for preventing reintubation and post extubation respiratory failure.

A study done by Maggiore et al[23] conducted a study in 105 critically ill patients to compare the effects of the Venturi mask and the high-flow nasal oxygen therapy. They found that HFNO oxygen therapy resulted in significantly less reintubation rate (3.8%) during the 48 hrs of the study period than conventional oxygen therapy (21.2%) (p=0.005) and also resulted in better oxygenation, better patient comfort in HFNO group than conventional oxygen therapy.

Song HZ et al[10] conducted a single-centre, prospective, randomized, controlled pilot trial in 60 patients to investigate the value of high-flow nasal oxygen therapy after extubation in patients with acute respiratory failure. Among the 60 patients, 46 were successfully treated by initial oxygen therapy within 24 hr after extubation, including 27 in the HFNO group and 19 in the air entrainment mask group. The success rate of oxygen therapy by HFNO (27/30, 90%) was significantly higher than that by the air entrainment mask (19/30, 63.3%) (p=0.01) Finally concluded that

compared to the air entrainment mask group, the success rate of oxygen therapy and the partial pressure of arterial oxygen were significantly higher and the respiratory rate was lower in the high-flow nasal oxygen group compared to air entrainment mask group.

Early weaning to non-invasive ventilation has also been studied in some populations to decrease invasive mechanical ventilation days. Perkins GD et al[13] performed a Randomized, open-label, multicentre clinical trial in 364 respiratory failure patients comparing the effects of protocolized weaning with early extubation to non-invasive ventilation on time to liberation from ventilation. The median time to liberation was 4.3 days in the non-invasive group vs 4.5 days in the invasive group (adjusted hazard ratio, 1.1; 95%CI, 0.89-1.40). Competing risk analysis accounting for deaths had a similar result (adjusted hazard ratio, 1.1; 95%CI, 0.86-1.34). The non-invasive group received less invasive ventilation (median, 1 day vs 4 days; incidence rate ratio, 0.6; 95%CI, 0.47-0.87) and fewer total ventilator days (median, 3 days vs 4 days; incidence rate ratio, 0.8; 95% CI, 0.62-1.0). There was no significant difference in reintubation, tracheostomy rates, or survival. Adverse events occurred in 45 patients (24.7%) in the non-invasive group compared with 47 (25.8%) in the invasive group.

Vaschetto R et al[14] conducted the pilot study aimed to assess the feasibility of early extubation followed by immediate NIV vs conventional weaning, in patients with resolving hypoxemic respiratory failure patients. Arterial blood gases were similar during IMV, 1 hr after NIV application following extubation, and after 12, 24 and 48 hrs. Respiratory rate was higher after 1h in the NIV group, but no different after 12, 24 and 48 hr. The number of invasive-ventilation-free-days at day 28 was 20

± 8 (min = 0, max = 25) days in the treatment group and 10 ± 9 (min = 0, max = 25) days in the control group (p = 0.014). The rate of extubation failure, ICU and hospital mortality, tracheostomies, septic complications, days and rates of continuous sedation, and ICU length of stay were not significantly different between the two groups.

There is currently no data on the use of HFNO to facilitate the process of early weaning and extubation from IMV in hypoxemic respiratory failure patients in order to avoid complications associated with invasive mechanical ventilation.

This study was aimed to assess the feasibility of early extubation followed by immediate HFNO application, compared with conventional weaning in patients with resolving hypoxemic respiratory failure.

AIMS AND OBJECTIVES

The aim of this prospective randomized controlled trial was to assess the feasibility of early extubation followed by immediate HFNO, compared with conventional weaning method in patients with resolving hypoxemic respiratory failure.

PRIMARY OBJECTIVE

To compare weaning failure (defined by need of reintubation within 48hrs of extubation) in both groups.

SECONDARY OBJECTIVES

To compare total invasive mechanical ventilation days, incidence of ventilator associated pneumonia (VAP), ICU length of stay, invasive mechanical ventilation free days, days of sedation requirement & all-cause mortality during ICU stay.

MATERIALS AND METHODS

STUDY DESIGN:

The single-centre, open label, prospective randomized controlled trial

STUDY DURATION:

This study was conducted between Jan 2021 to June 2022

PLACE OF STUDY:

This study was conducted at adult ICU in the Department of Anaesthesiology and Critical Care, AIIMS, Jodhpur.

After getting approval from the institutional ethical committee (IEC Reg. No. AIIMS/ IEC/ 2021/ 3313) and registration with Clinical Trial Registry-India (CTRI/2021/07/034659), this study was carried out in adult ICU patients who received invasive mechanical ventilation for more than 48 hrs in hypoxemic respiratory failure patients.

Inclusion criteria:

All adult pts (age above 18yrs) who received invasive mechanical ventilation through endotracheal tube for more than 48 hrs for hypoxemic respiratory failure.

Exclusion criteria:

- Age less than 18yrs
- Type 2 respiratory failure
- Tracheostomized patients

- Profound neurological deficit and altered sensorium
- Contraindication to HFNO application (base of skull fracture, known nasal obstruction and nasal trauma)
- Psychiatric, agitated or non-cooperative patients

Patients were randomly allocated into two groups by a computer-generated randomization table. All the patients received appropriate continuous sedation with titration of sedation based on Richmond Agitation Sedation Scale score[19] to −2 to 0 (ANNEXURE-6). All the patients recruited in our study were screened daily for readiness to wean based on clinical criteria[20] & RSBI [21] (Rapid Shallow Breathing Index) (Respiration rate/ Tidal volume) mentioned below and sedation was stopped 1 hr prior to spontaneous breathing trial according to our institution protocol

Common criteria used to determine readiness for weaning:

- Mental status awake and alert or easily arousable
- The cause of respiratory failure has improved
- Adequate cough reflex
- Ability to initiate an inspiratory effort (with trigger flow of -2cm H2O)
- Hb ≥ 7gm/dl
- PH > 7.25
- Core temperature ≤ 38 to 38.5°c
- Hemodynamic stability (no or minimal inotropic support)

And

RSBI <105 (rapid shallow breathing index) (Respiration rate/ Tidal volume)

Following a decision by the treating clinician based on the above criteria, all patients underwent SBT.

Conventional weaning group: In the conventional group**,** patients received SBT with Pressure support of 5-8 cm H2O, PEEP of 5 & FiO2 of 0.4 after achieving PaO2/FiO2ratio of ≥ 200 with FiO2 of 0.4.

HFNO group: Patients received SBT with Pressure support of 5-8 cm H2O with same PEEP and FiO2 on achieving PaO2/FiO2ratio of ≥ 150 with PEEP of 5-8 and FiO2 of ≤0.5.

During the weaning trial, patients monitored for vital signs and ventilator parameters such as the tidal volume and respiratory rate (minute ventilation). In addition, patients assessed for respiratory distress and mental status changes, alertness and responsiveness. At the end of the 30min of spontaneous breathing trial (SBT), an arterial blood gas (ABG) was obtained. SBT success was defined by maintaining the same PaO2/FiO2 ratios (PaO2/FiO2 ratio of ≥ 200 in conventional group and PaO2/FiO2 ratio of ≥ 150 in HFNO group) and RSBI of <105 with acceptable clinical parameters. At the end treating clinician confirmed about success or failure of SBT based on clinical, objective parameters and ABG.

All the patients were extubated after successful SBT. Then shifted to HFNO with 60 litres flow & 100% FiO2 and titrated to maintain SPO2 of ≥94% and RR ≤ 30 in HFNO group or patients were placed on oxygen supplementation via venturi mask

with FiO2 titration to maintain SPO2 of ≥94% and RR ≤ 30 in conventional weaning group.

All the patients monitored in the postextubation period for vital signs, SPO2, ECG, respiratory rate, signs of distress such as accessory muscle use, tachypnoea, tachycardia, chest retractions, agitation and mental state changes. ABG was repeated 30 min after extubation. In case of failed extubation based on clinical parameters and unacceptable ABG assessed by treating clinician, patients were reintubated again and put on IMV and noted as weaning failure (if reintubated within 48hrs of extubation) and continued further mechanical ventilation and weaning based on conventional method.

STATISTICAL ANALYSIS

The data collected was entered in Microsoft Excel and checked for any inconsistency. All the statistical analysis was carried out using Statistical Package for Social Sciences (SPSS, version 23.0 for Windows).

The results of this study were presented as absolute numbers and percentages or means and standard deviations for continuous data if normally distributed and medians and interquartile ranges if not normally distributed. Comparisons between the two groups were performed using indirect t test or Mann-Whitney U test for metric data and the chi-square test for categorical data. A two-sided p-value of less than 0.05 was considered significant.

The sample size was calculated based on the previous study[10] (Song HZ et al) where outcome proportions between the two groups were 90% and 63.3%. By having a confidence interval of 95% and power of the study as 80% the sample size required for this study was 36 in each group. Additional 10% will be added to ensure that loss of follow up and loss of data the sample size of 40 in each group was taken in this study.

OBSERVATIONS AND RESULTS

During the study period between January 2021 to June 2022, a total of 176 hypoxic respiratory failure patients received invasive mechanical ventilation for more than 48hrs in adult ICU, AIIMS, Jodhpur and were assessed for eligibility; of these, 66 patients were excluded (58 patients not meeting inclusion criteria & 8 patient's relatives refused to participate). Remaining 110 patients were randomized using a computer-generated randomization table. 56 patients were enrolled in the HFNO group and 54 patients were enrolled in the conventional group. 12 patients in the HFNO group and 14 patients in the conventional group did not receive the proposed intervention due to mortality prior to extubation or tracheostomized due to prolonged mechanical ventilation. In addition, 4 patients in HFNO group were also excluded due to rapid improvement of PaO2/FiO2 ratios to ≥ 200. Eventually, 40 patients in each group received the intervention based on the proposed protocol and they were statistically analysed (Figure 1). All the patients were monitored for the signs of respiratory distress throughout the ICU stay. Required data was obtained and the results were statistically analysed, which are presented as follows.

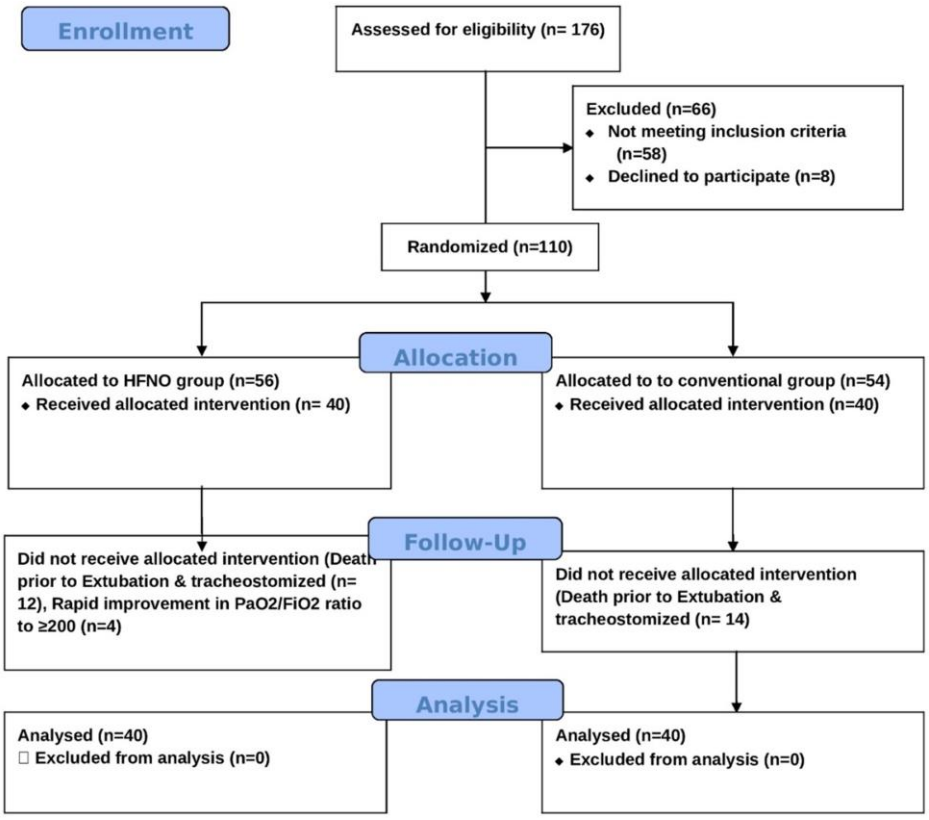

Figure 1: Consort flow diagram

Demographic data & Patient baseline characteristics:

Age:

The mean± SD age of HFNO and Conventional group were 43±14yrs and 48±17yrs respectively (P=0.167). Patients in the HFNO group were comparable to the conventional group. (Table 1 & Figure 2)

Table 1: Age

	HFNO (n=40)	Conventional (n=40)	Mean difference (95% confidence interval)	P value
AGE (yrs)	43±14	48±17	-5.02 (-12.18 to 2.13)	0.167

Values expressed as Mean (Standard deviation) and analysed using independent t test wherever applicable.

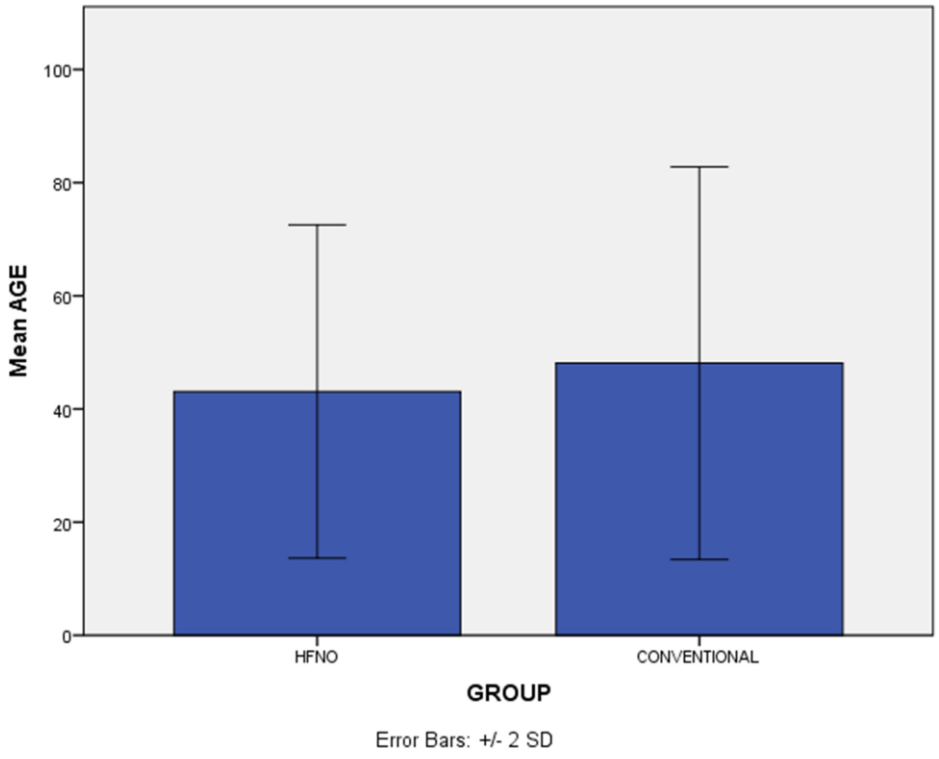

Figure-2: Age distribution

Gender distribution:

The number of males and females were 25 (62.5%) & 15 (37.5%) in the HFNO group and 28 (70%) & 12 (30%) in the conventional group respectively (P=0.637). Both the study groups were comparable with respect to the gender of the patients enrolled (Table 2 & Figure 3)

Table 2: Gender

		HFNO (N=40)	Conventional (N=40)	Chi-square value (P value)
GENDER	Male	25 (62.5%)	28 (70%)	0.503 (0.637)
	Female	15 (37.5%)	12 (30%)	

Values expressed as number of patients (percentages) and analysed using chi-square test wherever applicable.

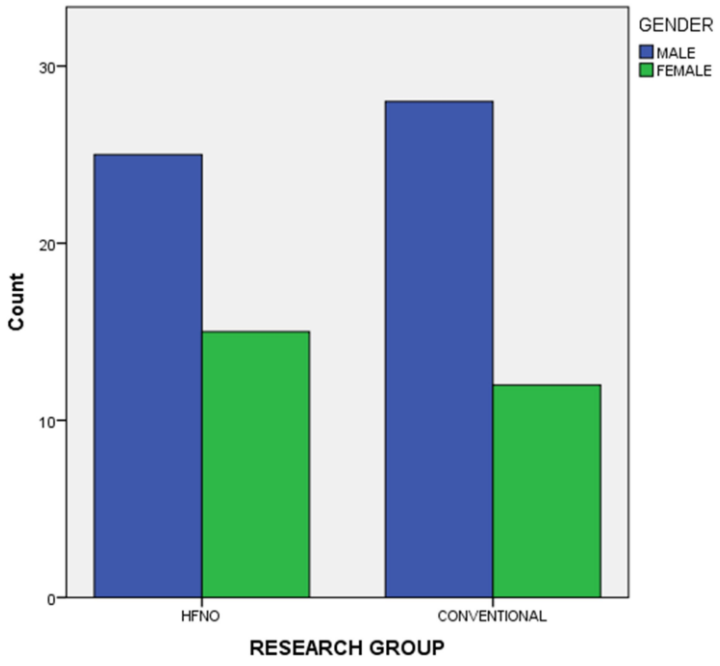

Figure 3: Gender distribution

Comorbidities:

17 (42.5%) patients in HFNO group and 26 (65%) patients in the conventional group have comorbidities like HTN, DM, Asthma, Coronary artery disease, Chronic kidney disease, Cerebrovascular accident and Seizure disorder while rest of the patients didn't have any comorbidities, which was comparable between the two groups (P>0.05) (Table 3& Figure 4).

Table 3: Comorbidities

		HFNO (N=40)	**Conventional (N=40)**	**Chi-square value (P value)**
COMORBIDITIES	DM	5 (12.5%)	4 (10%)	0.125 (1.00)
	HTN	7 (17.5%)	11 (27.5%)	1.147 (0.42)
	Asthma	1 (2.5%)	3 (7.5%)	1.053 (0.615)
	CAD	1 (2.5%)	2 (5%)	0.346 (1.0)
	CVA	0	2 (5%)	2.051 (0.494)
	CKD	1 (2.5%)	3 (7.5%)	1.053 (0.615)
	SEIZURE DISORDER	2 (5%)	1 (2.5%)	0.346 (1.0)

Values expressed as number of patients (percentages) and analysed using chi-square test wherever applicable. HTN=Hypertension, DM=Diabetes mellitus, CAD= Coronary artery disease, CVA= Cerebrovascular accident, CKD= Chronic kidney disease

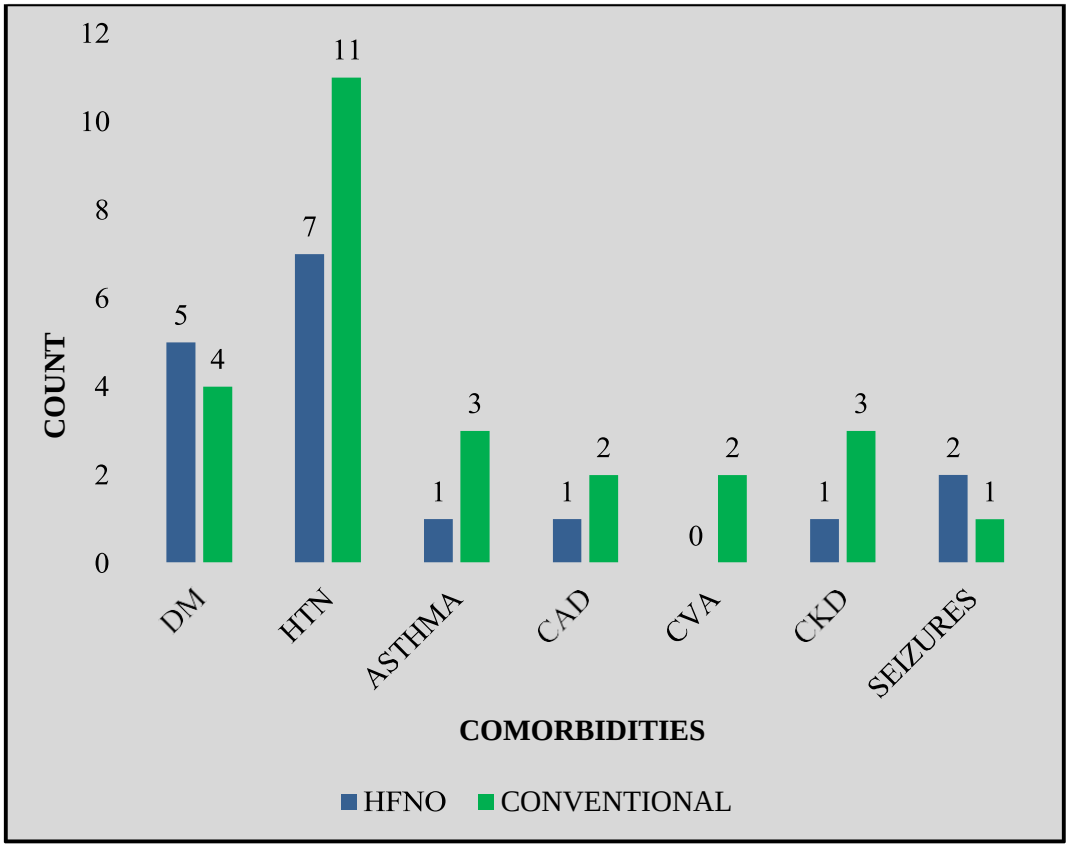

Figure 4: Co-morbidities

Diagnostic category:

Primary diagnosis of the patients was categorized as pulmonary and extrapulmonary (Trauma induced ARDS, Transfusion related acute lung injury, Pancreatitis associated ARDS etc.) causes of hypoxemic respiratory failure. There were 34 (85%) cases of pulmonary and 6 (15%) cases of extrapulmonary causes of hypoxemic respiratory failure in the HFNO group. In conventional group, 31 (77.5%) cases of pulmonary and 9 (22.5%) cases of extrapulmonary causes of hypoxemic respiratory failure, which was statistically not significant i.e., both the study groups were comparable with respect to the category of hypoxemic respiratory failure (P=0.568). (Table 4) (Figure 5)

Table 4: Diagnostic category

		HFNO (N=40)	**Conventional (N=40)**	**Chi-square value (P value)**
Diagnostic category	Pulmonary	34 (85%)	31 (77.5%)	0.738 (0.568)
	Extrapulmonary	6 (15%)	9 (22.5%)	

Values expressed as number of patients (percentages) and analysed using chi-square test wherever applicable

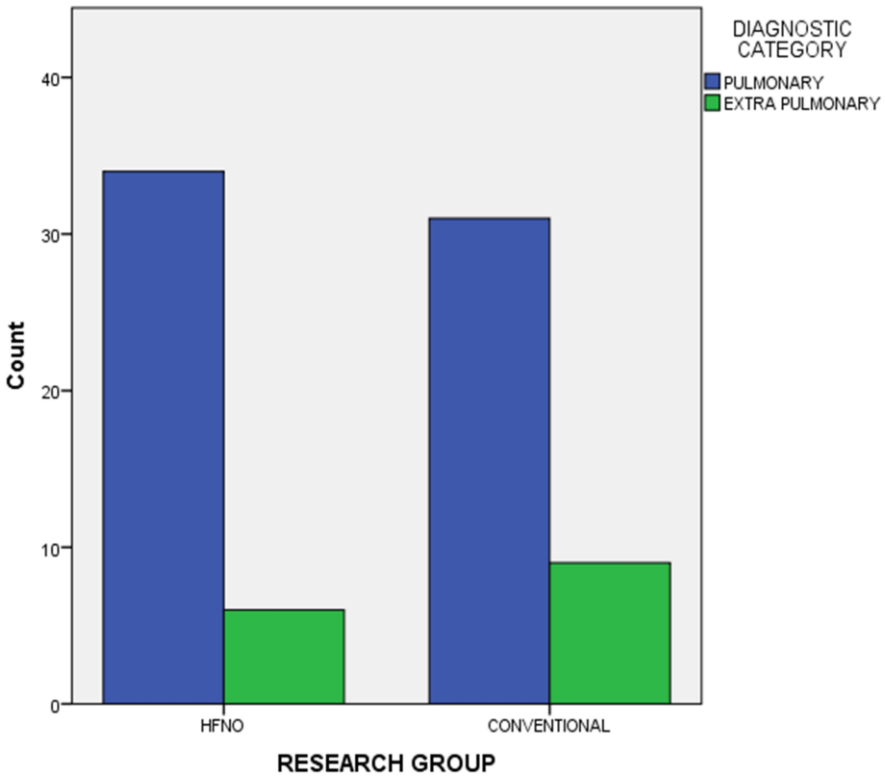

Figure 5: Diagnostic category

Duration of illness:

Median (IQR) duration (days) of illness prior to ICU admission were 7 (3-7) days in HFNO group & 5 (3-9) days in conventional group (P=0.607), which was comparable in both the groups (Table 5).

Table 5: Duration of illness prior to ICU admission (days)

	HFNO (n=40)	**Conventional (n=40)**	**Median difference (95% confidence interval)**	**p-value**
Duration of illness prior to ICU admission (days)	7 (3-7)	5 (3-9)	2 (-1.364 to 1.564)	0.607

Values expressed as Median (Interquartile range) and analysed using Mann Whitney U test wherever applicable

ICU admission scores: (Table 6 & Figure6)

Median (IQR) SOFA scores at admission in HFNO and conventional groups were 6 (4-7) & 7 (5-9) respectively, which was statistically not significant between the two groups (P=0.507). Median (IQR) APACHE-2 scores at admission in HFNO and conventional groups were 10 (8-16) & 16 (9-19) respectively. Median APACHE-2 score at admission was significantly less in the HFNO group compared to the conventional group (P=0.025). Overall, Both the groups were well matched with respect to demographic data (p>0.05) except the APACHE 2 score at admission.

Table 6: ICU scores at admission

	HFNO (n=40)	Conventional (n=40)	Median difference (95% confidence interval)	p-value
SOFA at admission	6 (4-7)	7 (5-9)	1 (-2.659 to -.191)	0.0507
APACHE-2 at admission	10 (8-16)	16 (9-19)	-6 (-6.073 to -.327)	0.025

Values expressed as Median (Interquartile range) and analysed using Mann Whitney U test wherever applicable.

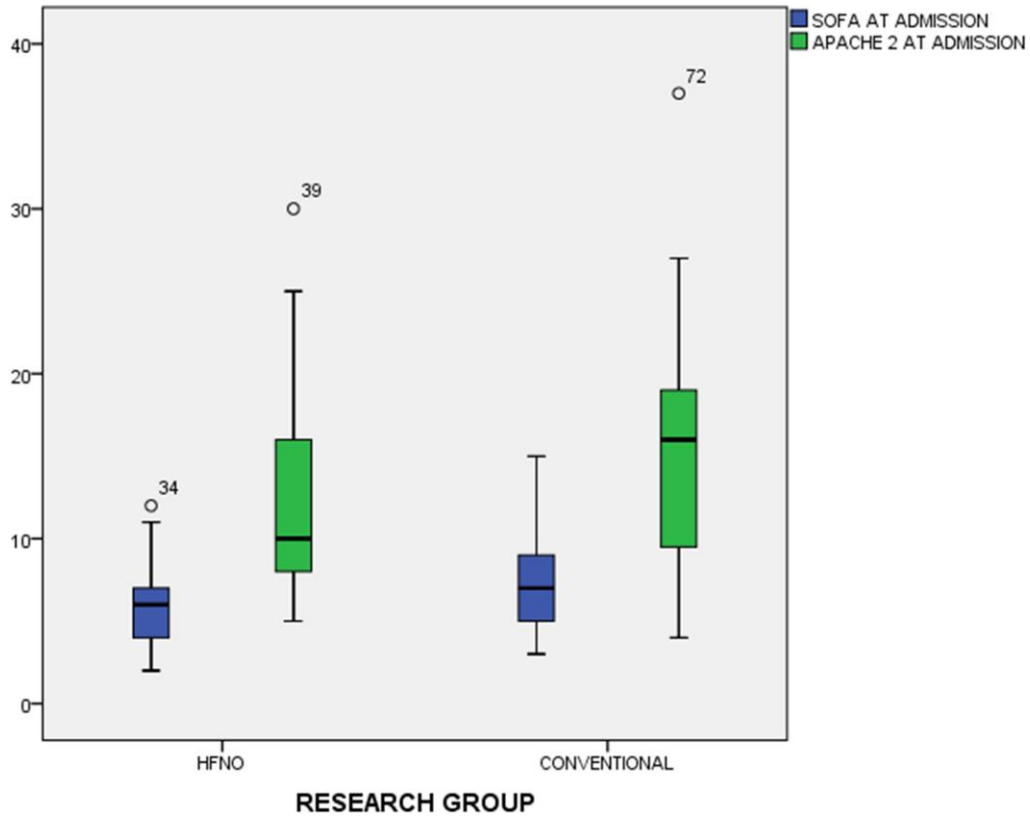

Figure 6: ICU scores at admission

PaO2/FiO2Ratios at different time intervals:

At admission, the mean PaO2/FiO2ratios in the HFNO group were significantly less than those in the conventional group (P<0.05), with mean and standard deviation of 99±29 in HFNO group and 133±38 in conventional group. According to the study protocol, patients in the HFNO group were extubated earlier, with mean± SD PaO2/FiO2Ratios of 173±14 compared to patients in the conventional group, who were extubated with mean± SD PaO2/FiO2Ratios of 265±60 (P<0.05). Post-extubation PaO2/FiO2ratios were significantly less in the HFNO group (168±22) compared with the Conventional group (264±55) (P<0.05). (Table 7 & Figure 7)

Table 7: PaO2/FiO2Ratios at different time intervals:

	HFNO (N=40)	**Conventional (N=40)**	**Mean Difference (95% Confidence interval)**	**P-value**
PaO2/FiO2AT ADMISSION	99 (29)	133 (38)	-33.9 (-48.0 To -18.8)	0.001
PaO2/FiO2PRIOR TO SBT	183(14)	291 (55)	-111.5 (-129.6 To -93.5)	0.001
PaO2/FiO2AFTER SBT	173(14)	265 (60)	-92.8 (-112.7 To -72.8)	0.001
PaO2/FiO2POST-EXTUBATION	168 (22)	264 (55)	-95.9 (-114.8 To -76.9)	0.001

Values expressed as Mean ±Standard deviation and analysed using independent t- test

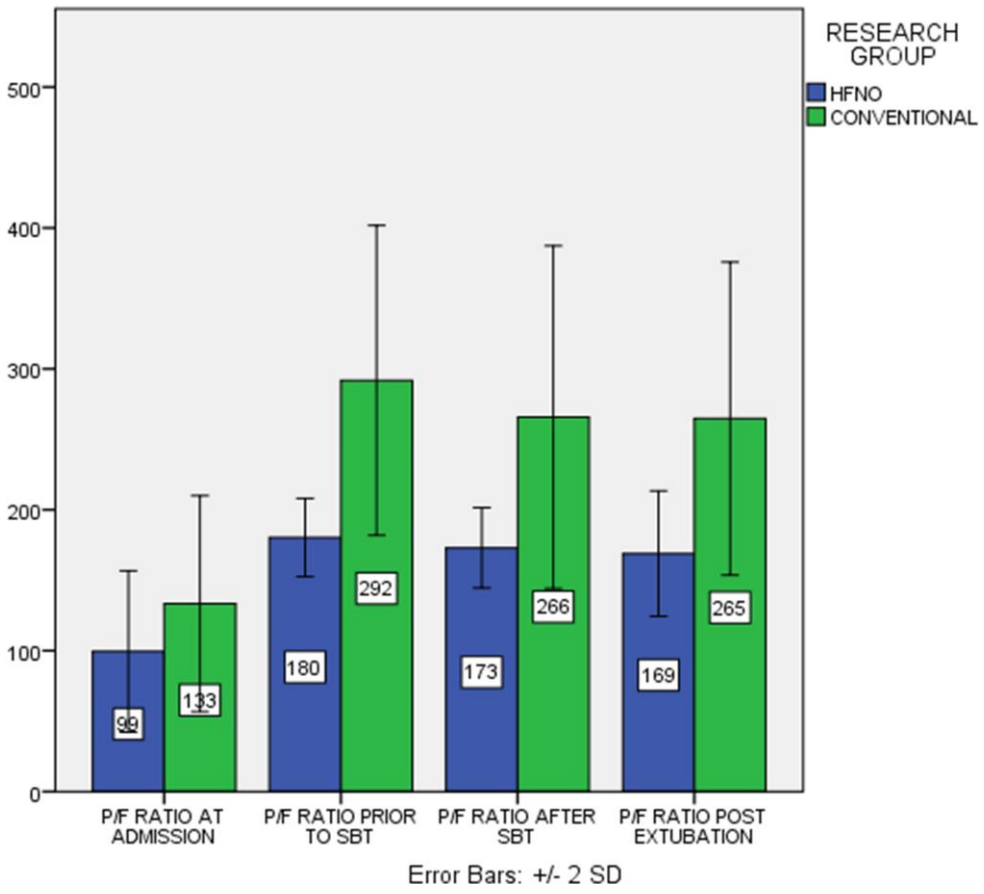

Figure 7: PaO2/FiO2Ratios at different time intervals

Rapid shallow breathing index values (RSBI):

Prior to the spontaneous breathing trial, mean± SD values of the RSBI in the HFNO and conventional groups were 70±12 and 64±14 respectively (P<0.05), while the RSBI following the SBT were 74±13 and 69± 14 respectively (P > 0.05) but both values were less than 105 and it was reasonable to wean the patients. (Table 8 & Figure 8)

Table 8: RSBI values:

	HFNO (N=40)	**Conventional (N=40)**	**Mean Difference (95% Confidence interval)**	**P–value**
RSBI PRIOR TO SBT	70 (12)	64 (14)	5.5 (-.18 To 11.3)	0.048
RSBI AFTER SBT	74 (13)	69 (14)	4.7 (-1.2 To 10.7)	0.119

Values expressed as Mean ±Standard deviation and analysed using independent t- test

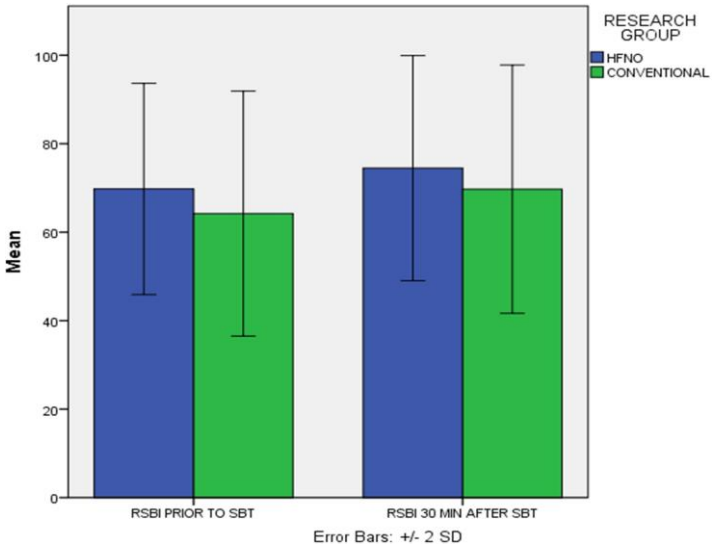

Figure 8: Rapid shallow breathing index values

Weaning failure (Extubation outcome):

According to study protocol weaning failure was defined as reintubation within 48hrs of extubation. Weaning failure was observed in 5 (12.5%) patients in HFNO group and 10 (25%) patients in the conventional group without any significant difference between the two groups (P=0.252) (Table 9 & Figure 9). Extubation failure risk was not significantly different with HFNO compared to conventional method [odds ratio,0.5; (95% confidence interval,0.188-1.332)].

Table 9: Extubation outcome

	HFNO (N=40)	**Conventional (N=40)**	**Chi-square value (P–value)**
FAILED EXTUBATION	5 (12.5%)	10 (25%)	2.051 (0.252)

Values expressed as number of patients (percentages) and analysed using chi-square test

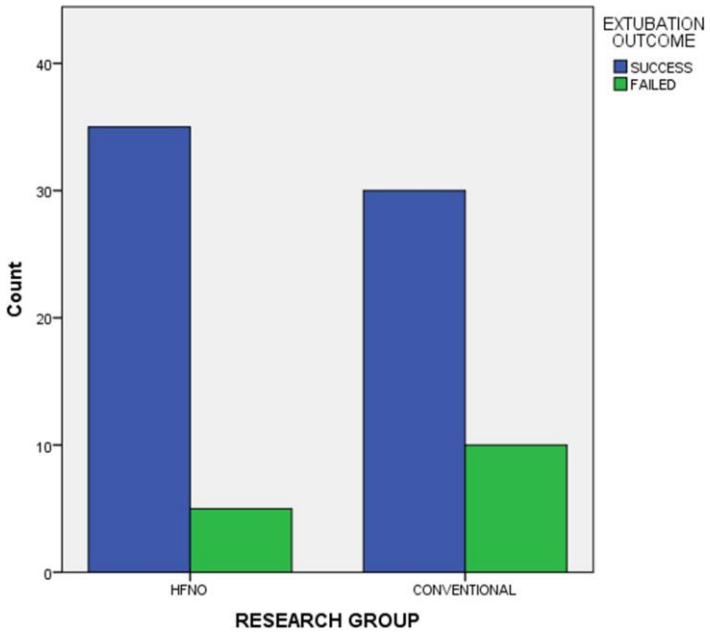

Figure 9: Extubation outcome

Invasive mechanical ventilation days:

Total median (IQR) invasive mechanical ventilation days in HFNO and Conventional groups were 5 (3.25-9.75) and 5 (3-7) respectively showing no significant difference between the two groups (P>0.05). (Table 10 & Figure 10)

Table 10: invasive mechanical ventilation days

	HFNO (N=40)	**Conventional (N=40)**	**Median difference (95% confidence interval)**	**P- value**
TOTAL IMV DAYS	5 (3.25-9.75)	5 (3-7)	0 (-1.00 to 3.00)	0.398

Values expressed as median (Interquartile range) and Mann Whitney U test was applied

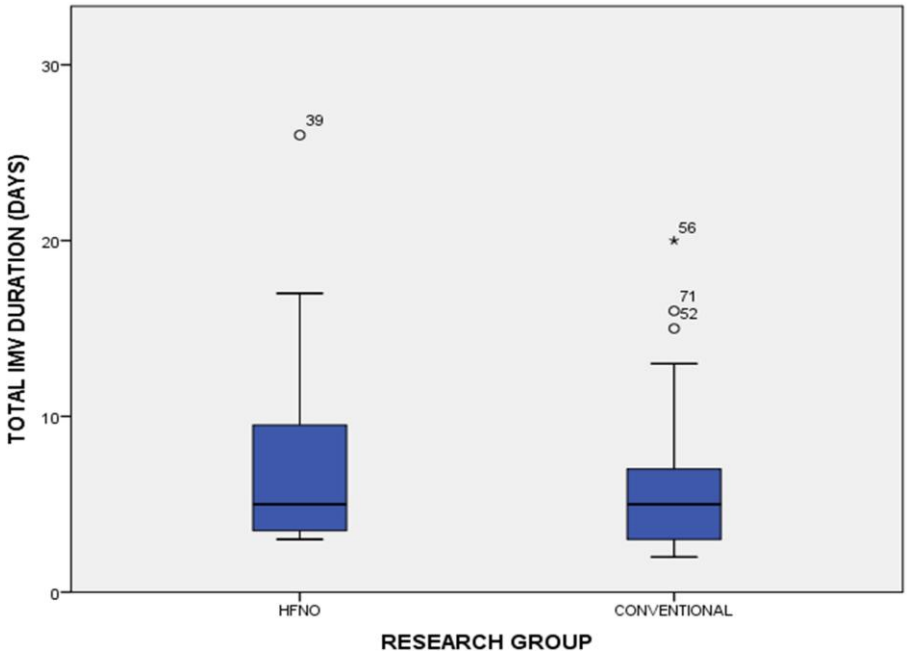

Figure 10: Invasive mechanical ventilation days

VAP Incidence:

Ventilator associated pneumonia was developed in 8 (20%) patients in the HFNO group and 5 (12.5%) patients in the conventional group without any significant difference (P>0.05). (Table 11 & Figure 11)

Table 11: VAP incidence

	HFNO (N=40)	Conventional (N=40)	Chi-square value (p-value)
VAP EVENTS	8 (20%)	5 (12.5%)	0.827 (0.546)

Values expressed as number of patients (percentages) and analysed using chi-square test

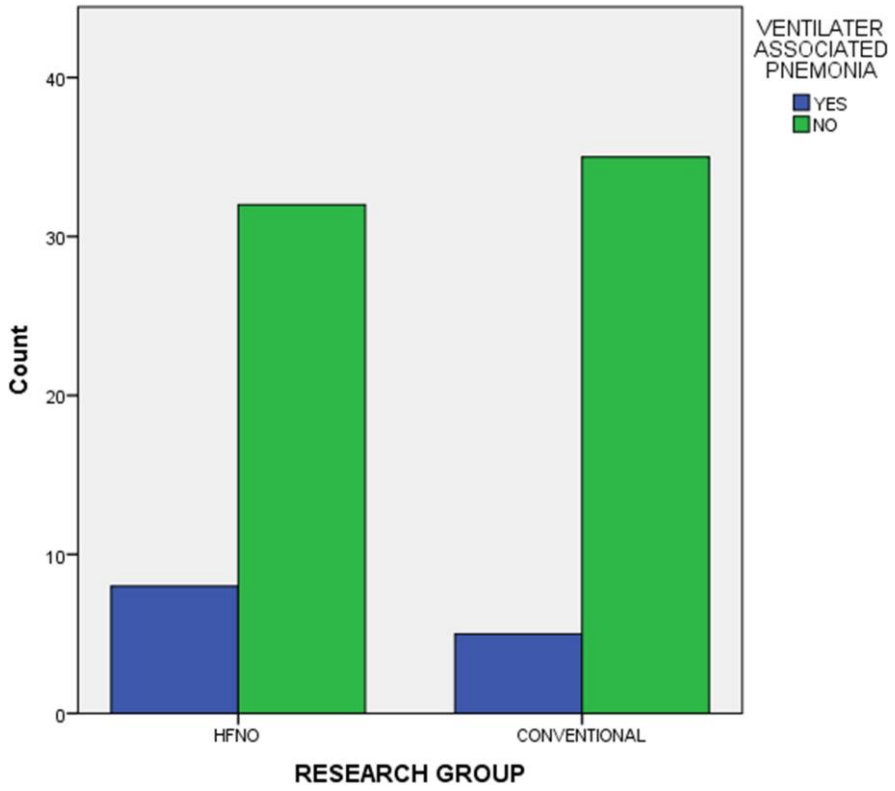

Figure 11: VAP Incidence

Total ICU length of stay (Days):

There was no statistically significant difference found in total days of ICU duration between HFNO and conventional group (p=0.067) (Table 12 & Figure 12)

Table 12: Total ICU length of stay (Days)

	HFNO (N=40)	Conventional (N=40)	Median difference (95% confidence interval)	P–value
TOTAL ICU LENGTH OF STAY	12 (7-17.5)	9.5 (7-13.75)	2.5 (-1.32 to 5.42)	0.067

Values expressed as median days (Interquartile range) and Mann Whitney U test was applied

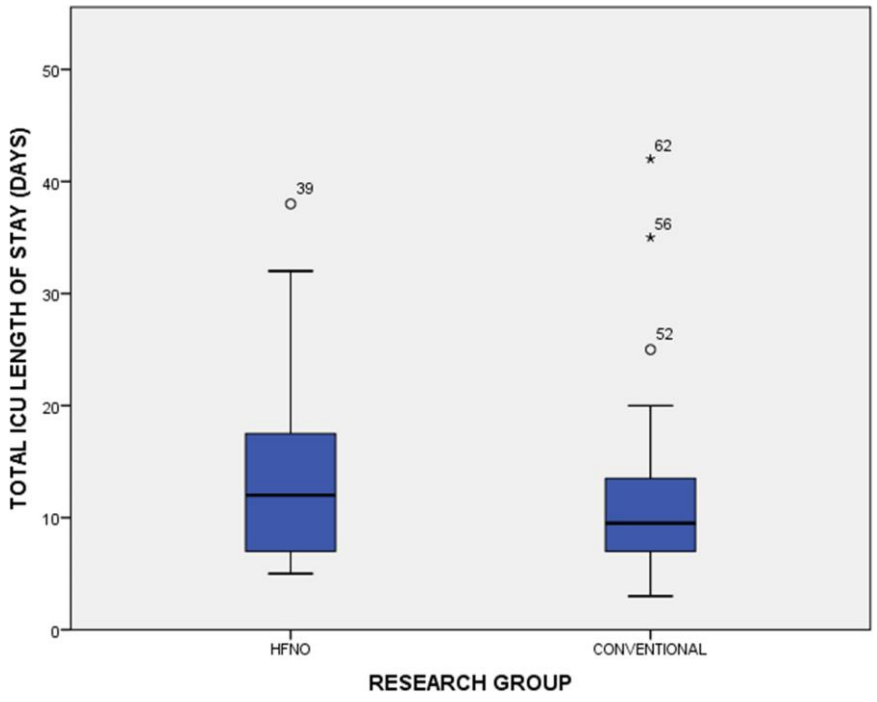

Figure 12: Total ICU length of stay (Days)

IMV free days:

The median (IQR) invasive mechanical ventilation free days in HFNO group and conventional groups were 5 (4-8) and 4 (2.25-6.75) respectively, which was significantly less in HFNO group (P=0.033) (Table 13 & Figure 13)

Table 13: IMV free days

	HFNO (N=40)	Conventional (N=40)	Median difference (95% confidence interval)	P–value
TOTAL IMV FREE DAYS	5 (4-8)	4 (2.25-6.75)	1 (-1.01 to 3.11)	0.033

Values expressed as median (Interquartile range) and Mann Whitney U test was applied

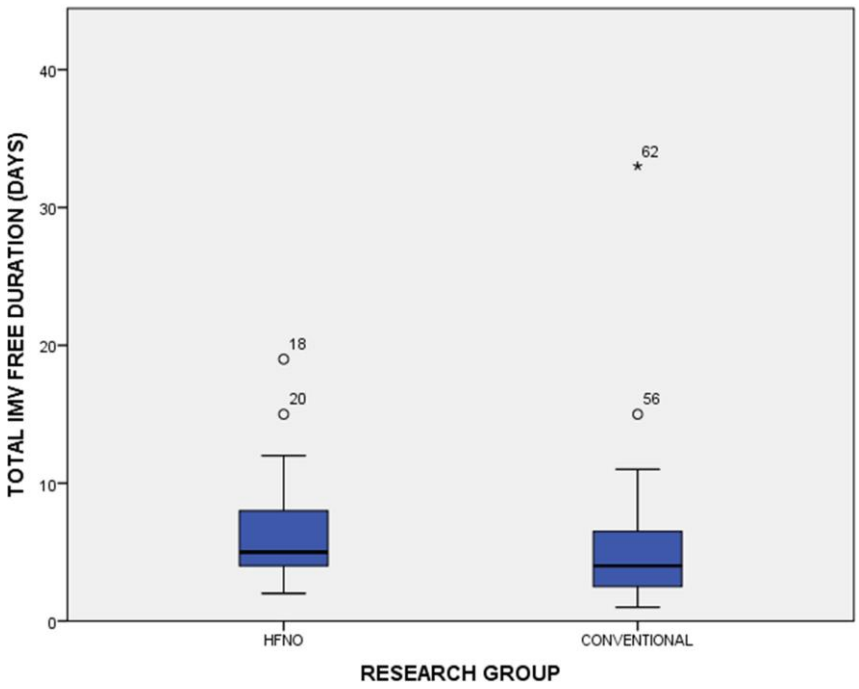

Figure 13: IMV free days

Total days of sedation requirement:

Total median (IQR) days of sedation requirement in HFNO and conventional groups were 5 (3-10) and 5 (3-7) respectively, which was comparable between the two groups (P=0.356). (Table 14 & Figure14)

Table 14: Total days of sedation requirement

	HFNO (N=40)	Conventional (N=40)	Median difference (95% confidence interval)	P–value
TOTAL DAYS OF SEDATION REQUIREMENT	5 (3-10)	5 (3-7)	0 (-.61 to 3.06)	0.356

Values expressed as median (Interquartile range) and Mann Whitney U test was applied

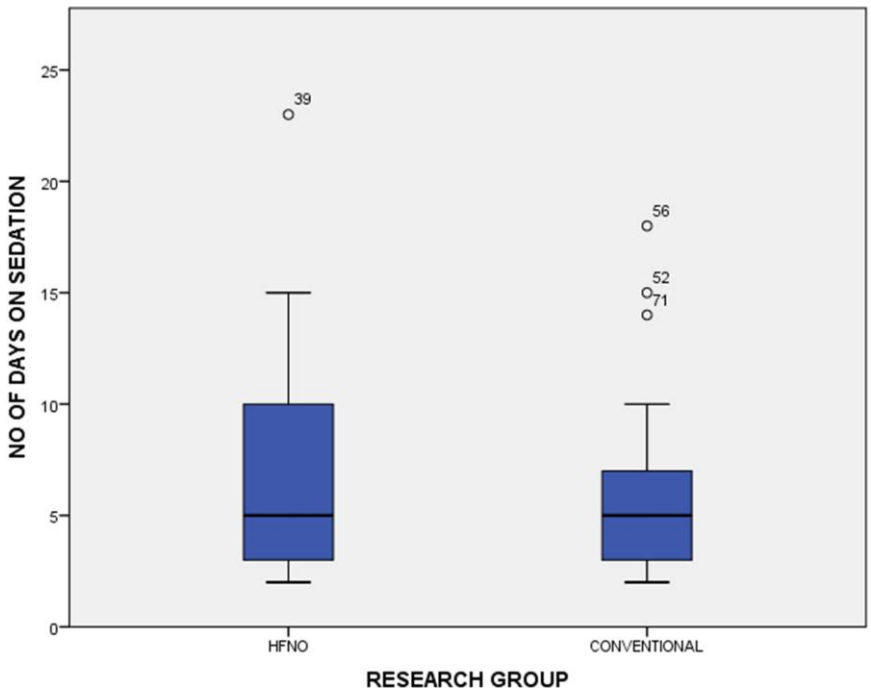

Figure 14: Total days of sedation requirement

All-cause mortality:

Out of a total 80 patients 2 (5%) patients in the HFNO group and 5 (12.5%) patients in the conventional group expired during ICU stay, which was comparable between the two groups (P=0.432). (Table 15 & Figure 15). All-cause mortality risk was not significantly different with early weaning using HFNO compared to conventional weaning method [odds ratio, 0.368 (95% confidence interval,0.067 – 2.023)]

Table 15: All-cause mortality

	HFNO (N=40)	**Conventional (N=40)**	**Chi-square value (P value)**
ALL CAUSE MORTALITY	2 (5%)	5 (12.5%)	1.409 (0.432)

Values expressed as number of patients (percentages) and analysed using chi-square test

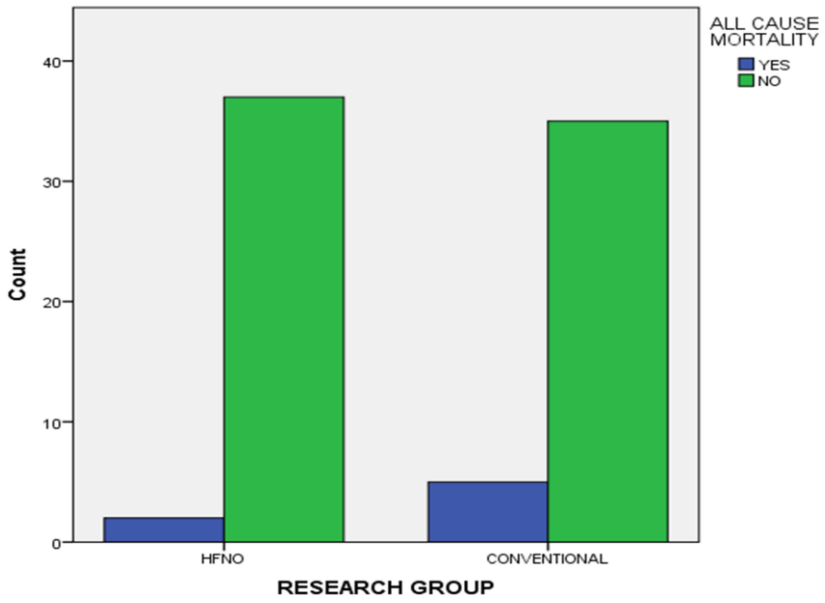

Figure 15: All-cause mortality

Reintubation after 48hrs of extubation:

Only 1 (2.5%) patient in the HFNO group and 3 (7.5%) patients in the conventional group were reintubated after 48hrs of extubation, which was comparable (p=0.615) between the two groups. (Table 16 & Figure 16)

Table 16: Reintubation after 48hrs of extubation

	HFNO (N=40)	Conventional (N=40)	Chi-square value (P value)
REINTUBATION AFTER 48HRS OF EXTUBATION	1 (2.5%)	3 (7.5%)	1.053 (0.615)

Values expressed as number of patients (percentages) and analysed using chi-square test

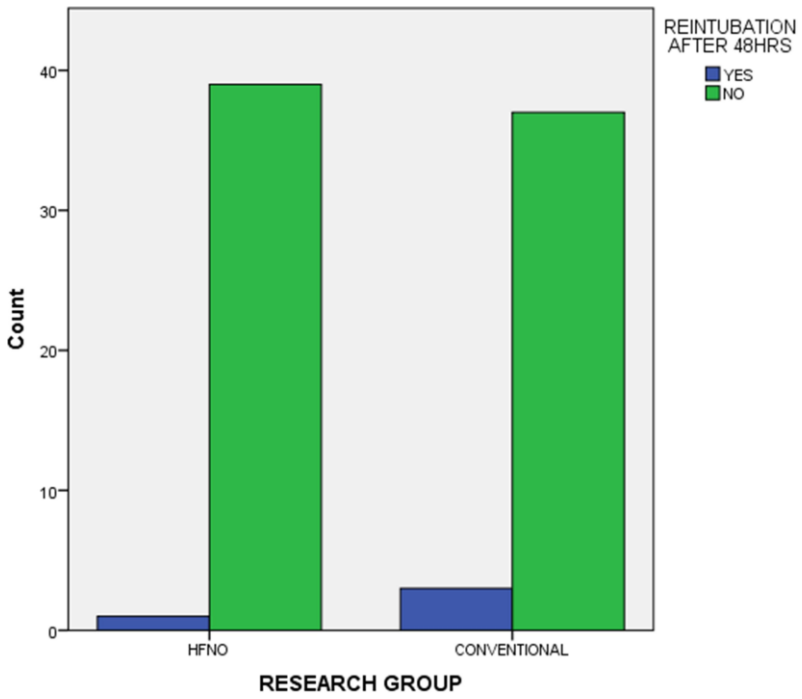

Figure 16: Reintubation after 48hrs of extubation

DISCUSSION

Invasive mechanical ventilation (IMV) requirement is one of the main reasons for intensive care unit (ICU) admissions. Invasive mechanical ventilation is a lifesaving therapy but prolonged invasive mechanical ventilation is associated with increase in mortality and morbidity.[1,2] Successful and early weaning from invasive mechanical ventilation is important to improve outcomes in critically ill patients in intensive care.[1] Physicians must weigh the benefits of prolonging IMV, which allows for better recovery, against the risks associated with prolonged invasive ventilation such as pulmonary infections, delirium, muscle atrophy and mortality.

Application of non-invasive ventilation (NIV) after early extubation have been studied in hypoxemic as well as hypercapnic respiratory failure patients.[13,14] NIV has a clear indication only in hypercapnic patients and this matter is still debatable in hypoxemic respiratory failure.[25,26] According to a study done by Vaschetto et al[14], NIV may be used to facilitate early discontinuation of mechanical ventilation in selected patients with resolving hypoxemic respiratory failure. In their study they extubated the patients after achieving PaO2/FiO2≥225 with a minimum of 8 cm H_2O PEEP and 10 cm H_2O of pressure support. But there is no data available so far on the use of HFNO as a means to facilitate the process of early extubation from IMV in hypoxemic respiratory failure patients. So, in our study we applied HFNO therapy for early extubation after achieving the PaO2/FiO2 ratio of ≥150 with minimum PEEP of 5-8 cm H_2O and pressure support of 5 cm H2O compared it to conventional weaning method, where weaning trial was given after achieving PaO2/FiO2ratio of ≥200 with minimum PEEP of 5 cm H_2O and pressure support of 5 cm H_2O.

HFNO device provides high inspiratory flows (upto60 L/min) of a controlled mixture of actively warmed (32–37 °C) and humidified (up to 100% relative humidity) oxygen and air through nasal prongs, producing a reasonable positive end-expiratory pressure (PEEP)[22]. HFNO may aid in the prevention of weaning failure in early extubation through different mechanisms. First, controlled oxygen concentration may reduce transient hypoxic episode[23]. Second, high flow minimises CO2 rebreathing by washing out the nasopharyngeal dead space, which in turn lowers respiratory rate and minute ventilation[8]. Third, the minimal amount of PEEP may improve gas exchange and decrease work of breathing by preventing lung collapse[24]. The potential reduction of airway inflammation[24] and improving the patient comfort provided by the warmed and humidified inspired gases improves drainage of respiratory secretions[23].

HFNO has also been studied mostly in comparison with NRBM and conventional therapy in different study populations and showed some benefits. However, there was no literature comparing the use of HFNO for early extubation compared with conventional weaning method. Our study's main objective was to compare the weaning failure (reintubation within 48hrs of extubation) in the HFNO group and the conventional group.

Hernandez et al[9] performed a trial on the effect of post-extubation HFNO vs conventional oxygen therapy after achieving the PaO2/FiO2ratio of ≥150 with stable clinical parameters on reintubation in low-risk patients found reduced the risk of reintubation within 72hrs of extubation in HFNO group. Despite the proposed PaO2/FiO2ratio of ≥150 for extubation, the mean PaO2/FiO2 ratios prior to extubation in their study were 227±25 in the HFNO group and 237±34 in the

conventional group. In our study we strictly followed the oxygenation criteria for extubation targeting PaO2/FiO2of ≥150 in the HFNO group and ≥200 in the conventional group.

The main finding of our study was that in critically ill hypoxemic respiratory failure patients, early extubation on HFNO is as effective as the conventional method of weaning. The reintubation rate in the HFNO group was 12.5%, which was similar to the rates from previous reports in critically ill population[28]. In our study, the HFNO group had a lower reintubation rate within 48hrs (weaning failure) (12.5%) than the conventional group (25%) without significance (P=0.252). The seemingly higher number of weaning failures in conventional group could be attributed to significantly higher APACHE-2 scores in the conventional group [16 (9-19)] than HFNO group [10 (8-16)] (P=0.025). Song et al[10] conducted a study on the value of HFNO therapy compared to the conventional oxygen (air entrainment mask) therapy after extubation in patients with acute respiratory failure and found a significant increase in success rate in HFNO group (90%) than air entrainment mask group (63.3%) (p=0.012). In their study, all the patients were extubated on achieving the PaO2/FiO2ratio of ≥150 with FiO_2 of ≤ 0.4 and PEEP ≤ 8 according to their research protocol. In order to reduce the failure rates in the conventional group, we extubated the patients after achieving a PaO2/FiO2of ≥200 in the conventional group and a PaO2/FiO2of ≥150 in the HFNO and found no significant difference in weaning failure rates in our research (p=0.252). The risk of weaning failure with HFNO was not significantly different from the conventional method in our study [odds ratio,0.5; (95% confidence interval,0.188-1.332)].

A study done by Maggiore et al[23] in 105 critically ill patients found that HFNO oxygen therapy resulted in significantly better oxygenation, better patient comfort, and a lower reintubation rate (3.8%) during the 48 hrs of the study period than conventional oxygen therapy. Similarly, Hernández et al[9] in 527 adult patients atlow risk for reintubation also showed that HFNO application resulted in a significantly lower reintubation rate (4.9%) than conventional oxygen therapy (12.2%) within 72 hrs. However, the influence of HFNO for early extubation (PaO2/FiO2≥150) was not studied in these two studies. Our study extended the application of the HFNO for early extubation and found an effective alternative to conventional weaning.

In our study, reintubation rate is matching with the reported reintubation rates, where it ranges from 5%[29] to 13%[29,30] in low-risk groups and 22% to 24% in high-risk groups.[31,32] The proportion of patients who need to be reintubated for reasons other than those linked to their respiration mostly depends on the case mix, which differs greatly amongst ICUs and is not usually been reported in clinical trials. In our study weaning failure was defined as reintubation within 48hrs of extubation to avoid misinterpretation of results and in our study the patients reintubated within 48hrs were purely due to respiratory failure. Although this was not the objective of our trial, we observed that only one patient (2.5%) in the HFNO group and three patients (7.5%) in the conventional group required reintubation after 48 hours, which was comparable in two groups (P=0.615). The optimal length of high-flow oxygen therapy is unknown. In our study, high-flow oxygen therapy was administered until the patient was ready to begin low-flow oxygen therapy.

Total median invasive mechanical ventilation free days were significantly reduced in the HFNO group [5(4-8)] compared to the conventional group [4(2.25-6.75)] in our study (P=0.033). VAP was observed in 8 (20%) patients in the HFNO group and 5 (12.5%) patients in the conventional group with no significant difference in our study. Although fewer IMV free days would be expected to reduce VAP incidence, no difference in this secondary outcome was observed, most likely due to no significant difference in total invasive mechanical ventilation days or the sample size was too low to affect outcome variables. Hernandez et al[9] discovered no difference in ICU length of stay despite the fact that the HFNO group was associated with a lower rate of reintubation compared to conventional group in low-risk population (p=0.004). These results support our study's findings that there was no difference between the groups total median IMV days (P=0.398) and total median ICU length of stay(P=0.067). In spite of early extubation in HFNO group no differences in total mean IMV days were found, probably due to the significantly low PaO2/FiO2ratio at admission in the HFNO group (99±29) compared to conventional weaning group (133±38) (P=0.001).

All-cause mortality was seen in 2 (5%) patients in the HFNO group and 5 (12.5%) in the conventional group, which was comparable between the two groups (P=0.432) in our study. The risk of all-cause mortality was not significantly different between early HFNO weaning and conventional weaning [odds ratio, 0.368 (95% confidence interval, 0.067 - 2.023)]. Hernandez et al[9] examined the effects of post-extubation HFNO vs. conventional oxygen therapy on reintubation in low-risk patients and discovered no difference in ICU mortality (p=0.99). These resultsprovide additional evidence to support our study's finding that early extubation on HFNO did not affect mortality when compared to conventional weaning strategy.

Our sample size may not be adequate to assess the significant differences in weaning failure and other secondary outcomes. Future, multi-centre trials with a larger sample size are required before our results can be generalised.

LIMITATIONS

However, our study is not without limitations. The main limitations of our study are single centre trial, small sample size and this study couldn't be blinded. Some patient's PaO2/FiO2ratios were rapidly improved to ≥200 and we had to exclude those cases enrolled in the HFNO group. Significantly high APACHE-2 scores in conventional group and significantly low PaO2/FiO2ratios at admission in HFNO group might affect the results of our study.

CONCLUSION

In this Prospective, randomized controlled trial, a total of 80 patients undergoing invasive mechanical ventilation for hypoxic respiratory failure were analysed. Patients were randomly allocated into 2 groups. The patients were given a spontaneous breathing trial (SBT), when the patient was ready to wean based on clinical parameters and rapid shallow breathing index (RSBI) criteria. In the Conventional group, SBT was given on achieving PaO2/FiO2 ratio of ≥ 200, while in HFNO group, SBT was given on achieving PaO2/FiO2 ratio of ≥ 150 with PEEP of ≤ 8. All the patients were extubated after successful SBT and put on oxygen supplementation. Patients in the HFNO group received O2 through HFNO at 60 litres flow & 100% FiO2 and titrated to maintain SPO2 of ≥94% and RR ≤30. In the conventional group, patients received oxygen via venturi mask with flow titration to maintain SPO2 of ≥94%.

The major findings of our study are:

1. The study results showed no significant difference in weaning failure (defined as reintubation within 48hrs of extubation) in HFNO group as compared to conventional weaning group.

2. Study results also confirmed no significant difference in the incidence of ventilator associated pneumonia between the two groups.

3. There was no significant difference in total median (IQR) invasive mechanical ventilation days between the HFNO and conventional groups.

4. The median (IQR) invasive mechanical ventilation free days were significantly less in the HFNO group compared to the conventional group (P=0.033) in our study.

5. There was no statistically significant difference found in total days of ICU duration between HFNO and conventional groups.

6. Total median (IQR) days of sedation requirement in HFNO and conventional groups were comparable between the two groups in our study.

7. We found no significant difference in all-cause mortality between the two groups in our study.

8. We also observed that there was no significant difference in reintubation after 48hrs of extubation in two groups.

Finally, this was the first study to compare the feasibility of HFNO-assisted early extubation to the conventional method. We discovered that early extubation on HFNO is equally effective as the conventional method of weaning.

ETHICAL CONSIDERATIONS

Approval was obtained from the Institute Ethical Committee (IEC Reg. No. AIIMS/ IEC/ 2021/ 3313) before initiation of study. An informed written consent was obtained from the patient attendant in English/Hindi.

According to the modified guidelines set by ICMR 1994 and the Helsinki declaration (modified 2000) the following was adhered for all patients enrolled in the study:

The patients involved in the research project were informed of the methods, anticipated benefits and potential risks of the study and the discomfort it may cause and the remedies thereof.

Written informed consent was obtained.

Every precaution was taken to respect the privacy and confidentiality of the patient.

The patient has been given the right to abstain from the study or to withdraw consent to participate at any time of the study without reprisal.

Due care and caution were taken at all stages to ensure that the patient is put to minimum risk or suffer from irreversible side effects and probably benefit from study.

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ANNEXURE-1

All India Institute of Medical Sciences, Jodhpur, Rajasthan

(Informed Consent Form)

TITLE: EARLY WEANING FROM MECHANICAL VENTILATION USING HFNO vs CONVENTIONAL METHOD IN HYPOXIC RESPIRATORY FAILURE: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

Name of the Student: Dr HAREESH AYYAWAR Telephone no: 9700528518

Patient Identification No:_____

I_____S/O, D/O, R/O_____

Resident of_____give my full, free, voluntary consent to be a part of the study "Title: Early weaning from mechanical ventilation using HFNO vs conventional method in hypoxic respiratory failure: A prospective randomized controlled trial", the procedure and nature of which has been explained to me in my own language to my full satisfaction. I confirm that I have had the opportunity to ask questions.

I understand that my participation is voluntary, and I am aware of my right to opt out of the study at any time without giving any reason. I understand that the information collected and any of my medical records may be looked at by responsible individuals from AIIMS Jodhpur or from regulatory authorities. I give permission for these individuals to have access to my records.

Date: _____ _____

Place: _____ Signature/Left thumb impression

This to certify that the above consent has been obtained in my presence.

Date: _____ _____

Place: _____ Signature of the student

Witness 1	Witness 2
_____	_____
Signature	Signature
Name	Name

ANNEXURE-2

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर , राजस्थान

(सूचित सहमति पत्र)

शीर्षक: होइपोक्सिक इंजरी फलता में एचएफएनओ बनाम परंपरागत विधि का उपयोग करके यांत्रिक वेंटिलेशन से शुरुआती वीनिंग: एक संभावित यादृच्छिक नियंत्रित परीक्षण

छात्र का नाम: डॉ हरीश अग्रवाल टेलीफोन नंबर: 9700528518

रोगी पहचान संख्या: _____

मैं_____एस/ओ, डी/ओ, आर/ओ_____

_____के निवासी अस्पताल का एक विषय बनने के
लिए अपनी पूर्ण, स्वतंत्र, स्वैच्छिक सहमति देते हुए "शीर्षक: होइपोक्सिक इंजरी फलता में एचएफएनओ बनाम पारंपरिक विधि का उपयोग करके यांत्रिक वेंटिलेशन से शुरुआती वीनिंग: एक संभावित यादृच्छिक नियंत्रित परीक्षण", जिसकी शुरुआत और शुरुआत मेरी पूरी संतुष्टि के लिए मुझे अपनी भाषा में समझाया। मैं पुष्टि करता हूं कि मुझे पूछने का अवसर मिला है।

मैं समझता हूं कि मेरी भागीदारी स्वैच्छिक है, और मैं बिना कोई कारण बताए किसी भी समय अस्पताल से बाहर होने के अपने अधिकार से अवगत हूं। मैं समझता हूं कि एकत्र की गई जानकारी और मेरे किसी भी मेडिकल रिकॉर्ड को ए.आई.जोधपुर के विशेषज्ञ निरीक्षकों या नियामक अधिकारियों द्वारा देखा जा सकता है। मैं इन निरीक्षणों को मेरे रिकॉर्ड तक पहुंच की अनुमति देता हूं।

तारीख:_____ _____

स्थान: _____ हस्ताक्षर/बाएं अंगूठे का निशान

यह प्रमाणित किया जाता है कि उपरोक्त सहमति मेरी उपस्थिति में
प्राप्त की गई है। तारीख:_____ _____

स्थान:_____ छात्र के हस्ताक्षर

साक्षी 1 साक्षी 2

_____ _____

हस्ताक्षर हस्ताक्षर

नाम **नाम**

ANNEXURE-3

PATIENT INFORMATION SHEET

1. **Risks to the patients:** No interventions or life-threatening procedures will be done.

2. **Confidentiality:** Your participation will be kept confidential. Your medical records will be treated with confidentiality and will be revealed only to doctors/ scientists involved in this study. The results of this study may be published in a scientific journal, but you will not be identified by name.

3. Provision of free treatment for research related injury. Not applicable.

4. Compensation of subjects for disability or death resulting from such injury: Not Applicable.

5. Freedom of individual to participate and to withdraw from research at any time without penalty or loss of benefits to which the subject would otherwise be entitled.

6. You have complete freedom to participate and to withdraw from research at any time without penalty or loss of benefits to which you would otherwise be entitled.

7. Your participation in the study is optional and voluntary.

8. The copy of the results of the investigations performed will be provided to you for your record.

9. You can withdraw from the project at any time, and this will not affect your subsequent medical treatment or relationship with the treating physician.

10. Any additional expense for the project, other than your regular expenses, will not be charged from you.

ANNEXURE-4

रोगी सूचना पा

1. ◌े डलए ज◌ो™खम: क◌ोई ह™◌ेपया ज◌ीवन-धमकी ◌ी जाएगी।
र◌ोडग ◌ंडिय◌ा नह◌ीक
य◌ोक

2. गोपनीयता: आपकी भागीदारी को गोपनीय रखा जाएगा। आपके

मेडिकलररकॉ◌ि◌षकोगोपनीयता के साथ इलाज डकया जाएगा

और के वलइस अ◌ंयन मőशाडमल

◌ि◌◌◌ॉ4र◌ो◌ं व◌ैy◌ाडनक◌ोपत◌ा चलगे ◌ा।इस अ◌ंयन के पररर◌् ◌ाम एक वैy
◌ाडनकपडाक◌ा

मő◌ंक◌ाडशत हो सकत◌े ह,ल◌े डकनआपक◌ो न◌ाम स◌े पहच◌ाना नह◌ी◌ं ज◌ाएग◌ा।

3. अनुसंधानसंबंधीचोट के डलए डन: शु७उपचार की Dव3था। लागूनही।◌ं

4. ऐस◌ी च◌ोट स◌े उ◌ा७ डवकल◌ा◌ंगत◌ाय◌ा म◌ृw◌ुके डलए डवय◌ाक◌ा म◌ु आवजा:ल◌ाग◌ूनह◌ीह

5. डकस◌ी भी समय द◌ं◌ि◌य◌ा लाभ◌ोके न◌ुकसानके डबना डकस◌ी भ◌ी समय भाग ल◌े नके
डलए

D◌ि™ क◌ो 4त◌ं◌ात◌ाल◌े न◌े और अन◌ुस◌ंध◌ानस◌े व◌ापस ल◌े न◌े कडलए

4त◌ं◌ात◌ा,डजसके तहत डवयअqथा हकदार होगा

6. आपक◌ोज◌ुम◌ाषन◌ाय◌ाल◌ाभके न◌ुकस◌ानके
डबनाडकस◌ीभ◌ीसमयभ◌ागल◌े न◌े औरअन◌ुस◌ंध◌ानस◌े व◌ापस

लेने की पूरीआजादी है,डजस पर आप अqथा हकदार होगे।

7. अ◌ंयन मőआपकी भागीदारी वैकि™कऔर 4◌ै◌ि™कहै।

8. ◌ंदशषनक◌ी ज◌ा◌ंचक◌ी ◌ी ◌ंडत आपके ररकॉ◌ि◌षके डलए आपको उपल◌्

पररर◌् ◌◌ाम◌ोकराई जाएगी।

9. आप डकसी भी समय पररय◌ोजन◌ा स◌े व◌ापस ल◌े सकत◌े ह,और यह आपके ब◌ाद के
डचडकT◌ा

उपचार या उपचार डचडकाक के साथ संबंधको◌ंभाडवत नहीकरेगा।

10. पररयोजना के डलए कोई भी अडतरर Dय, आपके डनयडमत खचों के अलावा,

आपसेश७नहीं डलया जाएगा।

ANNEXURE-5

CASE RECORD FORM

Patient Sticker:

Name of the patient: Age: Sex:

Height: Weight:

Registration number:

SOFA score at admission: APACHE-2 score at admission:

Group: HFNO / Conventional weaning

Duration of illness:

Comorbidities:

Medications:

Diagnosis:

Date of hospital admission: Date of ICU admission:

Date of intubation:

Date of readiness to wean:

Total number of SBT attempts:

Reason for failed SBT: 1.

2.

Date of successful SBT:

Time & Date of extubation:

Extubation outcome:

Days of HFNO requirement (HFNO group):

Condition of the patient at the end of HFNO therapy: improved / not improved:

Subsequent therapy: Low flow oxygen therapy / Reintubation /Other

Days of oxygen requirement via venturi mask (conventional weaning group):

Reintubation after failed extubation: Yes / No

1. Within 48 hrs: Yes / No

2. After 48 hrs: Yes / No

Total no of IMV days: Total no of ICU days:

Total no of IMV free days:

Development of VAP: Yes / No

Antibiotics used with total number of days:

Organism identified:

Total no of days on sedation:

All-cause mortality:

Day of death in ICU:

Primary cause of death:

Significant events in ICU:

1.

2.

3.

	AT THE TIME OF ICU ADMISSION	**PRIOR TO SBT**	**30MIN AFTER SBT**	**30MIN POST EXTUBATION**	**DAY 1**	**DAY 2**	**DAY 3**	**DAY 4**	**DAY 5**
PEEP									
FiO2									
PaO2									
PaO2/FiO2									
PACO2									
FLOW									
RSBI									
RR									
SPO2									
HR									
BP									
LACTATE									

ANNEXURE-6

The Richmond Agitation–Sedation Scale:

Score	Term	Description
+4	Combative	Overtly combative or violent; immediate danger to staff
+3	Very agitated	Pulls on or removes tube(s) or catheter(s) or has aggressive behaviour toward staff
+2	Agitated	Frequent non purposeful movement or patient–ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	Spontaneously pays attention to caregiver
-1	Drowsy	Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice
-2	Light sedation	Briefly (less than 10 seconds) awakens with eye contact to voice
-3	Moderate sedation	Any movement (but no eye contact) to voice
-4	Deep sedation	No response to voice, but any movement to physical stimulation
-5	Unarousable	No response to voice or physical stimulation

ANNEXURE-7

Institutional Ethics Committee Certificate

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2021/3478 **Date: 12/03/2021**

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2021/3313**

Project title: **"Early weaning from mechanical ventilation using HFNO vs conventional method in hypoxemic respiratory failure: A prospective randomized controlled trial"**

Nature of Project:	**Research Project Submitted for Expedited Review**
Submitted as:	**D.M. Dissertation**
Student Name:	**Dr. Hareesh Ayyawar**
Guide:	**Dr. Pradeep Kumar Bhatia**
Co-Guide:	**Dr. Nikhil Kothari, Dr. Sadik Mohammed, Dr. Bharat Paliwal & Dr. Ankur Sharma**

Institutional Ethics Committee after thorough consideration accorded its approval on above project.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.
- In case of any issue related to compensation, the responsibility lies with the Investigator and Co-Investigators.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

Please Note that this approval will be rectified whenever it is possible to hold a meeting in person of the Institutional Ethics Committee. It is possible that the PI may be asked to give more clarifications or the Institutional Ethics Committee may withhold the project. The Institutional Ethics Committee is adopting this procedure due to COVID-19 (Corona Virus) situation. If the Institutional Ethics Committee does not get back to you, this means your project has been cleared by the IEC.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Praveen Sharma
Member Secretary

Member secretary
Institutional Ethics Committee
AIIMS,Jodhpur

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