Efficacy of High Flow Nasal Cannula Vs Non Invasive Ventilation in Acute Exacerbation of Chronic Obstructive Pulmonary Disease-A Randomized Control Study

Dr. Praveen. R

Associate Professor, Department of Respiratory Medicine, Sri Manakula Vinayagar Medical College and Hospital, Puducherry

ABSTRACT:

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous disease characterized by various symptoms with a significant impact on morbidity and mortality. Non-Invasive Ventilation Bilevel Positive Airway Pressure (NIV BIPAP) is the gold standard modality of treatment in patients with acute exacerbation of COPD with hypercapnic respiratory failure. High Flow Nasal Cannula is a newer modality and its role in AECOPD with hypercapnic respiratory failure is debatable. As there is little evidence comparing the NIV BIPAP and HFNC, this study aims to find the efficacy of HFNC over BIPAP in AECOPD with hypercapnic respiratory failure.

Objectives: To compare the efficacy of High Flow Nasal Cannula with Non-Invasive Ventilation Bilevel Positive Airway Pressure as an initial modality in Acute Exacerbation of Chronic Obstructive Pulmonary Disease by clinical parameters and Arterial Blood Gas analysis.

Methods: This randomized control study was conducted at the Department of Respiratory Medicine, SMVMCH, Puducherry, from September 2022 to March 2024. The participants were assigned to NIV BIPAP or HFNC groups by block randomization. They were assessed in terms of MMRC grade of breathlessness, Respiratory Rate, Pulse Rate, SpO2 and ABG parameters like pH, pO2, pCO2 at baseline, 2 hours and 6 hours respectively.

Results: There was a significant reduction in grades of breathlessness, respiratory rate, pulse rate and PCO2 levels in both the HFNC and the NIV BIPAP group compared to the baseline. There was a significant rise in SpO2 and pH levels compared to baseline in both the groups. There was a significant rise in PO2 levels from baseline to 6 hours in NIV BIPAP group which was not there in the HFNC group.

Conclusion: As the efficacy of HFNC is similar to that of NIV BIPAP in the improvement of clinical and ABG values, HFNC can be considered as a non inferior modality compared to NIV BIPAP in acute exacerbation of COPD.

***Keywords*:** Chronic Obstructive Pulmonary Disease, acute exacerbation, High Flow Nasal Cannula, Non invasive Ventilation Bilevel Positive Airway Pressure, efficacy, clinical and ABG parameters, non inferior.

Introduction:

Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction.[1] COPD is the leading cause of morbidity and mortality with varying prevalence across countries. The global prevalence of COPD according to Burden of Obstructive Lung Disease (BOLD) and other large-scale epidemiological studies is 10% and research from India estimated that 5.3% of persons 40 years of age and older had COPD.[2]

Air pollution, high temperatures, and bacterial and viral infections of the respiratory tract are the main causes of acute exacerbations of COPD.[3,4] An exacerbation of COPD is defined as an event characterized by dyspnea and/or cough and sputum that worsens over < 14 days. Exacerbations of COPD are often associated withincreased local and systemic inflammation caused by airway infection, pollution, or other insults to the lungs.[5] In acute exacerbation of COPD, Non non-invasive

ventilation is the preferred modality of treatment which aims to reduce the work of breathing and diaphragmatic dysfunction improving hypercapnia.[6] Most significantly NIV is associated with decreased mortality and morbidity. Claustrophobia, stomach distension, nose sores, throat dryness and nasal difficulties were linked to poor adherence to NIV.[7]

The above mentioned side effects can be reduced by high flow nasal cannula (HFNC) which is mainly used for acute hypoxemic respiratory failure. However, its usage has caused improvement in the reduction of dead space, improving ventilation, oxygenation and lowering hypercarbia in exacerbation of COPD. Some of its limitations are cost and air leaks.[8] As there are very few studies comparing the NIV and HFNC, this study aims to provide clinicians with valuable insights into the optimal management of respiratory failure in COPD by critically evaluating the strengths and limitations of each approach.

Objectives: To compare the efficacy of High Flow Nasal Cannula with Non-Invasive Ventilation Bilevel Positive Airway Pressure as an initial modality in Acute Exacerbation of Chronic Obstructive Pulmonary Disease by clinical parameters and Arterial Blood Gas analysis.

Study area and setting: The study was conducted in Sri Manakula Vinayagar Medical College and Hospital, Puducherry in the Department of Respiratory Medicine.

Study design: This was a hospital based, randomized control study with patients who received Non Invasive Ventilation were enrolled in the control group and who received High Flow Nasal Cannula were enrolled in the experimental group. CTRI registration has been done for the study.(CTRI/2023/04/051659)

Sample size: Sample size was calculated using OpenEpi. Version 3, open source calculator SSMean (comparing means). Considering the lower PCO2 values in HFNC group compared to the NIV group (50.8 ± 9.4 mmHg versus 59.6 ± 13.9 mmHg), in the study by Papachatzakis et al,[9] the sample size for the present study was calculated to be 58 at 95% confidence interval and 80% power. This sample size was rounded off to 60 (30 each in the 2 study groups).

Study duration: The study was conducted from September 2022-March 2024

Study participants: Patients with acute exacerbation of COPD to the Respiratory Medicine OPD and Emergency Medicine Department diagnosed by clinical and ABG parameters and patients who consented for the study were included in the study.

Randomization: Patients were randomized into two groups to receive either HFNC (experimental group) or BIPAP (control group) as the initial modality of treatment for acute exacerbation of COPD. Block randomization was performed in 1:1 ratio, with 2 blocks each of size 30 to achieve a sample size of 60 for the two treatment groups. A sample block randomization list was attached. The study coordinator prepared opaque envelopes containing the labels that were opened just after the patient arrived in the casualty containing the label "A" was applied for patients with HFNC and the label "B" was subjected to NIV BIPAP respectively.

Inclusion criteria: Patients with acute exacerbation of Chronic Obstructive Pulmonary Disease with Moderate Hypercapnic Respiratory failure; PCO2:45-65 mm of Hg; pH:7.25 – 7.35 were included in the study.

Exclusion criteria: Patients with Type I respiratory failure, massive aspiration, intolerance to NIV or NIV failure, severe ventricular/supraventricular arrhythmias, patients with neck and face trauma and patients who could not remove secretions were excluded from the study.

Study procedure:

After getting clearance from institutional ethics committee, patients with exacerbation of COPD diagnosed by clinical and ABG parameters were selected according to the inclusion and exclusion criteria. Informed and written consent was obtained from all participants. After the randomization procedure, the patients in group A were subjected to high flow nasal cannula and group B were subjected to NIV BIPAP respectively.

The HFNC machine used was *"inspiredO2FLO"* from Vincent Medical Manufacturing co., Limited. The patients from group A were subjected to this HFNC machine with a flow rate of 30-35 lit/min and a FiO2 to maintain SpO2 above 92% for 6 hours from the time of

assignment of the group. If there is a worsening of clinical and ABG parameters, the patients will be shifted to NIV BIPAP immediately. The NIV BIPAP instrument used in our study is *ResMed Lumis 150 VPAP ST*. Patients enrolled in group "B" were subjected to this modality in ST mode where IPAP and EPAP settings were modified according to patients' weight and tolerance. After subjecting the patients to any one of these modalities, they were assessed in terms of MMRC grade of breathlessness, pulse rate, respiratory rate, SpO2 levels and ABG values such as pH, PO2, PCO2 and HCO3 levels were measured at baseline, at the end of 2 hours and 6 hours after commencing the therapy.

Analysis of data:

Statistical analysis was performed using IBM SPSS statistics version 24 for Windows. Baseline characteristics of all study participants were analyzed using descriptive statistics. The data was described as mean plus or minus standard deviation (SD) and Interquartile range. Association between sociodemographic details and disease outcome were tested using Chi Square test. Comparison of Median data between the categories were tested using Wilcoxon sign Rank test, as appropriate. For all statistical tests, probability of P-value < 0.05 was considered significant.

Ethical issues

Institutional ethics clearance was obtained from the Research Committee and SMVMCH Ethics Committee (EC/75/2022) of Sri Manakula Vinayagar Medical College and Hospital, Puducherry.

Guidelines: Strengthening the reporting of observational studies in epidemiology (STROBE) statements – checklist of items were included in reporting of the study.

RESULTS:

Table 1: Sociodemographic details, symptoms of the participants in the experimental and control groups (n=60)

Characteristics	**Total (N=60)**	**Experimental group (HFNC) (N=30)**	**Control group (NIV BIPAP) (N=30)**
Age			
31-50	11(18.3)	5(16.7)	6 (20)
51-70	27(45)	14(46.7)	13(43.3)
71-90	22(36.7)	11(36.7)	11(36.7)
Gender			
Male	37 (61.7)	19(63.3)	18 (60)
Female	23(38.3)	11(36.7)	12(40)
Symptoms			
Breathlessness	59 (98.3)	29(96.7)	30(100)
Cough	57 (95)	29(96.7)	28(9.3)
Loss of appetite	31 (51.7)	22(73.3)	14(46.7)
Fever	21(35)	13(43.3)	8(26.7)
Chest pain	11 (18.3)	8(26.7)	3(10)
Loss of weight	6 (10)	4(13.3)	2(6.7)
Smoking status			

Chronic smoker	18(30)	8(26.7)	10(33.3)
Ex smoker	9(15)	6(20)	3(10)
Non smoker	33(55)	16(53.3)	17(55)

Table 2: Comparison of MMRC grades of breathlessness, PR, SpO2,PH,PCO2,PO2 levels from baseline to 2 hours,baseline to 6 hours and 2 hours to 6 hours with their respective p values in the HFNC group (p values < 0.05 is considered significant)

Parameters	**Values of variables**			**P values**		
	Baseline	**2 hrs**	**6 hrs**	**Baseline vs 2 hrs**	**Baseline vs 6 hrs**	**2 hrs vs 6 hrs**
MMRC grade of breathlessness	3.87 ± 0.35	2.93 ± 0.25	2.90 ± 0.31	**<0.001***	**<0.001***	**0.32**
Pulse rate	110.8 ± 10.01	103.37 ± 9.89	99.40 ± 8.01	**<0.001***	**<0.001***	**<0.001***
Respiratory rate	30.23 ± 3.85	26.13 ± 3.48	23.73 ± 3.27	**<0.001***	**<0.001***	**<0.001***
SpO2 levels	79.67± 9.48	82.90 ± 7.03	84.70 ± 6.19	**<0.001***	**<0.001***	**<0.001***
PH levels	7.32± 0.02	7.36 ± 0.04	7.38 ± 0.04	**<0.001***	**<0.001***	**0.02***
PCO2 levels	60.77 ± 4.52	58.13 ± 7.87	56.90 ± 9.24	**0.033***	**0.01***	0.305
PO2 levels	60.00 ± 12.48	63.30 ± 14.38	67.60 ± 18.42	0.24	0.03	0.22

Table 3: Comparison of MMRC grades of breathlessness, PR, SpO2,PH,PCO2,PO2 levels from baseline to 2 hours,baseline to 6 hours and 2 hours to 6 hours with their respective p values in the NIV BIPAP group (p values < 0.05 is considered significant)

Parameters	**Values of variables**			**P values**		
	Baseline	**2 hrs**	**6 hrs**	**Baseline vs 2 hrs**	**Baseline vs 6 hrs**	**2 hrs vs 6 hrs**
MMRC grade of breathlessness	3.97 ± 0.18	3.00 ± 0.00	2.90 ± 0.31	**<0.001***	**<0.001***	**0.08**

Pulse rate	115.13 ± 10.24	104.30 ± 8.28	98.20 ± 7.52	**<0.001***	**<0.001***	**<0.001***
SpO2 levels	79.57 ± 6.97	82.83 ± 5.63	84.73 ± 5.00	**<0.001***	**<0.001***	**<0.001***
Respiratory Rate	31.57 ± 5.19	26.53 ± 4.15	23.10 ± 3.81	**<0.001***	**<0.001***	**<0.001***
PH levels	7.32 ± 0.03	7.37 ± 0.04	7.39 ± 0.05	**<0.001***	**<0.001***	**0.02***
PCO2 levels	59.80 ± 5.12	55.87 ± 7.32	54.67 ± 10.49	**0.002***	**0.008***	0.397
PO2 levels	63.07 ± 26.47	68.20 ± 16.89	68.97 ± 12.34	0.21	0.16	0.71

Table 4: Comparison of p values of MMRC grades of breathlessness, Pulse Rate(PR), Respiratory Rate (RR), SpO2 levels, pH, PCO2, PO2 levels among HFNC and NIV BIPAP groups at baseline, 2 hours and 6 hours respectively.

PARAMETER	FREQUENCY	HFNC	NIV BIPAP	P VALUES
MMRC grades	**BASELINE**	3.97 ± 0.18	3.87 ± 0.35	0.16
	2 HRS	3.00 ± 0.00	2.93 ± 0.25	0.15
	6 HRS	2.90 ± 0.31	2.90 ± 0.31	1
Pulse rate	**BASELINE**	115.13 ± 10.24	110.8 ± 10.01	0.1
	2 HRS	104.30 ± 8.28	103.37 ± 9.89	0.69
	6 HRS	98.20 ± 7.52	99.40 ± 8.01	0.55
Respiratory rate	**BASELINE**	31.57 ± 5.19	30.23 ± 3.85	0.26
	2 HRS	26.53 ± 4.15	26.13 ± 3.48	0.69
	6 HRS	23.10 ± 3.81	23.73 ± 3.27	0.49
SpO2 levels	**BASELINE**	79.57 ± 6.97	79.67± 9.48	0.96
	2 HRS	82.83 ± 5.63	82.90 ± 7.03	0.97
	6 HRS	84.73 ± 5.00	84.70 ± 6.19	0.98
PH levels	**BASELINE**	7.32 ± 0.03	7.32± 0.02	0.76
	2 HRS	7.37 ± 0.04	7.36 ± 0.04	0.48
	6 HRS	7.39 ± 0.05	7.38 ± 0.04	0.43
PCO2 levels	**BASELINE**	59.80 ± 5.12	60.77± 4.52	0.44
	2 HRS	55.87 ± 7.32	58.13 ± 7.87	0.25

	6 HRS	54.67 ± 10.49	56.90 ± 9.24	0.39
PO2 levels	**BASELINE**	63.07 ± 26.47	60.00± 12.48	0.56
	2 HRS	68.20 ± 16.89	63.30 ± 14.38	0.23
	6 HRS	68.97 ± 12.34	67.60 ± 18.42	0.74

DISCUSSION:

This study recruited 60 participants who had acute exacerbation of COPD presented to a tertiary care hospital in South India. Acute exacerbation of COPD contributes to significant morbidity and mortality among the elderly population. The majority of the participants in this study had an age group of more than 50 years of which males contributed to 61.7%.

Patients subjected to HFNC had a significant decrease in MMRC grade of breathlessness and respiratory rate (RR) compared to baseline values in similarity with a study done by Lise Piquilloid et al.[10].Likewise, there was a significant decrease noted in respiratory rates compared to baseline in patients receiving NIV BIPAP which was similar to a study conducted by Farmer MJ et al. which described the same.[11]

The fall in PCO2 in our study was pronounced compared to the baseline PCO2 levels in the HFNC group unlike the study from McKinstry et al. which concluded that there was an undetermined significance of HFNC in the reduction of PCO2 levels.[12]

Unlike the study by Yanping du et al. which showed a similarity in increasing PO2 levels among HFNC and NIV groups, there was no significant difference in PO2 levels in HFNC group noted in our study. But there was a significant increase in SpO2 levels in both the groups.[13]

Our study, when pH and PCO2 were concerned, there was a decrease in values of PCO2 and increase in the values of pH noted in NIV BIPAP as well as the HFNC group. A similar study by Cong et al.[14] compared the levels of pH and PCO2 with HFNC and NIV BIPAP. They concluded that the levels of PCO2 and pH were significant but among the groups there was no significant change noted.

REFERENCES:

1. Celli B, Fabbri L, Criner G, Martinez FJ, Mannino D, Vogelmeier C, Montes de Oca M, Papi A, Sin DD, Han MK, Agusti A. Definition and nomenclature of chronic obstructive pulmonary disease: time for its revision. American journal of respiratory and critical care medicine. 2022 Dec 1;206(11):1317-25.

2. Adeloye D, Chua S, Lee C, Basquill C, Papana A, Theodoratou E, Nair H, Gasevic D, Sridhar D, Campbell H, Chan KY. Global and regional estimates of COPD prevalence: Systematic review and meta–analysis. Journal of global health. 2015 Dec;5(2).

3. Konstantinoudis G, Minelli C, Vicedo-Cabrera AM, Ballester J, Gasparrini A, Blangiardo M. Ambient heat exposure and COPD hospitalisations in England: a nationwide case-crossover study during 2007–2018. Thorax. 2022 Nov 1;77(11):1098-104.

4. Li N, Ma J, Ji K, Wang L. Association of PM2. 5 and PM10 with acute exacerbation of chronic obstructive pulmonary disease at lag0 to lag7: a systematic review and meta-analysis. COPD: Journal of Chronic Obstructive Pulmonary Disease. 2022 Dec 31;19(1):243-54.

5. Celli BR, Fabbri LM, Aaron SD, Agusti A, Brook R, Criner GJ, Franssen FM, Humbert M, Hurst JR, O'Donnell D, Pantoni L. An updated definition and severity classification of chronic obstructive pulmonary disease exacerbations: the Rome proposal. American journal of respiratory and critical care medicine. 2021 Dec 1;204(11):1251-8.

6. Brochard L, Mancebo J, Wysocki M, Lofaso F, Conti G, Rauss A, Simonneau G, Benito S, Gasparetto A, Lemaire F, Isabey D. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. New England

Journal of Medicine. 1995 Sep 28;333(13):817-22.

7. Coleman III JM, Wolfe LF, Kalhan R. Noninvasive ventilation in chronic obstructive pulmonary disease. Annals of the American Thoracic Society. 2019 Sep;16(9):1091-8.

8. Fraser JF, Spooner AJ, Dunster KR, Anstey CM, Corley A. Nasal high flow oxygen therapy in patients with COPD reduces respiratory rate and tissue carbon dioxide while increasing tidal and end-expiratory lung volumes: a randomised crossover trial. Thorax. 2016 Aug 1;71(8):759-61.

9. Papachatzakis Y, Nikolaidis PT, Kontogiannis S, Trakada G. High-flow oxygen through nasal cannula vs. non-invasive ventilation in hypercapnic respiratory failure: a randomized clinical trial. International journal of environmental research and public health. 2020 Aug;17(16):5994.

10. Piquilloud L, Olivier PY, Richard JC, Thepot-Seegers V, Brochard L, Mercat A, Beloncle F. High flow nasal cannula improves breathing efficiency and ventilatory ratio in COPD patients recovering from an exacerbation. Journal of Critical Care. 2022 Jun 1;69:154023.

11. Farmer MJ, Callahan C, Hughes AM, Riska K, Hill N. How I Do It Applying non-invasive ventilation in treatment of acute exacerbation of chronic obstructive pulmonary disease using evidence-based interprofessional clinical practice. Chest. 2024 Feb 28.

12. McKinstry S, Singer J, Baarsma JP, Weatherall M, Beasley R, Fingleton J. Nasal high-flow therapy compared with non-invasive ventilation in COPD patients with chronic respiratory failure: A randomized controlled cross-over trial. Respirology. 2019 Nov;24(11):1081-7.

13. Du Y, Zhang H, Ma Z, Liu J, Wang Z, Lin M, Ni F, Li X, Tan H, Tan S, Chai Y. High-flow nasal oxygen versus noninvasive ventilation in acute exacerbation of chronic obstructive pulmonary disease patients: a meta-analysis of randomized controlled trials. Canadian Respiratory Journal. 2023 Jun 30;2023.

14. Cong L, Zhou L, Liu H, Wang J. Outcomes of high-flow nasal cannula versus non-invasive positive pressure ventilation for patients with acute exacerbations of chronic obstructive pulmonary disease. Int J Clin Exp Med. 2019 Jan 1;12(8):10863-7.