Original Article

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Comparison of High Intensity Non-Invasive Ventilation with Low Intensity Non-Invasive Ventilation in Patients with Acute COPD Exacerbation

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Author`s Contribution

[1,2]Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work, data collection, manuscript writing, Final approval of the version to be published
[3,4,5,6]Literature review/data analysis and Active participation in Methodology

Funding Source: None
Conflict of Interest: None

Received: June 6, 2021
Accepted: May 11, 2022

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ABSTRACT

Objective: To determine the outcome of high intensity non-invasive positive pressure ventilation (HI-NPPV) as compared to low intensity non-invasive positive pressure ventilation (LI-NPPV) in patients with chronic obstructive pulmonary disease (COPD) exacerbations.

Methodology: This randomized controlled trial study was conducted at the department of Pulmonology, Fauji Foundation Hospital Rawalpindi, from 31st December 2017 to 30th June 2018. Patients with COPD presenting in emergency and outpatient department of Fauji Foundation hospital in acute exacerbation are admitted. Arterial blood gases (ABGs) are taken at admission. Patients were randomly divided into two groups by lottery method. Group A receives HI-NPPV and Group B receives LI-NPPV by TRIOLOGY machine. Expiratory positive airway pressures (EPAP) remain between 4 to 6 cmH2O. ABGs done at baseline and then 72 h after admission. Improvement in PaCO2, HCO3, and FEV1 recorded 72 hours from baseline and collected on proforma.

Results: Mean age (years) in the study was 55.54+3.81. The outcome of the study was assessed in terms of mean PaCO2 (mmHg), HCO3 (mmol/L) and FEV1 at baseline and after 72 hours. Mean PaCO2, HCO3 and FEV1 at baseline was 64.87+5.22, 33.75+4.17 and 0.66+0.04 respectively. After 72 hours, mean PaCO2 (mmHg), HCO3(mmol/L), and FEV1 among both the groups were 63.98+6.58 vs 41.46+2.40, 33.10+4.81 vs 23.12+2.01, 0.66+0.05 vs 0.72+0.04 with following P value of (0,000, 0.000, 0.000) respectively.

Conclusion: HI-NPPV has no different outcome as compared with LI-NPPV in patients with acute COPD exacerbations.

Keywords: Chronic obstructive pulmonary disease (COPD), Non-invasive positive pressure ventilation (NPPV).

Cite this article as: sabir A, Khalil KF, Shafique A, Duad S, Ambreen A, Awan S. Comparison of High Intensity Non-Invasive Ventilation with Low Intensity Non-Invasive Ventilation in Patients with Acute COPD Exacerbation. Ann Pak Inst Med Sci. 2022; 18(2):98-103. doi. 10.48036/apims.v18i2.534

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by chronic inflammation of airways and lungs and is one of the major causes of morbidity and mortality worldwide.[1] It is fourth leading cause of death in the world.[2] The overall prevalence of COPD in Pakistan is 2.1%.[1] According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, the diagnosis of COPD is based on clinical symptoms, history of exposure to risk factors and confirmed by spirometery.[1] Risk factors for COPD include smoking, environmental tobacco smoke, genetic factors including alpha one (α_1) anti-trypsin deficiency, exposure to occupational dust, pulmonary infections, and bio-mass fuel exposure at home.[2] Other risk factors having COPD causing potential are under birth weight and specific

respiratory tract infection during earlier age in children, outdoor air pollution, and hypersensitivity of bronchi. Breathlessness, chronic cough and sputum production are major symptoms of COPD.[1]

Treatment of COPD comprises of pharmacological and non-pharmacological management including prevention of risk factors.[3] Non-invasive positive pressure ventilation (NPPV) is one of the non-pharmacological treatment that is considered the standard of care for managing acute exacerbation of COPD.[4] It is considered to reduce in-hospital mortality, improve blood gases and symptoms.[4] It is basically a delivery of positive pressure into lungs and is first option for ventilator support in acute exacerbation of COPD and should be considered in difficult weaning.[5]

Any patient who has a history of exposure to the COPD risk factors or has any symptoms, including Phlegm, chronic cough, or shortness of breath (SOB) should be evaluated clinically for COPD diagnosis. Spirometry is a necessary diagnostic tool, the reading of post-bronchodilator FEV1/FVC< 0.07 indicates the chronic airflow limitation and thus confirms COPD diagnosis.[6] Currently for the measurement of airflow limitation spirometry is the most reproducible tool.[6] It detects individuals with excessive lung function loss who are at higher risk of developing lung function impairment or who have disease already. Spirometric results are matched with standard reference values based on height, age, race and gender for evaluation. The reading of post-bronchodilator FEV1/FVC< 0.07 indicates the chronic airflow limitation and confirms COPD diagnosis.[6]

At present, no treatment has modified the rate of decline in lung function. The inhaled route is preferred.[7] The most important consequence of bronchodilator therapy appears to be airway smooth muscle relaxation and improved lung emptying during tidal breathing. The resultant increase in FEV_1 may be relatively small but is often accompanied by larger changes in lung volumes[7], with a reduction in residual volume and/or a delay of the onset of dynamic hyperinflation during exercise. Both of these changes contribute to a reduction in perceived breathlessness.[8] Generally, the more advanced the COPD, the more important the changes in lung volume become relative to those in FEV_1. Short-acting bronchodilators can increase exercise tolerance acutely.[8] Long-acting inhaled β-agonists (LABA) improve health status possibly to a greater extent than regular short-acting anticholinergics, reduce symptoms, rescue medication use and increase time between exacerbations compared with placebo.[9] Combining short-acting bronchodilator agents (salbutamol (albuterol/ipratropium) produces a greater change in spirometry than either agent alone.[9] Combining LABA and ipratropium leads to fewer exacerbations than either drug alone. No good comparative data between different LABA are currently available, although it is likely that their effects will be similar. Combining LABA and theophylline appears to produce a greater spirometric change than either drug alone.[10]

NPPV is delivered either through face mask or a nasal mask but Oronasal mask is best initial interface for leak prevention and patient's comfort.[11] Ventilator support can be achieved by variety of ventilator modes but Bi-level positive airway pressure (BiPAP) mode is mostly used. It generates inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP) gradients that compliment patient's own respiratory cycle, optimizing the lung's efficiency and reducing work of breathing.[11] High intensity non-invasive positive pressure ventilation (HI-NPPV) has physiological benefits compared to low intensity non-invasive positive pressure ventilation (LI-NPPV). HI-NVVP requires high inflation pressure (IPAP) and back up respiratory rate whereas LI-NVVP requires low IPAP and back up respiratory rate. Both approaches reduce hypercapnia and improve quality of life.[12] HI-NVVP is superior to LI-NPPV in decreasing raised PCO_2, improvement in dyspnoea during physical activity, lung function, and controlling nocturnal hypoventilation.[12]

International data have shown that HI-NIV has significantly better outcome in stable COPD in home settings.[18] However, its role in acute exacerbations is not clear. This study is being conducted to establish the role of HI-NIV over LI-NIV in acute exacerbations in the hospital based settings observing symptomatic and physiologic variables and arterial blood gases. This study aimed to determine the outcome of HI-NPPV compared with LI-NPPV in patients with acute COPD exacerbations.

Methodology

It was a randomized control trial conducted in Pulmonology Department at Fauji Foundation Hospital Rawalpindi. The duration of study was 6 months after approval of the synopsis i.e. 31st December 2017 to 30th June 2018. Simple random sampling was done for the

purpose of data collection. The sample size of 100 patients were included in the study with the following calculation by using WHO sample size calculator; Level of significance: 5%, Power of test: 80%, Population mean 0.649, Mean 0.979, Standard Deviation 0.28 and η 50 in each group.

There were eight male patients included in the study who met the inclusion criteria. Of these, 05 and 03 male patients were among both groups, respectively. Similarly, there were 92 female patients included in the study who met the inclusion criteria. Of these, 45 and 47 female patients were included in both the groups, respectively. Outcome of the study included mean change in paCO2 levels, HCO3 and FEV1 from baseline to 72hours after admission with $paCO_2$: Mean change from baseline to 72 hours as mean paCO2 in mmHg. Mean change from baseline to 72 hours as mean HCO3 in mmol/l. Mean change from baseline to 72 hours as mean FEVI in liters (L). Acute COPD exacerbation: Defined as increase in volume of sputum, change in sputum colour and increase dyspnea leading to decrease oxygen saturation (less than 88%). High inspiratory positive airway pressure (IPAP) up to 30cmH2O and high back up respiratory rate up to 18/mint. Low inspiratory positive airway pressure (IPAP) up to 15cmH2O and low back up respiratory rate up to 12/min.

Patients who were aged 40-80 years old with both genders, diagnosed cases of COPD with acute exacerbation, pH=7.25 to 7.35, paCO2 - 55 to75mmHg and current or Ex- smoker were taken as inclusion criteria whereas patients who refused to use NIV, Contraindication to use of NIV: these were as follow: Hemodynamic instability i.e., BP<90/60mmhg, pulse>140/min, Drowsy patient, Impending respiratory arrest, Pneumothorax, Inability to protect airway, Facial deformity/trauma, Significant comorbidities (unstable IHD, malignancy, psychiatric disorders), Obstructive sleep apnea syndrome, Exclusion criteria included other chronic respiratory diseases (tuberculosis, musculoskeletal disorders, pulmonary fibrosis, bronchiectasis, and acute upper GI bleed).

After approval from the hospital ethical committee and informed consent, COPD patients presenting in emergency and outpatient department of Fauji Foundation hospital in acute exacerbation were admitted. Arterial blood gases were taken at admission. If values of pH and $paCO_2$ met the criteria for non-invasive ventilation then patients were enrolled in the study. Patients were randomly divided into two groups by lottery method. GROUP A received high intensity NIV (HI-NPPV) and Group B (control group) received low intensity NIV (LI-NPPV) by TRIOLOGY 100 machine using S/T mode. Expiratory positive airway pressure (EPAP) were set between 4 to 6 cmH_2O. Arterial blood gases (ABGs) were done at baseline and then 72 hours after admission. Improvement in PaCO2, HCO3, and FEV1 was recorded 72 hours from baseline and collected on proforma.

The data was entered and analyzed using SPSS version 19. Descriptive statistics were calculated for qualitative variables like gender and quantitative variables like age, paCO2, HCO3 and FEV1 at baseline and after 72hrs. For qualitative variables, frequency and percentages were calculated, and for quantitative variables mean and standard deviation were measured. PaCO2, HCO3 and FEV1 were compared between the two groups by using independent student t test. Effect modifiers like age, gender, current and ex-smokers were controlled by stratification. Post stratification independent sample t test were applied. P-value ≤ 0.05 were considered as significant.

Results

The mean age (years) in the study was 55.54±3.81. The baseline readings for the outcome of the study were assessed in terms of mean $PaCO_2$ (mmHg), HCO3 (mmol/L) and FEV1. At baseline, the mean PaCO2 (mmHg), HCO3 (mmol/L), and FEV1 were 64.87+5.22, 33.75+4.17, and 0.66+0.04, respectively. The distribution of gender of patients was also calculated in terms of frequency and percentage of male and female patients among both the groups, as shown in Table I. Table II shows a comparison of the outcomes after 72 hours, including mean PaCO2 (mmHg), mean HCO2 (mmol/L), and mean FEV1.

Table I: Distribution of Gender,

		Two groups		Total
		group A	group B	
Gender	Male	5	3	8
		10.0%	6.0%	8.0%
	female	45	47	92
		90.0%	94.0%	92.0%
Total		50	50	100

Table II: Comparison of Outcome at 72 hours among both the groups,

Outcome	Two groups	n	Mean	Std. Deviation	p-value
$PaCO_2$ (mmHg)	group A	50	63.98	6.58	0.000
	group B	50	41.46	2.40	.
HCO_2 (mmol/L)	group A	50	33.10	4.81	0.000
	group B	50	23.12	2.01	
FEV1	group A	50	0.66	0.05	0.000
	group B	50	0.72	0.04	.

Discussion

Chronic obstructive pulmonary disease (COPD) is characterized by chronic inflammation of airways. Patients with COPD exacerbations have air trapping, hyperinflation, obstruction, increased respiratory effort and central respiratory drive, leading to increase level of blood carbon dioxide (paCO2) which readily crosses blood brain barrier causing altered mental status. Therefore such patients require rapid correction of alveolar hypoventilation which ensures an adequate tidal volume (8-12ml/kg)[2] .

The projection of the global burden of disease has estimated that the COPD may become the third leading cause of death worldwide by 2020 and the fourth cause of death by 2030.[13] Numerous surveys carried out by the Burden of Obstructive Lung Disease Stude (BOLD) have reported more severity in the disease as compared to the earlier estimated, and have reported a significant prevalence of COPD in the people who have never smoked.[14]

Treatment of COPD comprises pharmacological and non-pharmacological management, including prevention of risk factors.[3] Short-acting bronchodilators can increase exercise tolerance acutely.[15] In comparison to placebo, long-acting inhaled agonists improve health status, possibly more than regular short-acting anticholinergics[16], reduce symptoms, rescue medication use, and increase time between exacerbations.[17] Non-invasive positive pressure ventilation (NPPV) is one of the non-pharmacological treatments that is considered the standard of care to manage acute exacerbation of COPD.[4] It is considered to reduce in-hospital mortality, improved blood gases and symptoms.[4]

Ventilatory support can be achieved by variety of ventilatory modes, but Bi-level positive airway pressure (BiPAP) mode is mostly used. High intensity non-invasive positive pressure ventilation (HI-NPPV) has physiological benefits compared to low intensity non-invasive positive pressure ventilation (LI-NPPV). HI-NVVP requires high inflation pressure (IPAP) and back up respiratory rate, whereas LI-NVVP requires low IPAP and back up respiratory rate. Both approaches reduce hypercapnia and improve quality of life.[18]

Noninvasive ventilation (NIV) has been established as a useful and safe method to improve gas exchange for critically ill patients with different etiologies of acute respiratory failure (ARF). During past 20 years much research has been completed in comparing the effectiveness of NPPV (noninvasive positive pressure ventilation) to MV (mechanical ventilation). NPPV appears to improve pH levels and stabilize respiratory rates just as effective as MV without the complications often seen in latter. Its use has drastically increased in acute care setting to treat acute exacerbations of COPD, acute pulmonary edema related to heart failure, and acute respiratory failure.[19] Despite the positive outcomes of the use of noninvasive positive pressure ventilation (NPPV) in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), NPPV fails in approximately 15% of patients with AECOPD, possibly because the inspiratory pressure delivered by conventional low-intensity NPPV is insufficient to improve ventilatory status for these patients. High-intensity NPPV, a novel form that delivers high inspiratory pressure, is believed to more efficiently augment alveolar ventilation than low-intensity NPPV, and it has been shown to improve ventilatory status more than low-intensity NPPV in stable AECOPD patients.[20]

The study aimed to compare outcome of high intensity non-invasive positive pressure ventilation (HI-NPPV) as compared to low intensity non-invasive positive pressure ventilation (LI-NPPV) in patients with acute COPD exacerbations, these two groups were compared on basis of following 3 outcomes $PaCO_2$ (mmHg), HCO3 (mmol/L) and FEV1(L) at baseline and after 72 hours, where as another study conducted by Micheal Dreher and colleagues compared these outcomes at baseline and after 6 weeks. The mean age (years) in the study was 55.54$\pm$3.81, whereas another study conducted by killen herold and colleagues, showed that the mean age of all patients was 78.68 ± 10.42 years.[21]

In our study, there were 08 (8.0%) male patients who met the inclusion criteria. Of these, 05 (10.0%) and 03 (6.0%) male patients were distributed among both groups respectively. Similarly, there were 92 (92.0%) female patients meeting the inclusion criteria. Of these, 45

(90.0%) and 47 (94.0%) female patients were distributed among both groups respectively. As compared the study results, astudy conducted by killen herold showed that the ratio between female and male patients was 40.9% and 59.1% respectively.[21]

A study conducted by Micheal Dreher[18] showed much improvement in individuals who received HI-NPPV as compared to LI-NPPV but this study is conducted to see improvement in stable chronic hypercapnic respiratory failure and also included use of NIV in home settings over period of 6 weeks, where as our study was conducted on patients having acute COPD exacerbation in hospital settings over a limited duration of time, i.e, 72 hours.

There were a few limitations in this study. Most of our patients were female (92%) as Fauji Foundation Hospital is meant for families of x-servicemen, hence it may be a source of bias in our study. The study was conducted only on patients having acute hypercapnic respiratory failure, not in chronic type II respiratory failure. Mortality and future exacerbation risks were not assessed. The outcome was limited to improvements in arterial blood gas analysis. Results could be different if conducted by long term outcomes including 30 day mortality and exacerbations were evaluated. The study has many future implications. Better designed studies must be performed to assess long term mortality and future exacerbation risks. More male patients must be recruited in the studies to come. HI-NIV may be incorporated in separate NIV machines and cost of the devices can be reduced for wider application, usage and testing in more remote setups.

Conclusion

The study concluded that there was no significant difference in short term outcome using HI-NPPV and LI-NPPV in patients with acute COPD exacerbations. Further studies must be conducted in the future at multiple setups to know exactly the difference in terms of short term outcomes by using HI-NPPV and LI-NPPV for managing of acute COPD exacerbations.

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