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Effect of Oxygen Therapy Alone VS Home Non-Invasive Ventilation with Oxygen Therapy on Morbidity and Mortilty after an Acute Exacerbation of COPD

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Abstract:
Objective: To compare the effects of home non-invasive ventilation with oxygen therapy versus oxygen Therapy alone on patients of acute exacerbation of COPD
Study design: A Randomized Controlled Trial.
Place and Duration of Study: Department of Pulmonology Nishtar Hospital Multan from April 2016 to march 2018.
Methodology: A total of 194 patients were divided into two groups of 100 and 94. There were 100 patients who were randomized to home oxygen alone. The number of patients who were given oxygen therapy with non invasive ventilation was 94. The non invasive ventilation was applied according to preference of patients by using nasal or total face masks. To increase the oxygen level to 60 mmHg, oxygen therapy was started at the minimum flow rate in both groups. The patients who were on oxygen therapy alone were instructed to undergo at least 15 hours of oxygen therapy daily. For the patients of other group, a minimum of 6 hours nightly use of ventilator was instructed.
Results: Ninety four patients were put on oxygen therapy combined with non-invasive ventilation and 100 patients were put on just oxygen therapy. Both the groups were comparable in all baseline variables. After one year follow up, there was significant improvement in PaCO2, PaO2, St. George Respiratory Questionnaire summary score and Severe Respiratory Insufficiency Questionnaire summary score at most of the occasions (p-value <0.001 for all at 3 months; .060, .013, .527 and .002 at 6 months; and .011, .001, .002 and .090 at 12 months, respectively).
Conclusion: It can be concluded from this study that the amount of time it takes to be readmitted to the hospital or suffer death from acute exacerbation in patients suffering from COPD can be improved by adding non-invasive ventilation to the oxygen therapy.
Keywords: Chronic obstructive pulmonary disease (COPD), Non-invasive ventilation (NIV), Acute exacerbation of COPD.

Introduction:

Chronic obstructive pulmonary disease is a kind of lung disease which is obstructive in nature and is characterized by poor airflow and chronic breathing problems [(1)]. Symptoms of COPD include cough with sputum and shortness of breath [(2)]. It is a chronic progressive disease which gets worse with the passage of time. It gets so bad that it gets impossible to carry out everyday activities and the health related quality of life worsens with time [(3)]. Chronic obstructive lung disease can be either of two conditions; chronic bronchitis and emphysema. A person is said to have chronic bronchitis if he has productive cough for at least three months each year for two years. The most common cause of COPD is tobacco smoking. Air pollution and genetics are minor factors. Inflammatory response to the irritants results in breakdown of lung tissue and narrowing of lung airways [(4)]. Lung function tests are used to diagnose COPD. It can be differentiated from asthma as airway obstruction in asthma is intermittent and reversible and it gets better with the use of bronchodilators [(5)]. According to an estimate, it affected about 174.5 million of global population in 2015 [(6)]. It is the third leading cause of death worldwide [(7)]. Acute exacerbation of COPD can be defined as increased cough in someone suffering from COPD, increased sputum production and change of color of sputum from clear to yellow or green [(8)]. Signs of acute exacerbation may include sweating, fast breathing, confusion and combative behavior.

The best prevention for COPD is to reduce the exposure from risk factors like smoking and air pollution. Treatment can slow down the progression of disease but there is no definite cure. Treatments include respiratory rehabilitation, vaccination, inhaled steroids and bronchodilators, long term oxygen therapy and lung transplantation [(9)]. One treatment option for COPD is to do an oxygen therapy while other option is to add non invasive ventilation to this oxygen therapy. In this randomized controlled trial, we hypothesized that the time to

death or readmission in patients suffering from acute exacerbation of COPD will be prolonged by adding non-invasive ventilation to simple oxygen therapy.

Materials and Method:

This controlled trial was conducted at department of pulmonology in Nishtar Hospital Multan over a period of two years. The number of patients was 194 which were divided into two groups of 100 and 94. Ethical approval regarding this study was taken from the hospital ethics committee. The study which was taken as a reference for this trial was done by Patrick B. et al [(10)]. There were 100 patients who were given just oxygen therapy at home. Average flow rate of oxygen for them was 1.0 L/min. The number of patients who were given oxygen therapy combined with non-invasive ventilation was 94. The ventilator settings for inspiration were 24 cm H_2O of air pressure which was positive, 4 cmH_2O airway pressure, and backup rate of 14 breaths per minute. The non invasive ventilation was applied according to preference of patients by using nasal or total face masks. To increase the oxygen level to 60 mmHg, oxygen therapy was started at the minimum flow rate in both groups. The patients who were on oxygen therapy alone were instructed to undergo at least 15 hours of oxygen therapy daily. For the patients of other group, a minimum of 6 hours nightly use of ventilator was instructed. The patients were on optimized COPD management which included long acting beta agonists, antimuscarinics, and steroids. They were also educated on COPD self-management.

The patients who were included in the study were bound to have hypercapnia, hypoxemia and slightly acidic arterial pH while inspiring room air. The patients, who required invasive ventilation and intubation, were currently on home mechanical ventilation, showed cognitive impairment, had coronary artery disease were excluded from the study. The primary outcome of the study was the amount of time it takes to be readmitted to the hospital or suffer death after 12 months of randomization. Secondary outcomes included mortality due to all causes, frequency of exacerbations, change in arterial concentration of CO_2 and O_2 while inspiring room air, breathlessness, and health related quality of life. Hospital readmission and exacerbation data was collected at each follow up visits at 6 weeks, 3 months, 6 months and 12 months.

The data was presented as mean or median as appropriate. All the analyses were assessed for superiority. The analysis was done according to intention-to-treat principle. Two-sided significance level of 0.05 was concluded. All the data was collected by the researcher himself on a preformed Performa. Data was analyzed using the software SPSS v.23.

Results:

Ninety four patients were put on oxygen therapy with non-invasive ventilation and 100 patients were put on just oxygen therapy. Both the groups were comparable in all baseline variables i.e. age, BMI, gender distribution, COPD related hospital readmissions, smoking duration, neck and waist circumference, FEV_1, FVC, FEV_1/FVC ratio, PaO_2, $PaCO_2$, arterial pH, Medical Research Council Dyspnea Score, Severe Respiratory Insufficiency Questionnaire summary score and St. George Respiratory Questionnaire summary score, except apnea hypopnea index which was statistically different between the groups (p=.001). Table-I

After one year follow up, there was significant improvement in PaCO2, PaO2, St. George Respiratory Questionnaire summary score and Severe Respiratory Insufficiency Questionnaire summary score at most of the occasions (p-value <0.001 for all at 3 months; .060, .013, .527 and .002 at 6 months; and .011, .001, .002 and .090 at 12 months, respectively). Table-II and Table-III

Table-I

Baseline variables

Variable	HO +NIV (N=94)	HO Alone (n=100)	P value	Total (n=194)
Age (years), mean ±S.D	63.20±5.30	62.43±4.56	.277	62.80±4.94
BMI (kg/m^2), mean ±S.D	31.32±4.33	31.24±4.34	.899	31.28±4.32
Gender, M/F	68/26	66/34	.340	134/60
Prior use of O2 therapy, n (%)	60 (63.8)	58 (58)	.406	118 (60.8)
≥3 COPD related readmissions, n (%)	71 (75.5)	66 (66)	.145	137 (70.6)
Smoking history (pack years), median (IQR)	38 (36-43)	38 (35-41)	.251	38 (35.75-42)
Apnea Hypopnea index, median (IQR)	3.5 (2.2-4.7)	2.7 (1.9-3.65)	.001	2.85 (1.9-4.1)
Neck circumference (cm), median (IQR)	37 (33-41)	37 (36-39)	.075	37 (35-39.5)
Waist circumference (cm), median (IQR)	94 (85-96)	94 (88.25-96)	.094	94 (87-96)
FEV_1 (Liter), mean ±S.D	.65±.29	.72±.25	.081	.68±.27
FEV_1 %Predicted, mean ±S.D	26.62±8.07	28.60±7.18	.073	27.58±7.70
FVC (Liter), mean ±S.D	1.89±.44	1.85±.49	.606	1.86±.47
FVC %Predicted, mean ±S.D	60.39±14.37	58.86±12.05	.427	59.49±13.25
FEV_1/FVC, mean ±S.D	.36±.12	.35±.12	.757	.36±.12
PaO_2 at room air breathing (mmHg), mean ±S.D	50.25±7.40	50.19±6.67	.955	50.21±6.99
$PaCO_2$ at room air breathing (mmHg), mean ±S.D	58.84±8.06	60.59±8.18	.136	59.74±8.13
Arterial pH at room air breathing, mean ±S.D	7.40±.12	7.39±.13	.576	7.39±.12
St. George Respiratory Questionnaire summary score, median (IQR)	71 (65-79)	74 (68-79)	.561	72.5 (65-79)
Severe Respiratory Insufficiency Questionnaire summary score, median (IQR)	48 (39-58)	51 (41.5-60.5)	.104	50 (41-59)
Medical Research Council Dyspnea Score, median (IQR)	4 (3-5.25)	4.5(3.25-5.75)	.973	4 (3-5.25)

BMI=body mass index; COPD=chronic obstructive pulmonary disease; FEV_1=forced expiratory volume of air in first second; FVC=forced vital capacity

Table-II

Daytime Gas Exchange

Factor	Visit	Number of Patients		Median (IQR)		P value
		HO+NIV	HO Alone	HO+NIV	HO Alone	
PaCO2	Baseline	94	100	59 (53-65)	60 (54-68)	.148
	3rd month	80	83	51 (47-56)	59 (54-63)	<.001
	6th month	69	71	51 (45-58)	54 (45-58)	.060
	12th month	58	59	47 (45-51)	51 (45-54)	.011
PaO2	Baseline	94	100	49 (47-56)	49 (46-56)	.623
	3rd month	80	83	59 (54-65)	48 (45-51)	<.001
	6th month	69	71	58 (54-65)	56(51-59)	.013
	12th month	58	59	63 (55-66)	56 (54-60)	.001

Table-III

Health Related Quality of Life

Factor	Visit	Number of Patients		Median (IQR)		P value
		HO+NIV	HO Alone	HO+NIV	HO Alone	
Severe Respiratory Insufficiency Questionnaire summary score	Baseline	94	100	48 (39-58)	51 (41.5-60.5)	.104
	3rd month	80	83	74 (65-79)	68 (63-74)	<.001
	6th month	69	71	78 (64-81)	74 (68-81)	.527
	12th month	58	59	81 (76-83)	74 (65-81)	.002
St. George Respiratory Questionnaire summary score	Baseline	94	100	71 (65-79)	74 (68-79)	.561
	3rd month	80	83	62 (58-65)	71 (68-78)	<.001
	6th month	69	71	62 (56-65)	54 (59-71)	.002
	12th month	58	59	55 (48.5-58.3)	58 (55-62)	.090

St. George Respiratory Questionnaire summary score (100=worst, 0=best); Severe Respiratory Insufficiency Questionnaire summary score (100=best, 0=worst). (Note: N=194, student t-test for continuous data, chi-square for percentages, Mann-Whitney U test for median (IQR))

Discussion:

In this randomized trial, an improvement was observed after adding non-invasive ventilation to oxygen therapy after an acute exacerbation of COPD in time to fatality or readmission.

A lot of studies support the results of our study. A reduction in need for endotracheal intubation can be observed in COPD patients treated with non invasive ventilation [(11)]. Addition of non-invasive ventilation with positive pressure decreases the trend to retention of carbon dioxide and improves quality of life and dyspnoea [(12)]. Non invasive positive pressure ventilation improves parameters like lung function, gas exchange and breathing pattern [(13)]. When non invasive ventilation is targeted to reduce hypercapnia, it improves the survival of patients with hypercapnic stable COPD [(14)] where long term ventilation provides a better ventilation-perfusion match [(15)]. The principle mechanisms by which non invasive ventilation improves gas exchange in patients with COPD are decreased gas trapping and increased sensitivity to CO_2 [(16)]. In high intensity non invasive ventilation, the component which plays a therapeutic role in the management of COPD is high pressure [(17)].

There were some studies which contradict the results of our study. These studies suggest that addition of home non-invasive ventilation did not improve the duration of hospital readmission or time to death [(18)]. One trial concluded that the risk of life threatening events in patients with COPD increases with the addition of non-invasive ventilation [(19)]. A study also concluded that while the addition of non invasive ventilation to oxygen therapy increases the survival rate, it worsens the quality of life [(20)].

Conclusion:

It can be concluded from this study that the amount of time it takes to be readmitted to the hospital or suffer death from acute exacerbation in patients suffering from COPD can be improved by adding non-invasive ventilation to the oxygen therapy.

Conflicts of Interest: Nil
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