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Comparing and Investigating the Effects of Bi-level Non-Invasive Ventilator with High and Low Inspiratory Pressure in a Group of Patients Suffering from COPD Exacerbation over the Period of 2015-2016

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Chronic obstructive pulmonary disease (COPD) will restrict the airflow in an irreversible way. Periods of COPD exacerbation are filled with worse respiratory symptoms of patient along with dyspnea, coughing and phlegm. Using non-invasive mechanical ventilation (NIV) will reduce the long term treatment side effects, need for intubation and mortality. The present research seeks to investigate and compare the NIV with high and low inspiratory pressure in patients with COPD exacerbation. the present research is an interventional or clinical trial study conducted on a population of 40 people suffering from COPD Exacerbation over the period of years 2015-2016. These people were randomly placed in two groups of 20 people and NIV with high and low inspiratory pressure was taken into consideration for each group. Finally, the O2 saturation(O_2 sat), number of breathes and ABG (Arterial Blood Gas) before and one hour after NIV was checked for all patients. the results indicated that both groups were similar in terms of their age and age had no effect on results (P-value = 0.3704). Low inspiratory pressure caused significant changes in PH (P-value = 0.028) and respiratory rate (P-value = 0.0178). Meanwhile, all the factors studied exhibited significant changes under high inspiratory pressure. It was also shown that a significant difference would be caused between the two groups in terms of changes in CO2, PH, SO2, and respiratory rate factors that favor high inspiratory pressure. the results of this study showed that using high inspiratory pressure for patients suffering from COPD Exacerbation will improve factors of CO2, HCO3, PH, SO2, and respiratory rate when compared to using low inspiratory pressure. This fact is indicative of superiority of NIV therapeutic strategy with high inspiratory pressure.

Keywords: COPD, COPD Exacerbation, NIV, Respiratory rate.

Chronic obstructive pulmonary disease (COPD) is diagnosed with the irreversible restriction of air tracts. The main symptoms of this disease are dyspnea , coughing and sputum production[1]. Here are the different types of COPD: Emphysema (an anatomic state diagnosed through destruction and enlargement of the lung alveoli), Chronic bronchitis (a clinical state defined by chronic cough and phlegm) and Small airway disease (a state when small bronchioles are narrowed)[2].

Smoking is the most common cause of COPD. However, other factors such as air pollution and inheritance also play minor roles in causing it[3]. One of the main sources of air pollution in developing countries are fires in ovens and heaters that have no appropriate ventilation[4]. Diagnosing

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this disease is based on dyspnea and its level is measured through pulmonary function tests[5].

COPD exacerbation is diagnosed through acute deterioration of symptoms and signs of COPD such as dyspnea, coughing and mucosa intensity (more than usual daily changes). This state is usually caused by infection with bacteria or virus and environmental pollutants. Generally, infections cause 75% of the cases of COPD exacerbation. Bacteria is responsible for 25% of these cases, viruses cause another 25% of the problem. Both of these factors (virus and bacteria) are observed in 25% of the cases. During COPD Exacerbation, inflammation of respiratory tract increases the resistance of air tract, reduces airflow and decreases gas transfer[6, 1].

Utilizing short acting bronchodilators is usually a good method to partially improve the general state of body[3]. These medicines contain a mixture of beta agonists and inhaled anticholinergics which can be given to the patient through metered dose inhaler (MDI) with a spacer or nebulizer. Both of them are equally effective, however, prescribing the medicine with nebulizer is much easier for unstable patient[7]. Using inhaled Corticosteroids and antibiotics enhances the chances and possibility of recovery and shortens the length of symptoms[8]. Many antibiotics are used for this purpose, such as Amoxicillin, Doxycycline or Azithromycin[9]. Another treatment method in the cases of COPD exacerbation with high levels of co2 is NIV (non-invasive ventilation) which reduces need for intubation and mortality rate[5].

NIV can be defined as a ventilation modality that supports breathing with using a special mask without the need for intubation or surgical airway. Compared to other techniques such as laryngeal mask, tracheostomy, and tracheal tube, this is a non-invasive method. Using non-invasive ventilation in COPD Exacerbation with respiratory failure ($PaCO_2 > 45$ mm Hg) resulted in improved clinical state of the patient, improvement of respiratory gases state, less need for intubation and a shorter period of hospitalization[10]. By applying positive pressure in inhaling and exhaling and providing pressure support, this device improved ventilation and co2 excretion. It is generally recommended that applying NIV for these patients be initiated with an inspiratory pressure of 8-10 cmH2o and an expiratory pressure of 4 cmH2o[11].

Keeping in mind the importance and negative effects of COPD Exacerbation in society and, on the other hand, positive influence of NIV and its importance as a non-invasive method for these patients, the present research was conducted in order to study the effect of high and low inspiratory pressure on respiratory gas changes, respiratory rate and O2 sat. If a high inspiratory pressure has better effects on the clinical state and arterial blood gases, we may enhance the pace of the process of recovery by applying high pressure since the beginning of the process of treatment, prevent wasting time, lower the costs and reduce side effects.

MATERIAL AND METHOD

The present research is an interventional or clinical trial study conducted on a group of people suffering from COPD Exacerbation over the period of years 2015-2016. As many as 40 patients with respiratory failures (PCO2 > 45) who required NIV were included in the research. This sample size was determined according to the total number of patients hospitalized in pulmonary diseases unit of hospital.impaired mental status, facial trauma, upper airway obstruction, copious sputum and secretions in tracts, cardiac or respiratory arrest, frequent vomiting and increased risk of aspiration and, finally, existence of comorbidity or other pulmonary diseases along with COPD were defined as exclusion criteria.

Having explained the experiment for patient and his aid and after gaining their consent, the patients were randomly divided into two groups, each with 20 members. In the first group (Group A), NIV commenced with low inspiratory pressure (IPAP: 9-10, EPAP: 4). In the other group (Group B), however, the process of NIV was utilized with a high inspiratory pressure (IPAP: 15-17, EPAP: 4).

The arterial blood gas of all patients was checked before and one hour after NIV. During these measurements, changes in the levels of PCO2, PH, and HCO3 were measured and studied. O2 SAT and Respiratory rate and hospital length of stay were the other factors studied and investigated in both groups.

The demographic and clinical data of patients was collected and entered in research papers based on patient's history and characteristics. Based on the result of the experiment reported from hospital's laboratory, the laboratory data was written in research forms. The data was written in research forms based on the results gained in each procedure. The data was then fed to SPSS v.20 software and t-test and paired t-test were used to statistically analyze the data.

RESULTS

In the present clinical trial, 40 patients were divided into two groups. The average age of the participants in group A (IPAP: 9-10) and group B (IPAP: 15-17) was 68.65 ± 7.33 and 66.50 ± 7.67 respectively. The length of hospitalization was also studied in both groups. This period for groups A and B was 8.1 ± 3.23 and 7.5 ± 2.82 days

Table 1. Within group comparison: Each arm of the study is being compared within itself. The number of observations in all instances has been 20 for each arm (total = 20)

Arm of the study	Variable	Pre Mean (SD)	Post Mean (SD)	Mean difference	P-value[+]
iPap=9 to 10	CO2	59.90 (10.28)	58.15 (13.07)	1.75	0.1959
	HCO3	29.05 (4.89)	28.65 (5.24)	0.4	0.0724
	PH	7.399 (0.04)	7.392 (0.05)	0.0075	0.028
	SO2	87.15 (3.34)	87.95 (3.69)	-0.8	0.0685
	Respiratory rate	20.6	19.65 (3.23)	0.95	0.0178
iPap = 15 to 17	CO2	70.7 (10.32)	58.6 (11.29)	12.1	0
	HCO3	29.35 (2.08)	28.8 (2.12)	0.55	0.0077
	PH	7.388 (0.03)	7.41 (0.04)	-0.22	0
	SO2	85.8 (5.17)	88.9 (3.75)	-3.1	0
	Respiratory Rate	21.1 (2.75)	17.7 (2.10)	3.4	0

* The number of comparisons was 19. [+] Paired t-test

Table 2. Comparisons between two arms of the study. The number of observations in all instances has been 20 for each arm (total = 40)

Variable	iPap = 9 – 10 Mean (SD)	IPap = 15 – 17 Mean (SD)	P-value T-test
Age	68.65 (7.33)	66.50 (7.67)	0.3704
FEV1	48.75 (9.34)	45.60 (9.77)	0.304
CO2 pre	59.90 (10.28)	70.70 (10.32)	0.002
CO2 post	58.15 (13.07)	58.60 (11.29)	0.9072
HCO3 pre	29.05 (4.89)	29.35 (2.08)	0.8022
HCO3 post	28.65 (5.24)	28.80 (2.12)	0.9062
PH pre	7.40 (0.04)	7.39 (0.03)	0.3776
PH post	7.39 (0.05)	7.41 (0.04)	0.1824
SO2 pre	87.15 (3.34)	85.80 (5.17)	0.3328
SO2 Post	87.95 (3.69)	88.90 (3.75)	0.4248
Respiratory rate pre	20.60 (3.41)	21.00 (2.75)	0.6854
Respiratory rate Post	19.65 (3.23)	17.74 (2.10)	0.0359
CO2 (post – pre)	1.75 (5.85)	12.10 (2.73)	0
HCO3 (post – pre)	0.40 (0.94)	0.55 (0.83)	0.5059
PH (post – pre)	0.01 (0.01)	-0.02 (0.01)	0
SO2 (post – pre)	-0.80 (1.85)	-3.10 (2.22)	0.001
Respiratory rate (post – pre)*	0.95 (1.64)	3.37 (2.36)	0.0006

*The number of comparisons was 19

respectively. The statistical analyses showed no significant difference between the two groups in terms of the average age and length of hospitalization. This fact pointed to the similarity of age and length of hospitalization in both groups. It can also be interpreted as the lack of influence on the side of these two variables on other factors.

Variables such as CO2, HCO3, PH, SO2 and Respiratory rate and their changes under the influence of NIV were studied in each group. The results indicated significant changes due to this therapeutic measure in group A in variables of PH (P-value = 0.028) and respiratory rate (P-value = 0.0178). however, all these factors exhibited significant changes under the influence of the therapeutic measures applied to group B (Table 1).

The values corresponding to each variable were also compared with one another. The results of this study indicate the significant difference between primary and secondary variables of CO2 and Respiratory rate in both groups. It was also shown that the difference between changes in factors of CO2, PH, SO2, and respiratory rate is statistically significant (table 2).

DISCUSSION

This was an interventional or clinical trial research conducted in a group of patients suffering from COPD Exacerbation over the period of 2015 to 2016 in order to study the high and low inspiratory pressures in respiratory gas changes and respiratory rate. The results of this research indicate the success of using NIV method, particularly by applying high inspiratory pressure in patients suffering from COPD Exacerbation. It has been proven that using high inspiratory pressure results in a significant improvement in all the factors measured and also Respiratory rate (table 1). The comparison of changes between groups A and B was indicative of the fact that a significant difference existed between pre- and post-NIV changes for each variable that points to the superiority of utilizing high inspiratory pressure for these patients (table 2). A review of the literature showed that the results achieved in this research are in line with the results of previous studies.

In order to confirm the importance and success of using NIV method, Becker *et al* (2011) showed that treatment with this therapeutic measure is a good strategy and, compared to other medical treatments, improves the blood gases [12]. Murphy *et al* (2013) introduced utilization of NIV in acute phase of COPD assault as an effective factor to improve hyper-capnia and acidosis and prognosis[13]. On the other hand, similar studies conducted in this field have also introduced utilization of NIV as the Gold Standard for treating COPD assault[14] which reduces intubation, mortality and the length of hospitalization[14, 15]. Of course, using these therapeutic measures over a long time is not recommended[15].

In a research conducted by Dreher *et al* (2011), the effect of NIV pressure on quality of sleep was studied. The results of this groups pointed to no significant difference in sleep quality of HI-NPPV and Low-NPPV groups. However, lower levels of PaCO2 were observed in HI-NPPV group. According to them, a higher pressure was more successful in preserving the appropriate ventilation of alveoli[16].

In another research conducted by Lukacsovits *et al* (2011), physiological changes while receiving low intensity and high intensity NIV were compared against one another. High intensity ventilation was assigned to one group in order to achieve the highest reduction of PaCO2 (IPAP = 27.6 ± 2.1, EPAP = 4, RR = 22), while low intensity ventilation was assigned for the other group (IPAP = 17.7 ± 1.6, EPAP = 4, RR = 12). The status of blood gases in comparison with spontaneos breathing had enhanced. In the group that had received HI-NPPV, blood gases had improved more, a greater reduction was observed in the PTP (Pressure Time Production) of diaphragm per minute and we witnessed a significant reduction of Cardiac Output[17]. As we see, the results achieved in the current research are in line with this report.

In 2009, Dreher *et al* conducted a research with the goal of the inductive analysis of high intensity and low intensity NIV effects on Stable hypercapnic COPD patient. This research included 17 patients suffering from severe hypercapnic COPD who were studied for 6 weeks under the 2 groups of HI-NPPV and LI-NPPV. It was finally stated that only among those treated by HI-NPPV, a significant improvement of shortness of breath, day long PaCO2, FEV1 and vital capacity was

observed[18]. The results achieved in our research confirmed this group's results.

CONCLUSION

As the results of this research indicate, using high inspiratory pressure for patients suffering from COPD yielded better results in terms of CO2, HCO3, PH, SO2, and Respiratory rate factors compared to low inspiratory pressure. Considering these results and comparing them against the results of other researches, it is recommended to use high inspiratory pressure as a therapeutic strategy in order to prevent wasting time, reduce costs, and improve the clinical state of patients as soon as possible.

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