

Efficacy of NiPPV in Management of Chronic Obstructive Pulmonary Disease in Intensive Care Unit

Ojum S.

Department of Anaesthesia, Rivers State University Teaching Hospital, Port Harcourt

Abstract: Chronic obstructive pulmonary disease (COPD) is a type of progressive lung disease characterized by chronic respiratory symptoms and airflow limitation. A cardinal symptom of COPD is the chronic and progressive shortness of breath, as most characteristic of the condition. Shortness of breath is often the most distressing symptom, responsible for the associated anxiety and level of disability experienced [28]. COPD is incompletely reversible poor airflow (airflow limitation) and inability to breathe out fully, trapping air. The poor airflow is the result of small airways disease, emphysema, and breakdown of lung tissue. The relative contributions of these two factors vary between people; air trapping precedes lung hyperinflation. COPD currently has no cure, but the symptoms are treatable, and its progression can be delayed by reducing exposure to risk factors, including offering non-pharmacological treatments, such as stopping smoking that will reduce the rate of lung function decline, which in turn reduces mortality. Current treatment involves vaccination, medical treatment, bronchodilators, and antibiotics. In the management of acute hypercapnic respiratory using non-invasive positive pressure ventilation (NiPPV), which is known to be effective in acutely raised levels of carbon dioxide, bi-level positive airway pressure BPAP can decrease mortality and the need for intensive care for end-stage disease; palliative care may be used to support breathing and also reduce daytime breathlessness. There are still great concerns in some patients; it is ineffective and causes delays in moving them to invasive ventilation, and this may worsen the outcomes. Hence, we conducted a retrospective study of 48 COPD patient records. Initially all patients underwent inhalational therapy. Group 1 was 23 and group 2, 25. (36)75% of the total had 3 times inhalational, while the remaining had 2 times only. Group 1 (18) had 78.2% had 3 times inhalational therapy, while group 2 had (15) 69.5% of the patients. Group 1 was treated with NiPPV in PSV or Bi-level mode and increased FiO₂; Group 2—with O₂ therapy only. Medical therapy was prescribed regardless of their group allocation. It was seen that the rate of intubation in group one was lesser than that of group 2. Intubation of patients in Group 1: only 6 (26%) that received non-invasive ventilation were intubated as compared to 17 (68%) in Group 2 that were not ventilated. The mortality rate in Group 1 was 21.7% (5 deaths), while in Group 2 the mortality rate was 36.0% (9 deaths). In the analysis of the length of stay in the hospital and ICU, the length of stay in the hospital was statistically near significance; the actual value for group 1 was 20.8±11.3 days, while in group 2 it was 29.1±12.3 days (p=0.063). While looking at the length of stay in ICU, no significant difference was found between the groups: 14.7±12.2 days and 10.8±7 days, respectively (p=0.178). There was evidence in favour of the efficacy of NiPPV in COPD patients with acute exacerbation in terms of mortality and tracheal intubation. No difference in hospital and ICU length of stay was found.

Key points: COPD, Hypercapnic Respiratory Failure, Mechanical Ventilation, Non-invasive ventilation.

Introduction

Chronic obstructive pulmonary disease is very fatal worldwide [8]. The World Health Organization has reported that in 2030 COPD will be the third leading cause of mortality [11]. The clinical states

of patients with chronic obstructive pulmonary disease (COPD) are often dominated by periods of intensification of symptoms; this aggravation leads to the worsening of the clinical state of the patient, which in turn requires frequent hospitalization and is sometimes often accompanied by ventilatory support [19]. There are airflow limitations and alveolar hypoventilation; hence, gas oxygen exchange is hampered, and this causes damage in these patients. [3] The main component in the disease or chain of activity of COPD is the worsening of the disease; there is hypoxemia and hypercapnia. This is caused by progressing peripheral airway obstruction, which reduces pulmonary gas exchange ability, the massive destruction of pulmonary parenchyma, and the development of abnormalities of pulmonary vessels, which increases the frequency of acute exacerbation. These patients develop severe disease characterized by chronic respiratory failure and hypercapnia with severe dyspnoea; these patients often have low quality of life and high mortality. [21]

It has been postulated that long-term oxygen therapy was helpful in the management of these patients, as it improves hypoxemia, quality of life, and dyspnea. [13] Non-invasive positive pressure ventilation could improve gas exchange, as it will increase tidal volume and exert a positive airway pressure [5]. This in turn will reduce the workload on respiratory muscles and their fatigue [24], and improvement is recorded and a better response of the respiratory center to CO₂ [27]. There are reports showing that patients with respiratory failure benefited from NIV, as it improves their outcomes [19, 23]; other research showed high mortality with persistent hypercapnia [6, 26]. It was also stated that most patients after discharge were readmitted to the hospital in a short time [1, 7]. In 2007 some authors in their work found out that early initiation and use of non-invasive positive ventilation in patients with aggravated COPD reduced the time of rehospitalization or death by 12 months [20]. It is also stated that NIPPV could reduce hospital rates (9). Despite all the works, randomized controlled trials have no agreement in the application of NPPV in the treatment of COPD patients. Few authors have tried to evaluate mortality, frequency of acute aggravation of diseases, and hospitalization rates; they were not able to deduct clearly due to the lack of support. [22], recently several RCTs have evaluated the efficacy of NIV on stable COPD patients, as it concerns mortality and acute exacerbation [17,25].

In this study we postulate that early use of non-invasive positive pressure ventilation (NiPPV), improves the patients' treatment outcomes, mortality, and reduce the intubation rate, as compared to patients treated with standard of care using oxygen therapy.

MATERIALS AND METHODS

Study Design and Data Collection.

This study is a retrospective study, where data of patients that were admitted into Braithwaite Memorial Hospital were collected; all patients were diagnosed with COPD. The study was from January 2012 to October 2014. All patients were admitted into the ICU through the medical team, some via the ER or medical ward. Inclusion criteria are as follows: a diagnosis of moderate to severe chronic obstructive pulmonary disease (COPD) according to Vogel Meier et al. [15], and an age range between 25 and 60 years. Clinical criteria for inclusion are as follows: patients with aggravated COPD with at least two of the following criteria present on admission: respiratory rate (RR) > 30 per minute and active respiratory distress involving the accessory respiratory muscles. In ABG blood gas analysis, hypercapnia (PaCO₂ > 50 mm Hg) and respiratory acidosis (pH < 7.33). The exclusion criteria were advanced heart disease (NYHA class > 2) and classes of heart failure by the American Heart Association [10]. Unstable hemodynamics requiring vasopressors were needed on admission. Patients that were intubated within 6 hours after admission and those with severe neurologic conditions were also excluded (non-hypercapnic coma, disabling stroke, cognitive impairment, and deformation of the face that cannot allow proper fitting of NIV accessories for oxygen delivery and early admission into ICU due to COPD with intubation or tracheostomy placement within a year).

Data collection and collation, all patients were allocated according to the treatment done, basically two group: group A (NIV+O₂) or group 2 treated with only O). Group 1 was patient who was treated for COPD exacerbation with medical treatment and NiPPV, using ventilator made by

Dragger Germany. We ventilated our patients using the pressure support (PSV) and biphasic positive airway pressure (BiPAP) modes. Initially, level of inspiratory support was placed at 12 cm H₂O, as demanded clinically respiratory volumes were to 6-8 ml/kg and respiratory rate < 30 per minute. PEEP level was the onset at 5 cm H₂O, and move to 1 cm H₂O to enable attain SpO₂ > 90% using the lowest possible FiO₂ level. [23]

In group 2, which received treatment without NiPPV or CPAP but was managed with medical treatment and supplementary oxygen, they had oxygen administered through a nasal cannula, Venturi mask, or non-rebreathing mask. The medical treatment was all administered by a fully qualified consultant who did their duties normally; treatments were monitored following the hospital policy and current guidelines. These consultants weren't a part of the study but were doing the normal duties.

Every patient that was intubated had the following criteria: respiratory arrest; severe hemodynamic instability; deterioration of consciousness level or increasing aggravation and agitation; respiratory rate > 35/min; SpO₂ less than 90%; PaCO₂ < 50 mm Hg; reduced cough reflex, by the patient's inability to effectively clear sputum or tolerate a facial mask. The staff on duty was permitted to intubate the patient if the clinical state was as per the above criteria.

Blood gas analyses were performed through an arterial blood withdrawal of 2 mL of arterial blood from the radial or femoral artery and were analyzed using an ABG blood analysis machine. Pulse oximetry (SpO₂) was monitored using a multi-parameter monitor made by the Mindray company. To access lung function, spirometry was performed by a respiratory therapist.

The main results were to see the outcomes between the two groups of the study and how it affects in-hospital mortality, as well as length of hospitalization and ICU. Statistical analysis of outcome was done using descriptive statistics calculated from baseline and while in treatment. Due to the small sample size, we used nonparametric tests. The differences between the two groups were then analyzed using the Mann–Whitney U-test, while the internal analyses were conducted using the Wilcoxon test. The significance level was set at 0.05. All analyses were performed using the statistical software Statistica (version 6.1).

RESULTS

90 moderate to very severe COPD patients in acute exacerbation were considered for the study. Among them, 42 were then excluded in all, as they did not meet the inclusion criteria either due to early intubation or unknown reason for admission into the ICU. 48 COPD patient were taken for the study all, and were placed on inhalational therapy. Group 1 was 23 and group 2, 25. (36)75 % of the total had 3 times inhalational while the remaining had 2 times only. Group 1 (18)78.2% had 3 times inhalational therapy while group 2, (15) 69,5% of the patients. Using medical scoring systems, acute physiology score and gold score social demographic data were compatible.

It was seen that the rate of intubation in group one was lesser that group 2. The group 1 that received non-invasive ventilation had 6 (26 %) compared to 17 (68 %) in group 2 that were not ventilated. In analysis of mortality rate in the study, it was found that more patients in group 2 died as compared to group 1, mortality rate in group 2 was 36.0 % (9 deaths), while in group 1 the mortality rate was 21.7 % (5 deaths). In analysis the length of stay in the hospital and ICU, the length of stay in hospital was statistically near significance, the actually value for group 1 was 20.8±11.3 days, while in group 2 is 29.1±12.3 days, (p=0.063). While looking at the length of stay in ICU no significant difference was found between the groups: 14.7±12.2 days and 10.8±7 days, respectively (p=0.178).

DISCUSSION

COPD is a common respiratory disease, which can be aggravated, it poses a significant major health issues with high mortality and morbidity. It has become a major public health concern worldwide [18]. It is very important to note several studies has been done on this topic and mortality differs in different studies, in a study by Nair et al mortality rate for patients with exacerbation of COPD is <

5% for outpatients, rises to 10 % of patients hospitalized in specialized departments and may exceed 30 % in patients admitted to the intensive care unit [12]. In some centres the mortality rate in patients with severe COPD rises up to 58% [3].

There are evidences showing that NiPPV is helpful in managing COPD in its aggravated state but many research has some reservations about that fact because its failure will lead to delayed intubation which will deepen and worsen the outcome. [12]. In this index retrospective clinical study, where patients are in severe hypercapnic respiratory failure the use of non-invasive ventilation reduced the intubation rate and in hospital mortality. It is important to note that, there no clear evidence to state that initial six hours NiPPV trial may worsen the outcome of patients with NiPPV failure. However, its usage was beneficial to the patients as it concerns outcomes. The influence of NIV in management of exacerbated COPD and its outcomes are controversial hence there are needs for more research and development of treatment protocol. In this study long term follow up was not done, as it was not within the scope of this study. However, some authors reported that a mortality rate of 20 % at the 6-year follow-up in a group of older COPD patients discharged after a non-acidotic exacerbation [3]. Other studies postulated that females are more predisposed to developing COPD, they further state that this might be because of the activity of cytochrome P450 enzymes. In comparative studies it was found that women with severe COPD have a higher risk of hospitalization and death from respiratory failure [14, 9]. This was not seen in this index study, is not within the scope of this study and was not investigated, and it will be the topic of future studies. No significant difference in ICU and hospital length of stay was found, which might be explained to some in-patient policies in the hospital, and hospital length of stay is not a key performance indicator (KPI) for department staff.

CONCLUSION

In this study, NiPPV was helpful in managing patients with severe COPD in exacerbation; proper timing of its usage will help in better outcomes in the population, and in the treatment done, there was an obvious significant decrease in lowering intubation rate and in-hospital patient mortality in patients who received non-invasive positive pressure ventilation compared to the standard of care. There was no significant difference as it concerns hospital length of stay and ICU length of stay. No evidence in favor of additional risk for patients with initial NiPPV failure was found.

REFERENCES

1. Atwood C.W. (2017). *Impact of Heated Humidified High Flow Air via Nasal Cannula on Respiratory Effort in Patients with Chronic Obstructive Pulmonary Disease*. *Chronic Obstr. Pulm. Dis. J. COPD Found.*; 4:279–286. Atwood C.W., Camhi S., Little K.C., Paul C., Schweikert H., Macmillan N.J., Miller T.L. doi: 10.15326/jcopdf.4.4.2017.0169.
2. Barnes P.J. (2016). *Sex Differences in Chronic Obstructive Pulmonary Disease Mechanisms*. *Am. J. Respir. Crit. Care Med.* 193:813–814. P. J. Barnes. doi: 10.1164/ rccm.201512-2379ED.
3. Bott J. (1993). *Randomised controlled trial of nasal ventilation in acute ventilatory failure due to chronic obstructive airways disease*. *Lancet.*; 341:1555– 1557. Bott J., Carroll M., Conway J., Keilty S., Ward E., Brown A., Paul E., Elliott M., Godfrey R., Wedzicha J., et al. doi: 10.1016/0140-6736(93)90696-E.
4. Brochard L. Noninvasive (1995). *Ventilation for Acute Exacerbations of Chronic Obstructive Pulmonary Disease*. *N. Engl. J. Med.* 333:817–822. Brochard L., Mancebo J., Wysocki M., Lofaso F., Conti G., Rauss A., Simonneau G., Benito S., Gasparetto A., Lemaire F., et al. doi: 10.1056/NEJM199509283331301.
5. Chest (1999). *Clinical indications for non-invasive positive pressure ventilation in chronic respiratory failure due to restrictive lung disease, COPD, and nocturnal hypoventilation – a consensus conference report*. 116(2):521–534. doi: 10.1378/chest.116.2.521. Anonymous.
6. Chu C.M., (2004). *Readmission rates and life threatening events in COPD survivors treated with non-invasive ventilation for acute hypercapnic respiratory failure*. *Thorax.*; 59:1020–1025.

- / Chu C.M., Chan V.L., Lin A.W.N., Wong I.W.Y., Leung W.S., Lai C.K.W. doi: 10.1136/thx.2004.024307.
7. Connors A.F., Jr., Dawson N.V., Thomas C., Harrell F.E., Jr., Desbiens N., Fulkerson W.J., Kussin P., Bellamy P., Goldman L., Knaus W.A. Connors A.F. (1999). *Outcomes following acute exacerbation of severe chronic obstructive lung disease. Prognoses and Preferences for Outcomes and Risks of Treatments*) Am. J. Respir. Crit. Care Med.; 154:959–967. doi:10.1164/ajrccm.154.4.8887592.
 8. Decramer M, Janssens W, Miravittles M. (2012). Chronic obstructive pulmonary disease. *Lancet*.;379(9823):1341–1351. doi: 10.1016/S0140-6736(11)60968-9.
 9. Gold report on diagnosis and initial assessment of COPD (2021). page 20-27 of chapter 2., Google scholar.
 10. Graham B.L (2019). Standardization of Spirometry Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. *Am. J. Respir. Crit. Care Med.* 2019;200: e70–e88. Graham B.L., Steenbruggen I., Miller M.R., Barjaktarevic I.Z., Cooper B.G., Hall G.L., Hallstrand T.S., Kaminsky D.A., McCarthy K., McCormack M.C., et al. doi: 10.1164/ rccm.201908-1590ST.
 11. Gudmundsson G. (2006). *Mortality in COPD patients discharged from hospital: The role of treatment and co-morbidity.* *Respir. Res.*; 7:109. / Gudmundsson G., Gislason T., Lindberg E., Hallin R., Ulrik S.C., Brøndum E., Nieminen M.M., Aine T., Bakke P., Janson C. doi: 10.1186/1465-9921-7-109.
 12. Köhnlein T, Windisch W, Kohler D, (2014). Non-invasive positive pressure ventilation for the treatment of severe stable chronic obstructive pulmonary disease: a prospective, multicentre, randomised, controlled clinical trial. *Lancet Respir Med.*;2(9):698–705. doi: 10.1016/S2213-2600(14)70153-5.
 13. McEvoy RD, Pierce RJ, Hillman D, (2009). Nocturnal non-invasive nasal ventilation in stable hypercapnic COPD: a randomised controlled trial. *Thorax.*;64(7):561–566. doi: 10.1136/thx.2008.108274.
 14. Murray I, Paterson E., Thain G., Currie G.P. (2011). Outcomes following non-invasive ventilation for hypercapnic exacerbations of chronic obstructive pulmonary disease. *Thorax.* 2011; 66:825–826: doi: 10.1136/thx.2010.152264.
 15. Nickol AH, Nicholas H, Hopkinson NS, E. (2008). Mechanisms of improvement of respiratory failure in patients with COPD treated with NIV. *Int J Chron Obstruct Pulmon Dis.*;3(3):453–462. doi: 10.2147/copd.2705.
 16. Ojo O, Lagan AL, Rajendran V, Y. (2014). Pathological changes in the COPD lung mesenchyme – novel lessons learned from in vitro and in vivo studies. *Pulm Pharmacol Ther.*;29(2):121–128. doi: 10.1016/j.pupt.2014.04.00
 17. Ranieri P. (2008). Predictors of 6-Month Mortality in Elderly Patients with Mild Chronic Obstructive Pulmonary Disease Discharged from a Medical Ward After Acute Nonacidotic Exacerbation. *J. Am. Geriatr. Soc.*; 56:909– 913. / Ranieri P., Bianchetti A., Margiotta A., Virgillo A., Clini E.M., Trabucchi M. doi: 10.1111/j.1532-5415.2008.01683. x.
 18. Schroff P. (2017). Pulmonary Rehabilitation Improves Outcomes in Chronic Obstructive Pulmonary Disease Independent of Disease Burden. *Ann. Am. Thorac. Soc.*; 14:26–32. Schroff P., Hitchcock J., Schumann C., Wells J.M., Dransfield M.T., Bhatt S.P. doi: 10.1513/AnnalsATS.201607-551OC.
 19. Slenter RH, Sprooten RT, Kotz D, Wesseling G, Wouters EF, Rohde GG (2014). Predictors of 1-year mortality at hospital admission for acute exacerbations of chronic obstructive pulmonary disease. *Respiration.* 2013;85(1):15–26. doi: 10.1159/000342036.

20. Struik FM, Lacasse Y, Goldstein RS, Kerstjens HA, Wijkstra PJ. Nocturnal noninvasive positive pressure ventilation in stable COPD: a systematic review and individual patient data meta-analysis. *Respir Med.*;108(2):329–337. doi: 10.1016/j.rmed.2013.10.007.
21. Struik FM, Sprooten RT, Kerstjens HA, A. (2014). Nocturnal non-invasive ventilation in COPD patients with prolonged hypercapnia after ventilatory support for acute respiratory failure: a randomised, controlled, parallel-group study. *Thorax.*;69(9):826–834. doi: 10.1136/thoraxjnl-2014-205126.
22. Suh E.-S., (2015). Neural respiratory drive predicts clinical deterioration and safe discharge in exacerbations of COPD. *Thorax.*; 70:1123–1130. / Suh E.-S., Mandal S., Harding R., Ramsay M., Kamalanathan M., Henderson K., O’Kane K., Douiri A., Hopkinson N.S., Polkey M.I., et al. doi: 10.1136/ thoraxjnl-2015-207188.
23. Tan WC, Mahayiddin AA, Charoenratanakul S, L. (2005). Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (UPDATE 2014) Global Initiative for Chronic Obstructive Lung Disease 2014 GOLD. *Respirology.*;10(1):9–17. doi: 10.1111/j.1440-1843.2005.00692.
24. Tuggey JM, Plant PK, Elliott MW (2003). Domiciliary non-invasive ventilation for recurrent acidotic exacerbations of COPD: an economic analysis. *Thorax.*;58(10):867–871. doi: 10.1136/thorax.58.10.867.
25. Vogelmeier CF, Criner GJ, Martinez FJ, T. (2017). Global strategy for the diagnosis, management and prevention of chronic obstructive lung disease 2017 report. *Am J Resp Crit Care.*;195(5):557–582. doi: 10.1164/rccm.201701-0218PP.
26. Windisch W, Kostli S, Dreher M, Virchow JC, Jr, Sorichter S. 2005). Outcome of patients with stable COPD receiving controlled non-invasive positive pressure ventilation aimed at a maximal reduction of PaCo₂. *Chest.*;128(2):657–662. doi: 10.1378/chest.128.2.657.
27. Zhang F. (2021). Effect of muscle training on dyspnea in patients with chronic obstructive pulmonary disease: A meta-analysis of randomized controlled trials. *Medicine.*;100: e24930. Zhang F., Zhong Y., Qin Z., Li X., Wang W. doi: 10.1097/ MD.00000000000024930.