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Noninvasive Ventilation plus Standard Medical Therapy versus Medical Therapy Alone in Acute Hypercapnic Respiratory Failure due to Post-tuberculous COPD

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Author`s Contribution

[1,6]Substantial contributions to the conception or design of the work; or the acquisition, Final approval of the study to be published [2,3,4]Drafting the work or revising it critically for important intellectual content, analysis, or interpretation of data for the work, [3]Active participation in active methodology,

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ABSTRACT

Objective: To compare the efficacy of noninvasive ventilation (NIV) plus standard medical therapy versus standard medical therapy alone in acute hypercapnic respiratory failure due to post-tuberculous chronic obstructive lung disease (COPD).

Methodology: This quasi-experimental study was done at the Department of Pulmonology, Fauji Foundation Hospital, Rawalpindi between August 2019 to January 2020 after ethical approval. After informed consent, 80 post-tuberculous COPD patients were enrolled by non-probability sampling. Patients were allocated into two groups with 40 participants in each group; Group A (intervention group) received NIV in addition to standard medical therapy, whereas patients in Group B were given standard medical therapy alone. Following history and examination, baseline arterial blood gases (ABGs) were done.

Results: Mean change in pH, paCO2, paO2 and respiratory rate in group A and group B at 6 hours were 7.38+0.06 vs 7.30+0.03, 44.63+8.24 vs 64.26+5.71, 73.55+14.94 vs 72.67+9.49 and 20.20+2.40 vs 25.32+3.18, respectively. Noninvasive ventilation plus standard medical therapy was more effective than medical therapy alone, with statistically significant results for pH, paCO2, and respiratory rate (p-value=0.001). The patient outcomes had no significant relation with age, gender and duration of post-tuberculous COPD (p-value ≥0.10).

Conclusion: Noninvasive ventilation plus standard treatment yields superior results to standard treatment alone in acute hypercapnic respiratory failure due to post-TB COPD. We recommend combination therapy in such patients.

Keywords: Chronic Obstructive Airway Disease, COPD, Tuberculosis, Non-invasive Ventilation, Acute Hypercapnic Respiratory Failure

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Introduction

Tuberculosis (TB) is a major communicable disease affecting almost 10.6 million people worldwide. Almost 1.6 million deaths are attributed to TB.[1] The majority of the cases of TB occur in adults (88%) followed by 12% in children.[2] South Asia has the highest prevalence of TB (44%) and 46% of the deaths occur in this region.[1,2] Tuberculosis is caused by Mycobacterium tuberculosis. The prevalence of tuberculosis increases with poor sanitation, overcrowding and undernutrition.[3]

Pulmonary tuberculosis can permanently damage lung anatomy and physiology with a significant loss of lung function.[4] A meta-analysis concluded that a greater percentage of individuals develop chronic obstructive pulmonary disease (COPD) with a history of pulmonary tuberculosis.[5] The 2022 updated executive summary of

the Global Initiative on COPD points to the role of tuberculosis in the development of COPD.[6] Chronic obstructive lung disease is a chronic lung disorder with progressive irreversible airway obstruction. Almost 329 million people are affected by the disease on the global scale.[7] After completion of tuberculosis treatment, around 12–31% of patients had a progressive decrease in lung function including airway obstruction and restriction. This increases the prevalence of COPD in post-tuberculous patients.[8] A study showed that 21% of the patients with pulmonary tuberculosis in the past developed COPD.[5]

Hypercapnic respiratory failure is a serious sequela of COPD attributing to disease exacerbations and recurrent ICU admissions.[9] Noninvasive ventilation (NIV) has a successful role in type 2 respiratory failure relieving shortness of breath, decreasing the incidence of complications such as endotracheal intubation, acute exacerbations, mortality and improving overall survival. It also decreases recurrent admissions in ICU per year and duration of hospital stay consequently resulting in a substantial cost saving for patients.[10] Noninvasive ventilation also results in in improvement of health-related quality of life (HRQOL) in these patients.[11] Our study determined the outcomes of noninvasive ventilation plus standard treatment with standard treatment alone in acute hypercapnic respiratory failure in patients with post-tuberculous COPD. The outcomes were assessed by pH, $PaCO_2$, PaO_2 and respiratory rate at baseline and 6 hours after treatment. There are numerous studies that evaluated the efficacy of NIV in patients with chronic hypoventilation syndrome, its use in acute hypercapnic respiratory failure due to post-tuberculous COPD has been less studied. There is a need to conduct studies to evaluate the efficacy of this procedure. By evaluating the outcomes of NIV in post-tuberculosis COPD we can improve the current management and treatment strategies for patients with post- tuberculous COPD.

Methodology

This quasi-experimental study was conducted in the Department of Pulmonology, Fauji Foundation Hospital, Rawalpindi from 1st August 2019 to 1st January 2020 after ethical approval. A sample size of 80 was estimated using the WHO calculator. Post-TB COPD patients were admitted to the hospital and enrolled by non-probability convenient sampling after informed consent. Patients with post-TB COPD were diagnosed based on radiological changes compatible with healed pulmonary tuberculosis i.e. calcified lesions and hyperinflated lungs for post-tuberculous COPD. Following history and examination, baseline arterial blood gases (ABGs) were done. Patients with pH < 7.35, PaCO2 > 50mmHg with normal or raised bicarbonate levels were labeled as having acute hypercapnic respiratory failure. Patients with hemodynamic instability i.e., BP <90/60 mmHg, pulse > 140/min, drowsy, impending respiratory arrest, excessive airway secretions, pneumothorax, inability to protect the airway, acute upper gastrointestinal bleeding, smear-positive pulmonary TB and facial deformity/trauma were excluded. Patients were allocated into two groups with 40 participants in each group; Group A (intervention group) received NIV in addition to standard medical therapy, whereas patients in Group B were given standard medical therapy alone.

Group A	Group B
Standard Medical Therapy plus NIV Non-invasive ventilation via a nasal mask or face mask by spontaneous/timed (S/T) setting of Trilogy machine with following instructions: Expiratory positive airway pressure (EPAP): 5 cm H_2O Inspiratory positive airway pressure (IPAP): 20 cm H_2O Respiratory rate (RR): 18 breaths per minute (BPM) Inspiratory to expiratory ratio (I:E): 1:3	**Standard Medical Therapy** Oxygen at 2L/minute via face mask, third-generation cephalosporin i.e. ceftazidime 1 gm bid via IV route, Steroids i.e. hydrocortisone 100 mg via IV sodium succinate 100mg tid and nebulization with salbutamol & ipratropium bromide 8 hourly.

Arterial blood gases and respiratory rate were documented at baseline and at the 6th post-admission hour to look for pH, $PaCO_2$ and PaO_2 on Performa. The demographic variables and duration of hospital stay (in days) were also noted.

The data was entered and analyzed using the Statistical Package for the Social Sciences (SPSS) version 25. Frequencies and percentages for categorical variables like gender and mean± standard deviation for quantitative variables like age, pH, $paCO_2$, paO_2, and respiratory rate were calculated. Independent student t-test was applied to compare quantitative variables like age, pH, $paCO_2$, paO_2, and respiratory rate between two groups. The relation of effect modifiers such as age, gender, and duration of post-tuberculous COPD with the outcomes was seen using the Chi-square test. The significance level was p-value ≤ 0.05.

Table I: Outcomes in Group A and B Participants.

Outcome	Group A	Group B	p-value
pH	7.38+0.06	7.30+0.03	0.001*
$PaCO_2$	44.63+8.24	64.26+5.71	0.001*
PaO_2	73.55+14.94	72.67+9.49	0.755
Respiratory rate	20.20+2.40	25.32+3.18	0.001*

Results

The study subjects had an average age was 58.26+8.15 years. Eight (10%) were males and 72 (90%) were females. The average duration of post-tuberculous COPD was 5±1.6 years. Mean pH, $PaCO_2$, PaO_2 and respiratory rate at baseline were 7.30+0.04, 62.15+5.58, 68.08+15.22 and 26.48+3.61, respectively, whereas, mean pH, $PaCO_2$, PaO_2, and respiratory rate at 6th hour were 7.34+0.06, 54.45+12.13, 73.11+12.44 and 22.76+3.81, respectively. Mean pH, $PaCO_2$, PaO_2 and respiratory rate in groups I and II at 6th hours was 7.38+0.06 vs 7.30+0.03, 44.63+8.24 vs 64.26+5.71, 73.55+14.94 vs 72.67+9.49 and 20.20+2.40 vs. 25.32+3.18, respectively. Independent student t-test was applied and the results were statistically significant results for pH, $paCO_2$, and respiratory rate (p-value=0.001) (Table I).

Effect modifiers like age, gender, and duration of post-tuberculous COPD were stratified on outcomes of either treatment at the 6th hour but the results were statistically insignificant ($p \geq 0.10$).

Discussion

Most of the studies available in the literature evaluated the effectiveness of NIV in chronic hypercapnic respiratory failure.[12,13,14] The studies that determined the role of NIV in acute hypercapnic respiratory failure due to COPD either studied its efficacy in all patients of respiratory failure without any comparison group[15] or compared outcomes between patients receiving NIV and invasive mechanical ventilation.[16,17]

In our study, patients had a mean age of 58.26+8.15 years and 72(90%) of them were females. In contrast, in another study, patients had a mean age of 66.8 years and 65% of them were male.[18] The mean age was 62.2±9.64 years in a study by Abdul-Aziz et al and 69.7% of the patients were male.[16] Patients were quite younger in another study having an average age of 39.3±18.4 years and 80% were males.[17]

Our study demonstrated that NIV plus medical therapy improved the pH, $PaCO_2$, and respiratory rate significantly versus standard medical therapy alone in post-COPD acute hypercapnic respiratory failure. The results of a systemic review and meta-analysis revealed that NIV improved the pH and $PaCO_2$ of patients markedly. $PaCO_2$ was also improved in that study but that was not significant. Noninvasive ventilation also had no effect in improving dyspnea in these patients. The study reported a remarkable decrease in the risk of mortality, intubation, and hospital stay period.[18] Another study revealed an improvement in respiratory rate and pH with NIV in post-COPD acute hypercapnic syndrome. However this improvement was only significant in patients with acidosis.[19] A study by Abdul-Aziz et al. reported a successful role of noninvasive ventilation in acute COPD exacerbations with a significant decrease in the duration of hospitalization and mortality. In this study, there were two patient groups: one receiving NIV and the other group included patients on mechanical ventilation. Patients who received NIV had a marked improvement in respiratory rate, whereas, the difference in pH, $PaCO_2$, and PaO_2 was insignificant between the patients receiving and not receiving NIV.[16] Another study demonstrated that NIV was successful in 70.2% of the patients, whereas the remaining 29.8% of the patients underwent mechanical ventilation. Noninvasive ventilation improved pH & $PaCO_2$ and decreased hospital stay duration & mortality in these patients.[17] Another study reported that NIV is an effective and safe modality in acute hypercapnic syndrome.[15] A review by Marwah et al. stated favorable outcomes in acute hypercapnic syndrome caused by COPD in terms of a decrease in hospital stay duration and less chances of intubation and mortality.[20]

Conclusion

Noninvasive ventilation plus standard treatment yields superior results to standard treatment alone in acute hypercapnic respiratory failure due to post-TB COPD. We recommend combination therapy in such patients.

LIMITATIONS OF THE STUDY: It was a single center trial with small sample size. Parameters like duration of hospital stay, readmissions after acute exacerbation, and risk of complications were not studied. Therefore, other

multicenter trials with larger population size and including these parameters should be conducted.

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