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EVALUATION OF THE EFFECT OF DEXMEDETOMIDINE INFUSION ON OUTCOME OF COPD PATIENTS ON NON-INVASIVE VENTILATION

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ABSTRACT

Objective: To evaluate of the Effect of Dexmedetomidine infusion on outcome of COPD patients on non-invasive ventilation.

Methods: Enrolled patients were randomly allocated to a (Dexmedetomidine) DEX group A (n=35) or (0.9% saline) control group B (n=35) using a randomized sequence generated by a computer, randomization process was centralized. The participating patients and nurses were blinded to the treatment.

Results: Differences in mean blood oxygenation were found to be statistically significant at all the follow up periods. Mean dyspnea grading of Group B (8.51±1.22) was found to be higher than that of Group A (7.09±1.31) and difference in dyspnea grading of both the groups at 1 hr. was found to be statistically significant ($p<0.001$). Comparison of mean heart rate between two groups showed significant stability in both the groups. ICU stay of patients of Group A ranged from 2-6 days while that of Group B from 9-17 days. Difference in mean ICU stay in patients of Group A (4.37±1.09 days) and Group B (12.23±1.94 days) was found to be statistically highly significant ($p<0.001$).

Conclusion: The desired level of oxygenation and improved outcome obtained by the effect of Dexmedetomidine on Non-invasive ventilation treatment in COPD patients improved many important aspects of critical care compared with the conventional treatment.

KEYWORDS : Dexmedetomidine, COPD,Oxygenation

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is an important public health challenge and is a major cause of chronic morbidity and mortality throughout the world. COPD is currently the fourth leading cause of death in the world (Mannino and Kiri, 2006)but is projected to be the 3rd leading cause of death by 2020. More than 3 million people died of COPD in 2012 accounting for 6% of all deaths globally. Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of the population (COPD Fact sheet, 2016).

COPD is defined by Global initiative of Chronic Obstructive Lung Disease 2017 as a preventable and reversible disease characterized by chronic airflow limitation (GOLD, 2017 recommendations for COPD patients).

Diagnosis of COPD can be made onpresence of risk factors like smoking and occupationaldustclinical symptoms, and chemicals and other tests.Spirometry is most commonly done to confirm diagnosis of COPD (Johns et al, 2014). Presence of a post-bronchodilator $FEV_1/FVC < 0.70$ confirms the presence of persistent airflow limitation.

Acute exacerbations of COPD often require ICU admission and supportive ventilation in form of either invasive or non-invasive ventilation (Mas A, Masip, 2014). Early use of non-invasive ventilation in mild to moderate acidotic COPD patients results in reduction of invasive ventilation related morbidity and also reduces mortality (Plant et al, 2000).

Dexmedetomidine which is a α2 receptor agonist is often used in ICU to provide sedation and facilitate NIV and also provides hemodynamic stability (Joseph et al, 2015). Dexmedetomidine in *in vitro* studies of human and animal bronchial tissue has shown improved oxygenation and also prevents bronchoconstriction which is a prominent feature of acute exacerbation of COPD (Zhang et al, 2017). A randomized blind trial done in patients of COPD undergoing one lung ventilation for lung cancer surgery showed that Dexmedetomidine not only improved oxygenation but also reduced dead space ventilation and also was effective in post-operative period (Su et al, 2016).

In this study we have determinedthe effect of lowest possible dose of Dexmedetomidine infusion on outcome of COPD patients admitted to ICU with acute exacerbations in terms of improvement in oxygenation, improvement in dyspnea, hemodynamic stability and ultimately resulting in decreased length of ICU stay.

MATERIAL AND METHODS

This study has been conducted after approval from the institutional review board of KGMU, with reference code 84th ECM 2 B Thesis /P 13, Lucknow.

All participants and attendants were explained in their language about the study & written informed consent taken before participation.

Patients expected to undergo non-invasive ventilation for acute exacerbation of COPD were included.

Patients with age between 40 to 80 years, Diagnosis of COPD of moderate grading, Forced expiratory volume in 1sec (FEV_1) of at least 50% and less than 80% of predicted, the presence of a post-bronchodilator FEV_1/FVC ratio less than 0.70 in a pulmonary function test and Patients with mild to moderate degree of hypoxemia on arterial blood gas analysis also included.

Patients with heart failure (New York Heart Association class > II), history of arrhythmia or treatment with antiarrhythmic drugs, bradycardia [(HR) <45 beats/min] or Atrio-ventricular block, severe functional liver or kidney disease, atrial fibrillation, diabetes mellitus, heart failure, cancer and age >80 years, obesity (body mass index >30 kgm^2), restrictive lung disease and/or, decreased lung diffusion capacity for carbon monoxide (DLCO <70%), patients with serum hypoxemia on arterial blood gas level of <40 mmHg, patients with altered sensorium (Glasgow Coma Scale<12) and unable to cough and deglutition, patients with ARDS or severe anemia and patients with severe sepsis and baseline serum procalcitonin level less than 2 ng/ml were excluded from the study.

Enrolled patients were randomly allocated to a (Dexmedetomidine) DEX group A (n=35) or (0.9% saline) control group B (n=35) using a randomized sequence generated by a computer, randomization process was centralized. The participating patients and nurses were blinded to the treatment.

Methods

A 20-gauge radial artery catheter was inserted for continuous

hemodynamic monitoring and to get repeated arterial blood sample. All patients received broad spectrum antibiotics upon arrival to ICU and changed according to their culture sensitivity report thereafter accordingly. All patients received IV fluids upon arrival to ICU. Dexmedetomidine or normal saline was given as bolus then continuous infusion was started after obtaining baseline ABG dyspnea grading vitals and then BiPAP support was applied with settings suitable for patients. 200 µg of injection Dexmedetomidine mixed in 50 ml of normal saline was prepared as a concentration of 4µg/ml and same volume of 0.9% saline was also used to prepare 0.9% saline infusion.

Statistical analysis

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean±SD.

RESULTS

Age of patients ranged from 41-80 years and mean age of patients included in the study was 60.67±11.00 years. Though proportion younger patients of Group B was higher as compared to Group A in lower age groups i.e. Up to 50 years (28.57% vs. 20.00%) and 51-60 years (37.14% vs. 14.29%) and proportion of patients of Group A was higher as compared to Group B in higher age groups i.e. 61-70 years (45.71% vs. 25.71%) and 71-80 years (17.14% vs. 5.71%) but this difference was not found to be statistically significant (p=0.090) (Table-1).

At mean baseline blood oxygenation of patients of Group B (82.09±13.02) was found to be higher than that of Group a (81.02±14.42) but difference in baseline blood oxygenation was not found to be statistically significant. Blood oxygenation of patients of Group A was found to be higher than that of Group B at follow up at 1 hour (145.51±38.70 vs. 109.74±11.19), at 2 hour (243.20±39.58 vs. 139.71±21.36) and at 12 hour (361.66±34.56 vs. 164.31±25.18). Differences in mean blood oxygenation were found to be statistically significant at all the follow up periods (Fig.1).

In both the groups, median baseline dyspnea grading was 10, though mean dyspnea grading of patients of Group B (9.69±0.63) was found to be higher than that of Group A (9.49±0.74) but difference in dyspnea grading of patients of both the groups was not found to be statistically significant.

At 1 hr., median dyspnea grading of Group A and Group B were 7.00 and 9.00 respectively. Mean dyspnea grading of Group B (8.51±1.22) was found to be higher than that of Group A (7.09±1.31) and difference in dyspnea grading of both the groups at 1 hr. was found to be statistically significant (p<0.001).

At 2 hr., median dyspnea grading of Group A and Group B were 4.00 and 7.00 respectively. Mean dyspnea grading of Group B (6.71±1.46) was found to be higher than that of Group A (3.97±1.36) and difference in dyspnea grading of both the groups at 1 hr. was found to be statistically significant (p<0.001) (Fig. 2).

Comparison of mean arterial pressure between group A and B showed that mean blood pressure of group A was comparable to group B at all follow up periods. Difference in mean arterial pressure of two groups was within 10% of their previous baseline at all -time intervals (Fig. 3). Comparison of mean heart rate between two groups showed significant stability in both the groups. Difference of mean heart rate of both the groups was within 10 % of their baseline. Decrease in heart of both group was within normal limits at all follow up interval (Fig. 4).

ICU stay of patients of Group A ranged from 2-6 days while that of Group B from 9-17 days. Difference in mean ICU stay in patients of Group A (4.37±1.09 days) and Group B (12.23±1.94 days) was found to be statistically highly significant (p<0.001) (Fig. 5).

DISCUSSION

COPD is currently the fourth leading cause of death in the world. As a result of aging populations, the absence of prognosis-modifying treatments, and the decline in mortality in other chronic diseases, the prevalence of COPD is increasing and it is estimated that by 2020 it will be the third leading cause of death worldwide(Mannino and Kiri, 2006).

COPD is a chronic disease, and its course is punctuated by acute exacerbations of respiratory impairment. These exacerbations are the leading causes of death or hospital admission for patients with COPD. Exacerbations and related hospitalizations also heavily impact the quality of life of affected people (Carballo et al, 2017).

Our study was to evaluate the effect of Dexmedetomidine infusion on outcome of COPD patients on non-invasive ventilation. The primary outcomes of our study were improvement of breathlessness using Modified Borg Scale, improvement in oxygenation and hemodynamic stability and secondary outcome was to evaluate its effect on length of ICU stay.

In our study total 70 patients between age group of 40-70 years with diagnosis of COPD included who were categorized as having moderate degree of COPD on their basal pulmonary function test and presented with acute exacerbations. The age of patients ranged from 41-80 years and mean age of patients included in the study was 60.67±11.00 years. This compares with the study done by Cassiano et al (2011) (mean age 74±10), Georg-Christian Funk et al (2013) (mean age -62.5 ± 17.3), Mihaela Stefan (2015) et al (mean age- 67) Carballo et al (2017) (mean age- 74) Out of 70 patients included in our study 33 (47.14%) were females and rest 37 (52.86%) were males. Male: Female ratio in overall patients was 1:0.89. Similar gender distribution was found in study by Georg-Christian Funk et al (2013) (males – 57.4%) and Carballo et al (2017) (males -54%) Various studies using Dexmedetomidine intraoperatively for one lung ventilation and on animals showed that it improves oxygenation and reduces dead space ventilation.[84-91] Su et al (2016) performed a randomized double-blinded controlled trail to evaluate the effect of Dexmedetomidine in patients with moderate grade COPD undergoing lung cancer surgery. Patients in their study were divided in Dexmedetomidine and control group and they concluded that Dexmedetomidine improves oxygenation and lung mechanics in COPD patients. In our study also, there was rapid improvement of PaO_2/FiO_2 ratio in Dexmedetomidine group (Group A) as compared to control (Group B) while in both the group patients were on non-invasive ventilation. Blood oxygenation of patients of Group A(Dex) was found to be higher than that of Group B(control) at follow up interval of 1 hour (145.51±38.70 vs. 109.74±11.19), 2 hour (243.20±39.58 vs. 139.71±21.36) and at 12 hour (361.66±34.56 vs. 164.31±25.18) Karlaet al (2000) studied usefulness of Modified Borg Scale in assessing the effectiveness of this scale to correctly correlate with the changes in Pulmonary function test and oxygen saturation in COPD patients. Their study showed that mean Modified Borg Scale changed from 6 to 3 post treatment. In our study, though baseline dyspnea grading of both groups was 9.69 and 9.49 respectively which was not statistically significant, but at all-time intervals difference in dyspnea grading was significantly lower in Dexmedetomidine group than control.

Both groups of patients showed a significant improvement of their hemodynamic parameters but were better in group A (Dex) as compared to group B (Control).The difference between two groups for the mean blood pressure and heart rate, was statistically significant at all the follow up intervals (p<0.001). Carballo et al (2017) determined the factors associated with the risk of death and/or new admission up to 5 years after an initial hospitalization for an exacerbation of COPD. The mean heart rate was 98/ min in their study which when comparable with ours was 100-110/ min. Effect of Dexmedetomidine infusion was predictable at all-time intervals. In our study mean arterial pressure decreased around 10 % in group A and B as in study of Xiaoyan et al (2016)mean blood pressure decreased at all-time intervals.

Infections developing in ICU patients are associated with increased lengths of ICU stay and cost. Thiago et al (2015) in their study showed that length of ICU stay was 12 days (8–31) in NIV group vs. 2 days in invasive ventilation group (1–4); p < 0.001. Whereas, in our study ICU stay of patients of Group A(Dex) ranged from 2-6 days while that of Group B(control) from 9-17 days. Difference in mean ICU stay in patients of Group A(Dex) (4.37±1.09 days) and Group B(Control) (12.23±1.94 days) was found to be statistically significant (p<0.001).

CONCLUSION

The desired level of oxygenation and improved outcome obtained by the effect of Dexmedetomidine on Non-invasive ventilation treatment in COPD patients improved many important aspects of critical care compared with the conventional treatment.

Table-1: Demographic profile

Variables	Group A (n=35)	Group B (n=35)	p-value
Age	63.80±10.42	57.54±10.80	0.0161
Weight	65.60±6.16	65.21±7.62	0.84
Height	158.23±6.39	159.81±8.42	0.37
Sex (M/F)	19/16	18/17	0.81

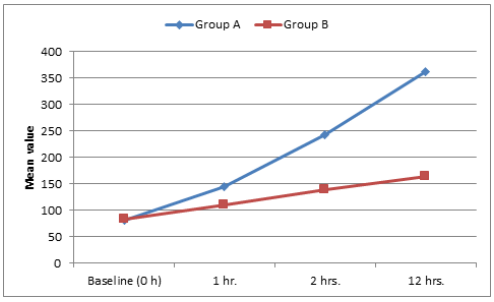

Fig. 1: Comparison of Blood Oxygenation (PaO2/FiO2 ratio) between two groups at different time intervals

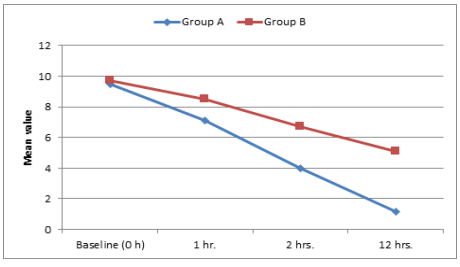

Fig. 2: Comparison of Dyspnea Grading between two groups at different time interval

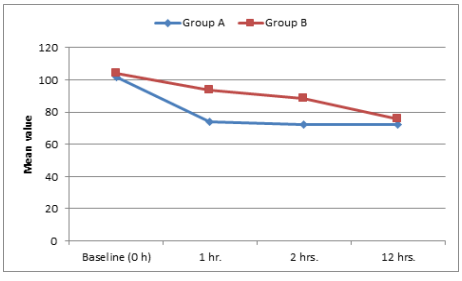

Fig. 3: Comparison of Mean arterial pressure of group A and B

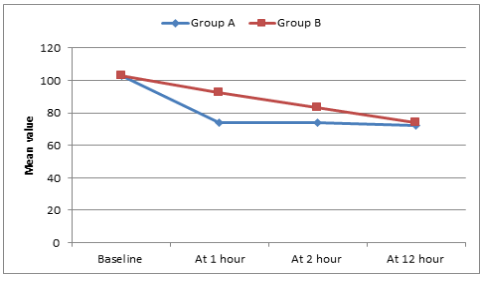

Fig. 4: Comparison of heart rate of group A and B

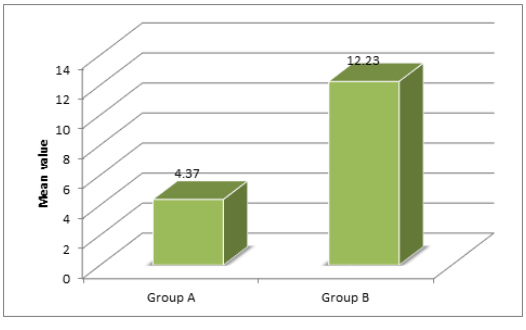

Fig. 5: Comparison of ICU Stay between two groups

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