

Echocardiographic Evaluation of Changes in Right Ventricle Functions After Oxygen Therapy in Patients with *Corpulmonale*

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ABSTRACT

Background: Long term oxygen therapy is the only therapy shown to improve survival in patients with COPD. Two controlled trials by the Medical Research Council in the United Kingdom and the National Institute of Health in North America have shown that long term oxygen therapy improves survival in patients with COPD. However, statistical proof correlating improvements in pulmonary hemodynamics with increased survival is lacking. The presence of pulmonary artery hypertension has been associated with a reduced rate of survival in patients with COPD and episodes of right ventricular failure have been reported to be major contributor to morbidity from the disease.

Methods: This study was conducted in the Department of Medicine at Hindu Rao Hospital; New Delhi. This hospital is the largest multi-speciality hospital in North Delhi catering to all section of society. All patients were in a stable condition which was defined as the absence of any acute exacerbation of dyspnoea, cough and expectoration or respiratory tract infection for at least 5 weeks prior to entry into the study.

Results: The administration of 100% oxygen for 15 to 20 minutes resulted in an average decline in pulmonary artery pressure (PAP) of 2.9 mm Hg, Burrows et.al., (1972).² The effect of oxygen on PAP was more striking on exertion. PAP raised an average 17 mm Hg on air breathing and 10 mm Hg on 100 % oxygen administration during exercise.

Conclusions: Oxygen administration resulted in a significant

decrease in pulmonary artery diameter in patients with *corpulmonale*. Oxygen therapy with 30 percent oxygen for 30 minutes brought about a significant increase in arterial oxygen saturation in patients with *corpulmonale*. All patients with COPD, *corpulmonale* does not show improvement with oxygen therapy. Identification of these patients would spare the expense, inconvenience and hazard of long term oxygen therapy. A fall in mean PAP of more than 5 mm Hg after 24 hours of oxygen breathing indicates a good response and can predict two year survival of 88% with domiciliary home oxygen treatment.


Key words: Oxygen, Hemodynamics, Medical, *Corpulmonale*, Right Ventricular Function.

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INTRODUCTION

Corpulmonale is an important consequence of COPD. Several factors contribute to the development of *corpulmonale* in patients with chronic obstructive pulmonary disease, but its primary cause is chronic alveolar hypoxia resulting in pulmonary vasoconstriction, vascular remodeling and pulmonary hypertension. The presence of pulmonary artery hypertension has been associated with a reduced rate of survival in patients with COPD and episodes of right ventricular failure have been reported to be major contributor to morbidity from the disease.

In the long term survivors it would appear that long term oxygen therapy prevented progression of the fall in PaO₂ and in the rate of rise of pulmonary vascular resistance without provoking further

rise in PacCO₂. Various studies demonstrated an improvement in survival of patients with long term domiciliary oxygen therapy. However, a number of patients show no improvement with oxygen therapy.

Identification of these patients would spare the expense, inconvenience and hazard of long term oxygen therapy and it also might turn the attention of the physician to potentially more effective measures such as control of heart failure and infection. The importance of predicting a good response to oxygen therapy has been widely acknowledged, but most studies have failed to identify the prognostic indicator have proposed criteria with only weak predictive value.

MATERIALS AND METHODS

This study was conducted in the Department of Medicine at Hindu Rao Hospital; New Delhi. This hospital is the largest multi-speciality hospital in North Delhi catering to all section of society. It has three units in Medicine Department. We studied the treatment of chronic hypoxemic COPD with Corpulmonale with Oxygen therapy and its effect on echocardiography parameters. The patient was studied before and after administration of oxygen. This study included both indoor and outdoor patients. Patients with history and clinical features suggestive of COPD with Corpulmonale were selected from Medicine Wards of Hindu Rao Hospital. The study was performed after stratification of their condition with adequate medical treatment i.e. they were in a condition to be discharged from the hospital.

Inclusion Criteria

Expiratory airflow limitations as revealed by an absolute value of FEV1 less than 80percent predicted and/or ratio FEV1 / FVC < 0.7 predicted on a well performed test on a spirometer which was largely irreversible i.e. less than 15percent change in FEV1 in response to two puffs of beta-2 agonists.(400µg salbutamol or equivalent)

All patients were in a stable condition which was defined as the absence of any acute exacerbation of dyspnoea, cough and expectoration or respiratory tract infection for at least 5 weeks prior to entry into the study.

All patients were taking bronchodilators and/or prednisolone. No change in treatment was made at the time of entry into the study.

Exclusion Criteria

Patient with a history of asthma or any other associated respiratory diseases were excluded from the study.

Patients with associated evidence of coronary artery disease, hypertension, congenital or valvular heart disease or previous history of myocardial infarction were excluded from the study.

Procedure

Patients underwent detailed history and clinical examination. Thereafter ECG, chest roentgenogram and pulmonary function test was done. Patients found suitable for the study were taken up for Echocardiography. The pulse oximeter was attached to the right index finger and ECG electrodes were attached to obtain simultaneous oxygen saturation and ECG display respectively. An attempt was made to secure adequate ECHO window to record as many of the parameters, listed above, as possible.

Arterial oxygen saturation is assessed by measuring partial pressure of oxygen in arterial blood (PaO₂) and when PaO₂< 60Torr, hypoxemia sufficient to treat with oxygen is present, oxygen therapy is given. The goal of oxygen therapy was to increase PaO₂ to at least 60Torr, equivalent to an arterial oxygen saturation of 90%. Increasing PaO₂ beyond 65Torr is associated with relatively minor further increase in arterial oxygen content. Patients with COPD can take 20 to 30 minutes for steady state to be achieved after a change in the inspired gas mixture. Also inspired concentration of oxygen of less than 40 percent is uncommonly associated with rapidly rising PaCo₂ and it is rare with an inspired concentration of less than 30 percent. Patients with an arterial oxygen saturation of less the 90 percent were administered 30 percent oxygen with a ventimask for a period of 30 minutes. The Echocardiographic study was repeated thereafter.

RESULTS

1. The mean age of patients in the study was 50.5years in Corpulmonale patient. Seventy percent of patients studied were males and thirty percent of patients studied were female.
2. The mean heart rate of patients with corpulmonale was 116 beats per minute. This was significantly more than that of control subjects. After oxygen administration; mean heart rate of corpulmonale patients decreased to 108 per minute which was statistically significant.
3. Only 30 percent of patients with corpulmonale could perform the pulmonary function tests. Means FEV1 was 0.67 lit. FVC was 1.23 Lit and FEV1/ FVC ratio 54.83 in this group.
4. Mean oxygen saturation of patients with corpulmonale was 70.5 percent before entry into the study. Oxygen therapy with 30 percent oxygen for 30 minutes brought about a significant increase in arterial oxygen saturation in patients with corpulmonale. Mean oxygen saturation after Oxygen administration was 88.9 percent (p value 20 mm Hg, PaO₂45 mm Hg, FEV1
5. All patients with corpulmonale had ECG evidence of right ventricular hypertrophy.
6. There was significant change in interventricular septal thickness after administration of oxygen in diastole.
7. Oxygen administration resulted in a significant decrease in pulmonary artery diameter (2.51 cm to 2.37 cm, p value .007) in patients with corpulmonale.
8. The peak velocity of pulmonary flow as assessed by pulsed Doppler was not significantly different in the four groups studied.
9. Mean acceleration time of patients with corpulmonale was 93.6 ± 12.3 msec. Oxygen administration to patients with corpulmonale resulted in significant change in acceleration time.
10. Pre-ejection period of pulmonary flow of patients with COPD was significantly lesser than that of controls (p value 0.0009). It was lesser than that seen in patients with corpulmonale (57.8 msec. versus 66 msec.). However the difference was not statistically significant. Oxygen administration to patients with corpulmonale did not result in any significant change in PEP
11. The mean ejection time of pulmonary flow was significantly lesser in patients with corpulmonale. Oxygen administration had no significant effect on this parameter.
12. The ratio of pre-ejection period to ejection time was significantly increased in patients with Corpulmonale. Oxygen administration resulted in a further increase in this ratio (mean value 0.323) but this difference was not significant (P value .08).
13. The ratio of pre ejection period to acceleration time was increased in patients with Corpulmonale (mean value 0.716). Oxygen administration resulted in a further increase in this ratio (mean value 0.930). The increase was statistically significant (p value .008).
14. Velocity time integral of pulmonary flow was significantly lesser in patients with Corpulmonale. Oxygen administration resulted in significant change in velocity time integral of flow (P value 0.03).
15. The mean E velocity of tricuspid flow was significantly increased in patients with Corpulmonale. Oxygen

administration had no significant effect on E velocity.

16. A velocity was increased in patients with Corpulmonale. Oxygen administration had no significant effect on A velocity.

17. The mean right atrial diameter in patients with Corpulmonale had larger RA dimension (Mean value 42 mm). Oxygen administration result in significant change in right atrial size (p value 0.003).

18. Patients with Corpulmonale had a mean RV free wall thickness of .762 cm. Oxygen administration did not result in any significant change in RV free wall thickness.

19. The mean right ventricular diameter in systole and diastole was more in patients with Corpulmonale (mean values 2.909 cm and 3.839 and respectively). Oxygen administration had no significant effect on right ventricular diameters in patients with Corpulmonale.

REVIEW OF LITERATURE

Long term oxygen therapy is the only therapy shown to improve survival in patients with COPD. Two controlled trials by the Medical Research Council in the United Kingdom and the National Institute of Health in North America have shown that long term oxygen therapy improves survival in patients with COPD.

However, statistical proof correlating improvements in pulmonary hemodynamics with increased survival is lacking. The administration of 100% oxygen for 15 to 20 minutes resulted in an average decline in pulmonary artery pressure (PAP) of 2.9 mm Hg, Burrows B et al.¹ The effect of oxygen on PAP was more striking on exertion. PAP rose an average 17 mm Hg on air breathing and 10 mm Hg on 100 % oxygen administration during exercise. All patients with COPD, corpulmonale do not show improvement with oxygen therapy. Identification of these patients would spare the expense, inconvenience and hazard of long term oxygen therapy. Ashutosh et al (1983)² a fall in mean PAP of more than 5 mm Hg after 24 hours of oxygen breathing indicates a good response and can predict two year survival of 88% with domiciliary home oxygen treatment.

Hypoxemic patients with COPD have symptoms thought to be caused by their hypoxemia. The most notable of these is pulmonary artery hypertension. The presence of pulmonary artery hypertension has been associated with a reduced rate of survival in patients with COPD and episodes of right ventricular failure have been reported to be major contributor to morbidity from the disease. These considerations led investigators to study the treatment of chronic hypoxemic COPD with long term Oxygen therapy 20 years back. The studies were done in single centres and involved series of 20 patients or less. They used each patient as his own control. The patient was studied before and after administration of oxygen and the results compared. These early studies did show that long term oxygen therapy reduced pulmonary hypertension and polycythemia in hypoxemic patients with COPD, it was not clear if these changes were associated with improved life expectancy. These studies showed that long term oxygen therapy was safe, it was not associated with CO₂ narcosis or increased hazard from fire or explosion. Also that long term oxygen therapy was not associated with changes in lung function no deterioration of function was noted that could be ascribed to oxygen therapy.

The Medical Research Council (MRC) of the United Kingdom and the National Institute of Health in the US conducted controlled

clinical trials on the effects of long term oxygen therapy. The MRC study was done in three Centres in the UK.³ The 87 patients, all less than 70 years of age, who participated in the study had chronic bronchitis or emphysema with irreversible airway obstruction, severe arterial hypoxemia, Co₂ retention and a history of CHF. The patients were randomised to oxygen therapy or no oxygen. Oxygen was given by nasal prongs for at least 15 hour daily, usually at 2L/Min. 19 of the 42 oxygen treated patients died in the five years of follow up compared with 30 of 45 controls. In the 66 men in this trial, survival advantage of oxygen did not emerge until 500 days had elapsed. Survival of the 12 female controls was poor 8 being dead in 3 years.

The rate of change in pulmonary hemodynamic and the mean pulmonary artery pressure showed little change in the men who survived longer, whereas it tended to rise in the 21 control men who survived over 500 days. The total pulmonary vascular resistance although rising slightly in the treated men surviving over 500 days raised much more in the control men who survived for this period. These objective measurements, although not significantly different between the groups, suggest that severity of respiratory failure progressed irrespective of the long term oxygen treatment in patients who died early. However, in the long term survivors it would appear that long term oxygen therapy prevented progression of the fall in Pao₂ and in the rate of rise of pulmonary vascular resistance without provoking further rise in Pao₂.

The Nocturnal oxygen therapy Trial Group (1980)⁴ conducted its study at six centres in the US. 203 patients with hypoxemic chronic obstructive lung disease were randomly allocated to either continuous oxygen therapy or 12 hour nocturnal oxygen therapy and followed for at least 12 months (mean 19.3 months). Overall mortality in the nocturnal oxygen therapy group was 1.94 times that in the continuous oxygen therapy group. This trend was striking in patients with carbon dioxide retention and also present in patients with relatively poor lung function, low mean nocturnal oxygen saturation, more severe brain dysfunction and prominent mood disturbances. Continuous oxygen therapy also appeared to benefit patients with low mean pulmonary artery pressure and pulmonary vascular resistance and those with relatively well preserved exercise capacity.

Neither oxygen therapy program resulted in correction or near correction of the baseline hemodynamic abnormalities. The Continuous oxygen therapy group did show improvement in pulmonary vascular resistance, pulmonary artery pressure and stroke volume index. The improvement in pulmonary vascular resistance was associated with improved cardiac function, as evidenced by an increase in baseline and exercise stroke volume index. The nocturnal oxygen therapy group showed stable hemodynamic variables. For both groups, change in mean pulmonary artery pressure during the first 6 months was associated with subsequent survival after adjustment for association with the baseline mean pulmonary artery pressure. Continuous oxygen therapy can improve the hemodynamic abnormalities of patients with COPD. The hemodynamic response to this treatment is predictive of survival.⁵

The above mentioned trials have demonstrated an improvement in survival of patients with long term domiciliary oxygen therapy. However, a number of patients show no improvement with oxygen therapy. Identification of these patients would spare the expense,

inconvenience and hazard of long term oxygen therapy and it also might turn the attention of the physician to potentially more effective measures such as control of heart failure and infection. The importance of predicting a good response to oxygen therapy has been widely acknowledged, but most studies have failed to identify the prognostic indicator have proposed criteria with only weak predictive value.

In an early study of patients with COPD pulmonary artery pressure and PVR declined acutely with oxygen administration continual oxygen therapy led to a gradual and significant decline (10 mm Hg) in mean pulmonary artery pressure over 4 to 8 weeks.⁶ Once therapy was discontinued, pulmonary artery pressure gradually increased. These data suggest that relief of hypoxia causes a gradual improvement in the vascular abnormalities related to hypoxic pulmonary vasoconstriction.

The prognostic value of pulmonary artery pressure was evaluated by Weitzenblum E et al (1981)⁷ with PAP>20 mm Hg, PaO₂45 mm Hg, FEV₁ml combined with an age of 60 years or older were associated with an increased four year mortality. However, this study did not address itself specifically to patients with corpulmonale. Also, the number of patients who received LTDO is not specified.

Kumar Ashutosh et al (1983)¹ conducted a study to develop criteria for predicting survival and clinical improvement with long-term domiciliary oxygen therapy (LTDO) in patients with COPD and corpulmonale. Twenty eight such patients were divided into two groups, responders (R) and non-responders (NR) on the basis of the fall in their mean pulmonary artery pressure (DPAP) while breathing 28 percent oxygen for 24 hours. The R (n = 17) and NR (n=11) had DPAP greater than and less than 5 mm Hg. Respectively. 88 percent of responders but only 22 percent of the non-responders were alive at the end of 2 years of LTDO. 85 percent of R, but only 11 percent of NR achieved end exercise maximal oxygen consumption (Max V_{O2}) greater than 6.5 ml/mm/kg. Left ventricular ejection fraction improved while breathing oxygen for 48 hours in the R only. They concluded that change in mean PA pressure greater than 5 mm hg and/or max V_{O2} 6.5 ml/kg/mm or greater predict 2 year survival with LTDO in patients with COPD and corpulmonale and can be useful in planning their management.

CONCLUSION

The following conclusion can be drawn from this study

1. Mean oxygen saturation of patients with corpulmonale was 70.5 percent before entry into the study. It was significantly lower that of patients with COPD and of controls. Oxygen therapy with 30 percent oxygen for 30 minutes brought about a significant increase in arterial oxygen saturation in patients with corpulmonale.
2. All patients with corpulmonale had ECG evidence of right ventricular hypertrophy.
3. Interventricular septal thickness in patients with corpulmonale was significantly more than that of patients of COPD and control. There was significant change in interventricular septal thickness after administration of oxygen in diastole.
4. Pulmonary artery diameter of patients with COPD was significantly more than that of control. Patients with corpulmonale had significantly larger mean PA diameter

as compared with the COPD group and control. Oxygen administration resulted in a significant decrease in pulmonary artery diameter in patients with corpulmonale.

5. The mean right atrial diameter was comparable in patients with COPD and controls. Patients with Corpulmonale had significantly larger RA dimension. Oxygen administration result in significant change in right atrial size.
6. Right ventricular free wall thickness in diastole was significantly more in patients with COPD as compared to controls. Patients with Corpulmonale had a mean RV free wall thickness of .762 cm which was significantly more than that of the other two groups. Oxygen administration did not result in any significant change in RV free wall thickness.
7. Right ventricular diameter was comparable in patients with COPD and in controls. The mean right ventricular diameter in systole and diastole was significantly more in patients with Corpulmonale. Oxygen administration had no significant effect on right ventricular diameters in patients with Corpulmonale.
8. Diastolic flow duration was significantly reduced in patients with COPD as compared with controls. The decrease in diastolic flow duration in patients with Corpulmonale was highly significant with control.
9. Left ventricular internal diameter in diastole and systole was significantly smaller in patients with corpulmonale as compared with controls and COPD patients. There was no significant change in left ventricular diameter after oxygen administration to corpulmonale patients.
10. Left ventricular volumes in diastole and systole of patients with COPD were not significantly different from controls. However, they were lesser than those of controls subjects in patients with corpulmonale. Oxygen administration had no significant effect on left ventricular volumes in patients with corpulmonale. Left ventricular volumes as estimated by two dimensional Echo were lower than those estimated by M mode Echo, but showed similar trends.
11. Left ventricular posterior wall thickness in diastole was significantly more in patients with corpulmonale. Oxygen administration demonstrated no significant change in this parameter.

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