Original Article

Long-Term Oxygen Therapy in Patients with Pulmonary Artery Hypertension

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Abstract

Introduction: Dyspnea associated with pulmonary arterial hypertension (PAH) requires supplemental oxygen to maintain oxygen saturation. Many researches related to oxygen therapy in chronic obstructive pulmonary disease and cor pulmonale are available, but the effect of long-term oxygen therapy (LTOT) has not been explored in PAH patients. **Aim:** This study aimed to determine the effect of LTOT in patients diagnosed with PAH. **Methodology:** All adult patients with PAH, primary or secondary to respiratory disease who require LTOT, were included in the study. The following parameters were collected: age, gender, severity of PAH based on echocardiogram, body mass index, comorbidities, type of oxygen therapy device, amount and duration of oxygen usage, mortality, frequency of readmission, oxygenation, and vital sign parameters. **Results:** This was a retrospective study which included 332 participants diagnosed to have PAH after detailed echocardiogram assessment. Out of these, 32 participants were prescribed LTOT at the time of discharge. At the time of discharge, there was a significant improvement in all the vital signs and oxygenation variables. The increase in oxygenation, hemoglobin, and reduced respiratory rate after LTOT was statistically significant ($P < 0.001$). During follow-up after 1 year, 26 (81.3%) participants survived, 3 participants (9.4%) expired, and 3 participants (9.4%) were lost to follow-up. **Conclusion:** The use of oxygen therapy is beneficial in patients with PAH in terms of improvement in oxygenation and reduction in hospital readmission. Survival at 1 year is 81% in patients using LTOT.

Keywords: Hypoxemia respiratory care, long-term oxygen therapy, pulmonary arterial hypertension

Introduction

Pulmonary arterial hypertension (PAH) is a heterogeneous disease primarily affecting small pulmonary arteries, which leads to reduction in cardiac output due to right heart failure and eventually death.[1] Dyspnea associated with PAH requires supplemental oxygen to maintain oxygen saturation (SpO_2) above 90% at all times.[2] There is a lack of evidence on the effectiveness of long-term oxygen therapy (LTOT) in PAH.

We aimed to determine the effect of LTOT in patients diagnosed with PAH. We hypothesized that LTOT decreases mortality rate and frequency of hospital readmission in PAH secondary to respiratory disease.

Methodology

A retrospective study was conducted from January 2014 to December 2015. Patients diagnosed to have PAH aged more than 18 years using LTOT were included in the study. Details were collected from the Medical Record Department over a 2-year period. The study was approved by the Institutional Ethical Committee.

As shown in Figure 1, the following parameters were collected: age, gender, severity of PAH based on echocardiogram, body mass index, comorbidities, type of oxygen therapy device, duration of oxygen usage, oxygen usage in L/min, mortality, frequency of readmission, oxygenation, and vital sign parameters.

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Statistical analysis

Descriptive data were expressed as mean ± standard deviation (SD) and percentage. Paired *t*-test was used for continuous data and Chi-square test was used for categorical variables. Statistical tests were performed using the SPSS v 16.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 332 participants diagnosed to have PAH after detailed echocardiogram assessment were included in the study. Out of this, 32 participants were prescribed LTOT at the time of discharge. The demographic data are summarized in Table 1. Two-thirds of the patients were women.

The study group was classified based on the World Health Organization classification of PAH. The comorbidities associated with pulmonary hypertension in these patients and the severity of pulmonary hypertension are also listed in Table 1. The severity of pulmonary hypertension and the gender distribution in each are illustrated in Figure 2.

Changes in oxygenation, respiratory rate, and hemoglobin from admission to discharge are summarized in Table 2. Changes in oxygenation are also shown in Figure 3. The changes in each of these parameters were highly significant. Figure 4 describes the BMI and Figure 5 describes the diagnosis according to WHO classification. Table 3 lists out the types of oxygen therapy devices and Table 4 describes the survival on follow-up and

Table 1: Baseline characteristics

Baseline characteristics	Parameters
Age (years) (mean±SD)	
Male	65±10
Female	54±10
Gender, *n* (%)	
Male	11 (34.4)
Female	21 (65.6)
Severity of PAH based on echocardiogram, *n* (%)	
Mild	1 (3.1)
Moderate	15 (46.9)
Severe	16 (50)
Respiratory and cardiac illness, *n* (%)	
Congestive heart failure	6 (18.8)
Ischemic heart disease	1 (3.1)
Asthma	6 (18)
COPD	12 (37.5)
Bronchiectasis	3 (9.4)
Tuberculosis	2 (6.3)
OSA	1 (3.1)
CTEPH	1 (3.1)

PAH: Pulmonary arterial hypertension, OSA: Obstructive sleep apnea, COPD: Chronic obstructive pulmonary disease, SD: Standard deviation, CTEPH: Chronic thromboembolic pulmonary hypertension

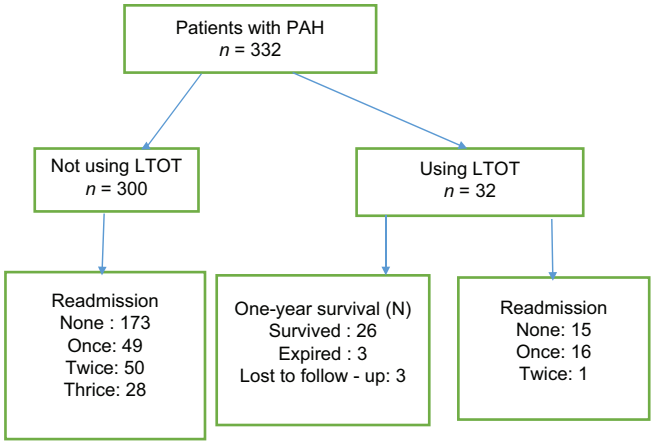

Figure 1: Consort diagram of the study

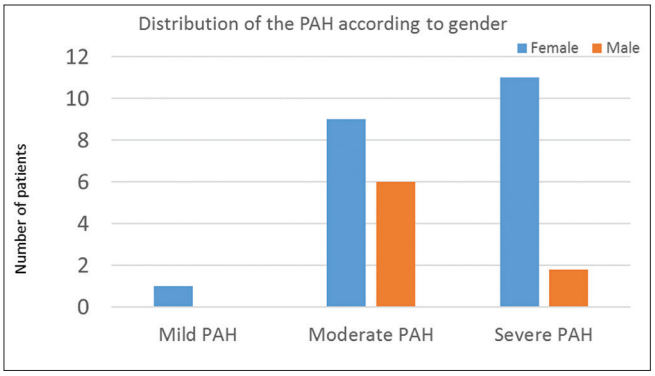

Figure 2: Severity of pulmonary arterial hypertension

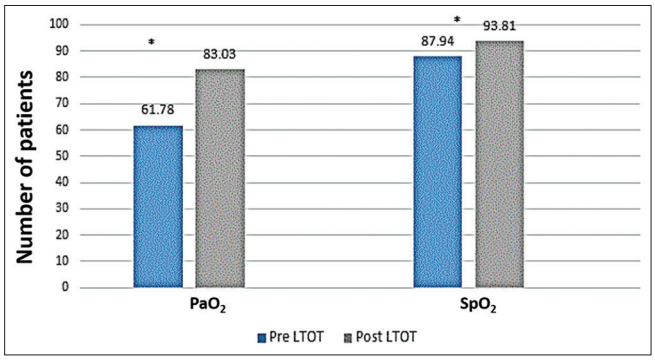

Figure 3: Changes in oxygenation

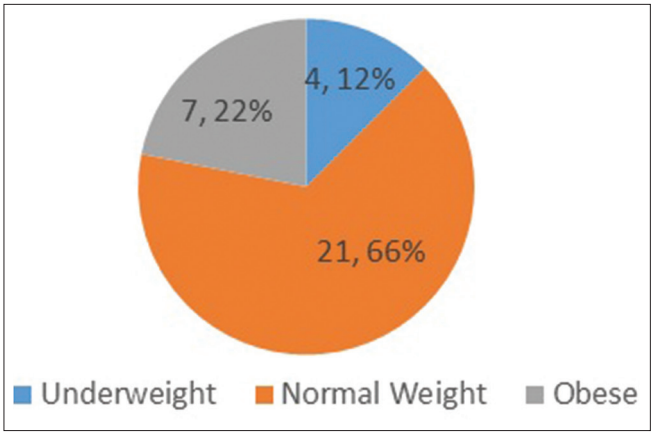

Figure 4: Body mass index

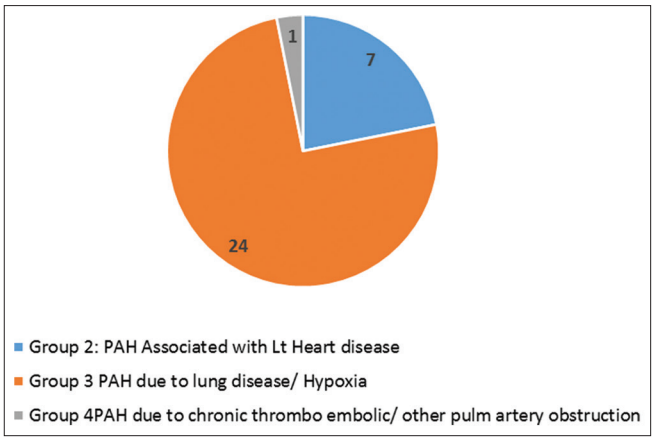

Figure 5: According to the classification of the World Health Organization

readmission pattern. There was a significant difference in the frequency of readmission in PAH participants who did not use LTOT.

Discussion

Two randomized controlled trials (RCTs) in chronic obstructive pulmonary disease (COPD) showed survival benefits when LTOT was used for 15 h/day.[3,4] An RCT on nocturnal oxygen therapy trial (NOTT) included 203 patients at six centers and they were randomly allocated to receive nocturnal oxygen therapy and continuous oxygen therapy. Baseline parameters such as arterial oxygen and carbon dioxide tensions (PaO_2 and $PaCO_2$), SpO_2, and demographics were recorded. Oxygen was administered by nasal prongs with a flow rate of 1–4 L/min. This trial reported a decrease in mortality rate after using LTOT and they concluded that continuous oxygen therapy was associated with lower mortality rates than nocturnal oxygen therapy.[3]

Cooper *et al*.[5] conducted a 12-year retrospective survival study in patients with hypoxic cor pulmonale prescribing LTOT as cor pulmonale is a maladaptive response to pulmonary hypertension. They included 72 patients in their study, 22 of whom were using oxygen concentrator and the rest cylinders. Baseline parameters were recorded before the therapy. The 1-year survival with oxygen therapy was found to be 88% and the overall 5-year survival was 62%. These study reports were considered to be better than the earlier report of 5-year survival without oxygen therapy, i.e., 40%. Weitzenblum *et al.* found out that LTOT for 15–18 h/day can reverse the progression of pulmonary hypertension in a high percentage of patients with severe COPD. The rationale behind the study was to report survival benefit with the use of oxygen therapy and to identify which group of PAH with their subtypes will be benefited with oxygen therapy.[6] Many researches related to oxygen therapy in COPD and cor pulmonale are available, but the effect of LTOT has not been explored in PAH patients.

Of the 332 patients with pulmonary hypertension enrolled in this study, 32 were prescribed LTOT. Two-thirds of the patients were women. The mean (±SD) age of men was 65 (±10) years and 54 (±14) years in women. Studies by Walker *et al*.[7] and Badesch *et al*.[8] showed that PAH is more prevalent among females with a ratio of 4.3:1. Up-to-date registries of PAH report older populations ranging from 50 ± 17 years to 65 ± 15 years.[9-12] In our study, 75% of participants who underwent LTOT were diagnosed as Group III which included asthma 6 (18%), COPD 12 (37.5%), bronchiectasis 3 (9.4%), tuberculosis 2 (6.3%), and obstructive sleep apnea 1 (3.1%). Chaouat *et al*. and Andersen *et al*. in their researches on the Global Initiative for Chronic Obstructive Lung Disease Stage IV revealed that most of these patients (90%) had PAH indicated by (mean pulmonary arterial pressure [mPAP]) >25 mmHg with most ranging between 20 and 35 mmHg and very few ranging between 3% and 5% with mPAP >35–45 mmHg.[13,14] Asthma and PAH are essentially separate diseases, but these

Table 2: Usage of oxygen in patients with pulmonary hypertension prescribed with long-term oxygen therapy

Type of oxygen therapy device	Patients
Cylinder (%)	19 (59.4)
Concentrator (%)	10 (31.3)
CPAP/cylinder (%)	3 (9.4)
Duration of oxygen usage/h (mean±SD)	15.22±1.963
Oxygen usage in (l/min)	
1 L/min	26
2 L/min	3
4 L/min	3

SD: Standard deviation, CPAP: Continuous positive airway pressure

Table 3: Changes in oxygenation, hemoglobin, and respiratory rate from baseline to discharge (pre- and post-long-term oxygen therapy)

	Baseline	Discharge	Difference in mean (95% CI)	*P*
PaO_2 (mmHg)	61.78±12.78	83.03±22.90	21.25 (−29.80-−12.69)	<0.001
SpO_2 (%)	87.94±4.127	93.81±2.520	5.875 (−7.284-−4.466)	<0.001
Hb (g%)	11.97±1.526	13.47±1.317	3.313 (4.139-8.175)	<0.001
RR (breaths/min)	25.66±1.961	22.34±1.537	1.503 (−1.919-−1.087)	<0.001

CI: Confidence interval, RR: Respiratory rate, Hb: Hemoglobin, SpO_2: Oxygen saturation

Table 4: Outcome data

Outcome variable	Patients
Mortality	
Survivors (%)	26 (81.3)
Died (%)	3 (9.4)
Dropouts (%)	3 (9.4)
Frequency of readmission	
No readmission	15
Once	16
Twice	1

two diseases have important pathological features in common which are inflammation, smooth muscle contraction, and remodeling.[15] In patients with COPD, chronic hypoxemia is a major reason for the development of pulmonary hypertension. Therefore, correction of alveolar hypoxia with supplemental oxygen appears suitable for treating pulmonary hypertension in COPD. The administration of LTOT has been shown to improve survival in COPD patients with chronic hypoxemia. Two major studies that reported the survival benefits of LTOT are Medical Research Council and the NOTT [3,4]

Our study showed significant improvement of oxygenation, respiratory rate, and hemoglobin in patients who used LTOT. The mean (±SD) duration of oxygen usage in our study was 15.22 (±1.963) hours during follow–up; at 1 year, 26 (81.3%) participants survived, 3 (9.4%) expired, and 3 (9.4%) dropped to follow-up. Sliwiński *et al*. suggested that the long-term use of oxygen may significantly improve survival, despite the lack of an acute oxygen effect on reducing pulmonary artery pressures.[16]

Weitzenblum *et al*.[6] suggested that LTOT for 15–18 h/day resulted in a small reduction in pulmonary hypertension after the first 2 years followed by a return to initial values and subsequent stabilization of PAPs over 6 years. In our study, patients who used LTOT had reduced hospital admission when compared to the patients who did not use LTOT.

A study by Ringbaek *et al*. shows that in hypoxemic COPD patients, LTOT is associated with a reduction in hospitalization.[17] Short-term readmission is common after PAH hospitalization. Patients admitted to high-volume PAH hospitals have lower rates of 30 days' readmission.[18] In the REVEAL Registry, PAH-related hospitalization was associated with relatively more re-hospitalization and worse survival at 3 years.[19] Our findings are similar to the findings in the literature. This study also calls for improvement in protocols, which lead to prescription of LTOT based on eligibility criteria, which aid to select the patients that might benefit most from such intervention. However, this study has not looked at the adverse effects of LTOT. The findings of this study should not be generalized due to its limitations.

This study has a few limitations: first, this was done on participants who were diagnosed by physicians seeking oxygen therapy. Therefore, it may not be generalized to the general population. Second, the diagnosis was not based on invasive measurements and 6-min walk test, and the study did not have a control group for comparison. Third, during follow–up, no vital sign parameters were measured as the patients were not visited by the research team. The values were recorded from the medical records available. Finally, the sample size was small.

Conclusion

Majority of patients with pulmonary hypertension are women. The use of LTOT is beneficial in patients with PAH in terms of improvement in oxygenation and reduction in hospital readmission. Survival of patients using LTOT is 81%.

A larger trial/RCT comparing PAH patients using LTOT compared to controls where patients are on standard therapy is required. A survey of the PAH with questionnaires based on the impact of LTOT on their activities of daily living and exercise tolerance pre- and post-treatment initiation and correlated with the level of hypoxia and the degree of pulmonary hypertension will help confirm these findings.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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