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Ambulatory Oxygen in Chronic Obstructive Pulmonary Disease

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Abstract

Ambulatory oxygen has been shown to improve pulmonary hemodynamics and reduce dynamic hyperinflation in patients with Chronic Obstructive Pulmonary Disease. Therefore, it is hypothesized to be of benefit in patients with either exertional desaturation or dyspnoea. There is evidence of short-term improvements in exercise distance, exercise time, breathlessness, oxygen saturation and minute ventilation. However, longer term studies only identified improvements in oxygenation and minute ventilation. The benefits were even more limited in patients with no resting hypoxemia. The role in improving exercise training in pulmonary rehabilitation by increasing exercise time and reducing dyspnoea was marginal and no improvements were detected in walking distance or quality of life. Practical considerations make compliance with ambulatory oxygen therapy a major issue with the weight of oxygen and social unacceptability the most often quoted problems. The evidence for any benefit of ambulatory oxygen is therefore limited despite the theoretical benefits.

Keywords: Ambulatory Oxygen, Pulmonary Rehabilitation, Long-Term Oxygen Therapy, Chronic Obstructive Pulmonary Disease (COPD)

1. Introduction

Since the 1980s, long-term oxygen therapy has been a non-surgical intervention proven to improve survival in Chronic Obstructive Pulmonary Disease(COPD) patients with severe resting hypoxemia. Treatment requiring 15 hours of oxygen has been shown to reduce mortality [1,2]. This forms the basis of standardized guidelines for the prescription and maintenance of home oxygen therapy. Long-term oxygen therapy may, however, be detrimental to patients' quality of life and hinder efforts at rehabilitation by rendering them homebound and connected to stationary oxygen concentrators that require direct wall currents for operation. It is postulated that ambulatory oxygen may contribute to the survival by enabling physical conditioning through improved mobility [3].

Exertional desaturation and dyspnoea portend a poorer morality prognosis. [4-6]. In a prospective study of 579 patients, exercise de-saturation of more than 4% to a saturation level of less than 90% conferred a 2.63 mortality risk in COPD patients [7]. The mechanisms behind exertional hypoxemia include ventilation perfusion mismatch, shunting and limitations in diffusion capacity [8]. Supplemental oxygen may delay diaphragmatic muscle fatigue and reduce lactic acidosis [9]. Oxygen has also been shown to have a beneficial effect on pulmonary hemodynamics by reducing the increase in pulmonary artery pressure and pulmonary wedge pressures that is experienced in exercise by patients with moderate to severe COPD [10].

Dynamic hyperinflation has also been demonstrated as a cause of exercise intolerance in COPD. A reduction in inspiratory capacity by 0.37 ± 0.39 liters in these patients during exercise showed a positive correlation with decreased maximum tidal volume attained during peak exercise ($r = 0.79$, $p < 0.0005$) [11]. The reduction of peak tidal volume in response to increased ventilatory demand contributes to exercise intolerance in COPD even in the absence of exertional desaturation [11]. Hyperoxia via supplemental oxygen is believed to reduce this ventilatory demand and reduce hyperinflation [12].

Currently there are no evidence-based guidelines for the prescription of ambulatory oxygen. To address this knowledge gap, this comprehensive review was carried out using a literature search through internet based research portal OvidSP and PubMed using the search terms: "ambulatory oxygen", "portable oxygen", "rehabilitation" and "oxygen", "air travel". A search for relevant meta-analyses of randomized controlled trials and systemic reviews via The Cochrane Library was also performed.

2. Use of Ambulatory Oxygen

2.1. Patients Already on Domiciliary Long-Term Oxygen Therapy

Long term oxygen therapy via an oxygen concentrator or cylinder can potentially limit mobility, debilitate function and risk deconditioning. There are meta-analysis data showing short-term benefit of ambulatory oxygen in COPD [13]. These data involve 31 studies consisting of 534 patients aged 47 to 73 with predominantly moderate to severe airflow obstruction and a mean resting arterial oxygenation of 52 mm to 85 mm Hg. Both maximal, as well as, endurance exercise testing were performed. The primary outcome of exercise capacity as measured by exercise distance in endurance testing improved by 18.86 meters (95% confidence interval CI was 13.11 to 24.61 meters, n = 238) with oxygen therapy. Similarly, exercise time increased by 2.71 minutes (95% CI, 1.96 minutes to 3.46 minutes, n = 77). In maximal exercise testing, ambulatory oxygen increased exercise distance by 32 meters (95% CI, 20.61 meters to 43.38 meters, n = 70) and exercise time by 1.06 minutes (95% CI, 0.67 minutes to 1.46 minutes, n = 50).

Secondary outcomes such as breathlessness, oxygen saturation and minute ventilation were not directly compared because of the dependence of exercise performance and instead were compared at isotime *i.e.* the time at which the group without oxygen ended the test. In endurance testing, oxygen reduced breathlessness by 1.15 points on the Borg scale (95% CI, –1.65 Borg points to –0.66 Borg points, n = 44); improved oxygen saturation by 8.36% (95% CI, 5.08% to 11.64%, n = 29) and reduced minute ventilation by 3.58 liters/minute (95% CI, –4.85 liters/min to –2.31 liters/min, n = 52). Similar findings were found on maximal exercise testing with improvements in oxygen saturation of 7.82% (95% CI, 4.89% to 10.74%, n = 31) and reductions in minute ventilation of 3.26 liters/minute (95% CI, –4.33 liters/minute to –2.19 liters/minute).

Although another systematic review [13] with studies of low heterogeneity provides evidence for the short-term improvements of ambulatory oxygen on exercise capacity in COPD, it is questionable if these statistically significant improvements are really clinically significant. The limitation in benefit achieved from supplemental oxygen may be due to the fact that COPD patients reach a ventilatory ceiling limit beyond which further improvements cannot be achieved with hyperoxia alone [9]. Furthermore, these studies do not provide guidance on what target oxygen saturation to dose titrate supplemental oxygen nor inform us of the long-term impact of this therapy.

Another systemic review involving 2 randomized controlled trials examined the longer-term effects of ambulatory oxygen on patients with COPD [14] and demonstrated a statistically significant reduction in minute ventilation during maximal exercise (weighted mean difference –11 liters/minute; 95% CI –17.53 liters/minute to –4.47 liters/minute; $p < 0.00097$) and increased PaO_2 at rest (weighted mean difference 17 mmHg; 95% CI 9.13 mmHg to 24.87 mmHg) after 12 weeks. There were modest but statistically insignificant improvements in Borg dyspnoea scores, distance walked and quality of life on the Chronic Respiratory Disease Questionnaire.

2.2. Patients with Exercise Desaturation or Dyspnoea

Ambulatory oxygen can improve exercise performance by reducing dynamic hyperinflation as deduced by a dose ranging study on non-hypoxaemic COPD patients compared to healthy subjects [15]. Significant reductions in minute ventilation, end-expiratory lung volume and respiratory rate with supplemental oxygen were found. Improved endurance time negatively co-related with end-expiratory lung volume ($r = 0.48$, $p = 0.002$) and dyspnoea rating correlated with reductions in respiratory rate at isotime. These benefits are seen in dose dependent increments of oxygen flow rates and oxygen fractions up to 50%.

Multiple small, single assessment studies have shown acute improvements in exercise tolerance, maximal exercise capacity and breathlessness (measured by Borg scores) in COPD patients on ambulatory oxygen. Oxygen increased exercise distance by 32 meters and significantly increased exercise time by 1.06 minutes. Dyspnoea improved by –1.16 Borg units [10]. 68% showed a 54 meter improvement in 6-minute-walk and 56% had clinically significant improvements in Chronic Respiratory Questionnaire [16]. Similarly, in a double-blind randomized controlled trial of 11 patients with severe COPD and exercise desaturation, the use of ambulatory oxygen prevented hypoxemia; improved the distance walked during 6-minut-walk test by 22%, and reduced the level of dyspnoea by an average of 2.09 units [17]. However, such acute responses to hyperoxia have not been found to be directly predictive of long-term exerse enhancements or quality of life [18,19].

Other recent studies have found no benefit of ambulatory oxygen over intranasal air in improving the extent of exertional dyspnoea or quality of life in patients with COPD. Results from a parallel, double-blinded, randomized controlled study [12], involving 139 patients, showed no significant differences between the ambulatory oxygen group versus placebo air in dyspnoea as measured by either the Transitional Dyspnoea Index or the Chronic Respiratory Disease Questionnaire; functional outcomes as measured by the 6-minute-walk, outings time or pedometer count; or health-related quality of life over 12 weeks. However, at baseline there was an improvement in 6-minute-walk distance in oxygen treated group by 10.7 ± 38.7 meters. The degree of exercise desaturation was also not predictive of therapeutic outcome [10,19]. These findings suggest that although oxygen supplementation may improve short term exercise tolerance, longer term benefits may depend on optimizing other factors that influence functional ability such as cardiovascular and muscle capacity. In another retrospective review of more than 400 patients with emphysema and exercise-induced hypoxemia over 8 years, no significant difference in survival was seen between the groups receiving continuous or intermittent oxygen [6].

The lack of standardized criteria in the definition of exercise desaturation continues to challenge research in establishing the effect of ambulatory oxygen on patients who develop hypoxemia on exertion. There are some proposals that recommend that ambulatory oxygen be prescribed to patients who demonstrate desaturation of ≥4% to an oxygen saturation of less than 90% on exertion [20,21]. The Long-term Oxygen Treatment Trial [LOTT] is an on-going multi-centre randomized controlled trial that aims to study the survival benefit of long-term domiciliary oxygen in 2 groups of COPD patients-a group with moderate hypoxemia (arterial saturation of 56 to 65 mmHg at rest) and a group with exercise desaturation. However, that study is unlikely to address many of the issues in this controversial area [22].

2.3. Role in Pulmonary Rehabilitation

Pulmonary rehabilitation in COPD patients has shown improvements in quality of life, exercise capacity and perception of dypsnoea [23]. If the benefits of exercise training lie in the duration and intensity of training; it was hypothesized that with supplemental oxygen, these patients could train longer. COPD patients with exertional desaturation area subgroup that may particularly benefit. In a meta-analysis of 2 randomized controlled trials comparing the use of ambulatory oxygen over placebo air in pulmonary rehabilitation, significant improvements were seen in exercise time (weighted mean difference 2.68 minutes; 95% CI 0.07 minutes to 5.28 minutes), as well as a reduction in Borg dyspnoea scores by a mean of –1.22 units (95% CI –2.39 to –0.06) [24]. No significant differences were seen in exercise outcomes, shuttle walk distance or health-related quality of life.

Wadell and colleagues demonstrated improved exercise performance (increased distance in 6-minute walk test by 14%), but there were no significant differences in exercise training effects between supplemental oxygen and air at the end of the rehabilitation period [25]. Similarly, Garrod *et al.* demonstrated improvement in dyspnoea scores by –1.46 units (95% CI –2.72 to 0.19) in patients with severe COPD on ambulatory oxygen compared to placebo room air, but there were no significant differences in other outcome measures such as shuttle walk test, Chronic Respiratory Disease Questionnaire, Hospital Anxiety and Depression Scale and London Chest Activity of Daily Living Scale [9]. There have been no studies to prove survival benefit in the use of supplemental oxygen in pulmonary rehabilitation. No recommendations have been made regarding the use of supplemental oxygen as an adjunct to pulmonary rehabilitation to improve survival [23]. Incidentally, there is also no evidence of any detrimental effects of supplemental oxygen during pulmonary rehabilitation.

3. Practical Considerations

Despite the relief of symptoms and acute improvement in exercise capacity, compliance to prescribed ambulatory oxygen is less than 50% [16,26] A qualitative study of 27 patients with COPD revealed several barriers to the use of ambulatory oxygen [27]. Patients listed weight of cylinder (92.5%), lack of patient education and perceived benefits (92.5%), embarrassment of being seen with an oxygen canister (77.8%) and lack of a carer (96.3%) as reasons as to why they were not compliant with their prescribed ambulatory oxygen [27]. Up to 50% of patients report difficulties with their oxygen cylinders because of poor portability or problems with the regulators [12]. Patients felt that despite the relatively lighter weight of an ambulatory oxygen system, it still contributed to their exertional dyspnoea and had a negative impact on their mobility. Comfort and costs were also other reasons cited by patients. Furthermore, relatively higher flow rates (6 liters/minute) may be needed in ambulatory oxygen therapy compared to domiciliary oxygen in order to alleviate exertional symptoms [12]. These higher flow systems may dry the upper airways and require more frequent refilling (**Table 1**).

Table 1. Practical considerations in the prescription of ambulatory oxygen.

	Factors	Implications
Equipment	Weight of cylinder	1). Increased exertional dyspnoea 2). Poor portability
	Oxygen flow rates	1). Higher flow rates increase discomfort 2). More frequent refilling required (leading to increased cost)
	Limited capacity of canister	1). More frequent refilling required (leading to increased cost)
Psychosocial	Embarrassment	1). Non-compliance
	Lack of patient education Lack of perceived benefits Lack of carer	1). Confusion over proper usage, duration of therapy 2). Non-compliance 3). Decreased community ambulation
	Costs	1). Increased economic burden
Other	Storage and handling	1). Fire hazard 2). Frostbite from liquid O_2 during refilling

4. Conclusions

The aim of ambulatory oxygen remains the relief of symptoms and the freedom to participate in activities of daily living without being debilitated by symptoms. The future calls for the development of more economical, highly portable and more efficient devices suitable for daily use. The benefits are not clearly defined, largely due to underpowered studies and lack of a standardized ethodology. There appears to be some role in acute relief of exertional dyspnoea and improved exercise capacity. However, short-term improvements in exercise testing may not necessarily lead to improved functional capacity in activities of daily living. Furthermore, no long term or survival benefit has been shown in the usage of ambulatory oxygen in patients with COPD. Patients also need to be fully engaged in their management and multiple practical limitations addressed before ambulatory oxygen is considered. Therefore, physicians should be extremely circumspect in the prescription of ambulatory oxygen. It should only be offered on a case-by-case basis to motivated and symptomatic patients after medical therapy with bronchodilators as well as inhaled steroids have been optimized and pulmonary rehabilitation has been completed. Patients who are hypercapneic at rest may also require blood gas analysis after initiating oxygen to exclude possibility of deterioration [12]. All cases should also be carefully monitored for clear evidence of symptomatic improvement before there is any commitment to long term therapy. More data on the efficacy of ambulatory domiciliary oxygen and to identify sub-groups who will clearly benefit are needed before definitive recommendations can be made.

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