

## Editorial

## Supplementary oxygen therapy in COPD: is it really useful?

P M A Calverley

Many patients with severe chronic obstructive pulmonary disease (COPD) develop hypoxaemia at rest when awake as their disease progresses. This may or may not be accompanied by hypercapnia but is a poor prognostic feature, independent of the forced expiratory volume in one second (FEV<sub>1</sub>).<sup>1</sup> For many years the scientific study of COPD was driven by the need to gain a greater understanding of the processes which led to these disorders of gas exchange. Ultimately this led to the introduction of effective treatment designed to increase the arterial oxygen tension beyond 8.0 kPa for at least 15 hours per day. The well known randomised controlled trials which confirmed the survival benefit of this treatment<sup>2-3</sup> are also the cornerstone of evidence based oxygen prescribing.<sup>4</sup> Since these results were published in the 1980s the costs of oxygen therapy have increased steadily in the UK and elsewhere<sup>5</sup> and constitute one of the largest medical expenses, particularly in the care of patients with COPD. Over half of this money is spent on providing oxygen for indications other than continuous domiciliary care. The rationale for these other indications is less secure and certainly less studied. The publication of two papers addressing different aspects of this treatment in this issue of *Thorax* is a welcome addition to our information about this common therapeutic problem.<sup>6,7</sup>

The physiological basis of exercise limitation in COPD has been challenged in recent years with the observation that end expiratory lung volume rises during exercise and is closely related to the degree of breathlessness.<sup>8,9</sup> Empirical studies have shown that supplementary oxygen increases the six minute walking distance compared with placebo in COPD,<sup>10,11</sup> and that these effects are most marked when tests of endurance rather than maximum exercise are conducted.<sup>12</sup> More detailed physiological studies suggest that this may be achieved by a reduction in minute ventilation rather than a specific "dyspnoegenic" effect.<sup>13</sup> These benefits have been shown in patients who are relatively normoxaemic at rest<sup>14</sup> but many COPD patients show periods of oxygen desaturation during exercise, the severity of which appears to be related to the carbon monoxide transfer factor (TLCO).<sup>15</sup> Indeed, the presence of such oxygen desaturations is required for the prescription of portable oxygen systems in North America. Pulmonary rehabilitation has been shown to be highly effective in improving exercise performance and reducing breathlessness in COPD.<sup>16</sup> However, there has been concern that, in promoting active exercise regimes, rehabilitation might worsen exercise hypoxaemia. Conversely, the correction of hypoxaemia during exercise might lead to more effective rehabilitation by permitting a greater degree of training than would otherwise be possible.

The role of supplementary oxygen in this setting has been addressed previously but a more thorough study is now reported by Garrod and colleagues<sup>6</sup> who followed 26

patients with moderate resting hypoxaemia and an FEV<sub>1</sub> of 30% predicted. They examined the effects of oxygen compared with air at the outset of a pulmonary rehabilitation programme and compared these results with the exercise performance and severity of breathlessness at the end of the exercise after the programme had been completed. They found in this parallel group design that oxygen therapy reduced the intensity of breathlessness without changing the distance walked before rehabilitation. After rehabilitation there was no significant difference between those who had trained while breathing oxygen and those who did not. Rehabilitation was effective and the authors were able to validate a new daily living scale which may be more appropriate for detecting change in patients with COPD.

This study raises a number of methodological points which apply to many other investigations. As the authors concede, it is a relatively small investigation and the effects of oxygen would need to be quite substantial before a study of this size would be able to show them, at least in terms of improved exercise capacity. Whether the extra inconvenience of training with oxygen is merited if there is no substantial gain to be made is an important point. It is a pity that the authors did not compare the interaction between rehabilitation and the acute effects of oxygen at the end of their study as this might be a justification for combining these modalities. They used the shuttle walking test as their measure of exercise performance.<sup>17</sup> This is a well validated tool which is certainly sensitive to change in rehabilitation, and is a halfway house between an endurance and maximum exercise test. However, the effects of oxygen are greatest in terms of endurance exercise and so it is possible that either a six minute walking test or the modified shuttle walking test<sup>18</sup> adapted for endurance purposes would have been a more sensitive outcome here. The fact that breathlessness was improved without changing the walking distance also raises the problem of studying any intervention where the response includes more than one degree of freedom. Patients who receive oxygen or undergo physical training may subsequently choose to exercise to the same level of breathlessness as previously but, because they are fitter or less distressed, they cover a greater distance. Alternatively, they may walk for the same distance but experience less breathlessness. The extent to which individuals consistently adopt a particular strategy has not been studied but clearly this complicates treatment studies such as this one and is a further reason for increasing the number of patients included. It is encouraging to see that oxygen desaturation in the placebo limb of this investigation was not associated with specific adverse effects, nor did it limit the benefits of pulmonary rehabilitation. Investigators have noted previously that acute treatment with bronchodilator drugs can worsen oxygen saturation but improve exercise performance and breathlessness,<sup>19</sup> so the

presence of desaturations alone should not discourage patients from undergoing active treatment.

Many patients with advanced COPD do not use oxygen during exercise, particularly in the UK where the availability of liquid oxygen systems is very limited. Much more commonly they resort to using oxygen as a way of rapidly relieving their breathlessness and this explains the large number of oxygen cylinders in peoples' homes. Surprisingly, there are remarkably few data about the frequency with which they are used or the effectiveness of this particular treatment. Administration of compressed gas, whether air or oxygen, can have a cooling effect on the face which itself may diminish the sensation of breathlessness, and this has been thought to explain the improvement in dyspnoea seen when breathing cool air in patients with COPD.<sup>20</sup> Very few studies have looked scientifically at whether or not oxygen is actually beneficial. In the most carefully conducted of these a significant benefit was seen in patients who were randomised to receive oxygen rather than compressed air when resting; breathlessness was used as the outcome measure.<sup>21</sup> However, many patients choose to use their oxygen only after breathlessness has been induced by some physical exercise and so the report by Killen and Corris<sup>7</sup> is very relevant to clinical practice. They examined the severity of breathlessness induced by standardised stair climbing in a group of 18 patients with severe COPD (FEV<sub>1</sub> 26% predicted) but who were not sufficiently hypoxaemic to merit domiciliary oxygen treatment. Only subjects who showed desaturations below 90% when exercising were included in the randomised crossover phase of the study. The intensity of breathlessness when they received air at rest and at the end of exercise was compared with the values after either oxygen before exercise or oxygen after exercise. Possibly because of the size of the investigation and the variability of the dyspnoea scores, individual comparisons between the three limbs were inconclusive. However, when treatment with oxygen was compared with treatment while receiving air, the oxygen treated patients clearly felt less breathless. Despite this, when asked to report their personal preference the patients could not distinguish air from oxygen. Clearly, it would be helpful to know how reproducible this kind of practical exercise task is and, in particular, whether patients show the kind of trade off between dyspnoea and exercise performance already noted elsewhere. Perhaps an even more relevant outcome would be the rate at which breathlessness resolved, and this is not clearly described in the present paper. The use of a different "short burst" exercise protocol may explain the benefits reported in this study compared with previous studies of pre-oxygenation in COPD. Moreover, the patient groups studied here are more severe than in most comparative investigations and are thus closer to the kind of patient likely to receive this treatment.

Investigation of the effectiveness of oxygen therapy has become unfashionable in the last decade following the key studies mentioned earlier. The papers by Garrod *et al* and Killen and Corris illustrate that there is still much to be

learned about the practical application of this expensive and widespread form of treatment. For many patients the use of "as needed" supplementary oxygen is likely to be as much a marker of their overall deterioration as an effective means of alleviating their symptoms, and behavioural considerations about who receives treatment and why are likely to be as important as physiological ones. Nonetheless, these data show that oxygen can have a useful role when applied acutely in the management of patients with COPD. Equally clearly, not everyone benefits and future studies should focus on identifying those people who are likely to experience most improvement with this treatment.

P M A CALVERLEY

*Pulmonary and Rehabilitation Research Group,  
University Clinical Department,  
Fazakerley Hospital,  
Liverpool L9 7AL,  
UK  
email: pmacal@liverpool.ac.uk*

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