The use of oxygen in the palliation of breathlessness. A report of the expert working group of the scientific committee of the association of palliative medicine

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Summary Dyspnoea is a common, distressing symptom and difficult to control with medical treatment. The role of oxygen in reducing the severity of the symptoms and improving quality of life is still unclear. A working party of the Association of Palliative Medicine Science Committee set out to examine the evidence concerning the use of oxygen for the palliation of breathlessness in COPD, advanced cancer and chronic heart failure and to make recommendations for clinicians working in palliative care. There were very few randomised controlled trails available for any of these conditions. There was no evidence available for heart failure, very little for advanced cancer and although there were a number of trails on the use of oxygen in COPD very few, until recently, used reduction of breathlessness as an outcome measure. Recommendations are made on the basis of the evidence available and expert opinion such as the Royal College of Physicians report on the use of domiciliary oxygen. Oxygen use has to be tailored to the individual and a formal assessment made of its efficacy for reducing breathlessness and improving quality of life for that person.

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KEYWORDS
Dyspnoea; Cancer; Heart failure; COPD; Palliation; Oxygen

Introduction

Breathlessness remains an enigma.1 It is a dominant symptom in the advanced stages of many disorders including cancer, cardio-respiratory and neurological disease. Clinicians are often unable to control breathlessness effectively2 in contrast with malignant pain management where it is now possible to offer relief for most patients with oral pharmacological therapy alone even in advanced disease. In their last year of life as many as 94% patients with chronic lung disease, 78% of those with lung cancer3 and more than 50% of patients with heart disease4 will experience breathlessness. Its prevalence is increasing in the population as a whole for a
number of reasons, paradoxically, for example, because of the success of the secondary prevention of the complications of myocardial infarction\(^5\) which delay but do not prevent the onset of heart failure and breathlessness. Breathlessness is a problem that is reaching epidemic proportions.\(^6,7\)

It is clear that a unitary theory of the causation of breathlessness is inadequate—it is not simply a disorder of the heart and lungs either singly or in combination. It is a complex multisystem disorder with evidence of neurohormonal abnormalities, peripheral and respiratory muscle dysfunction; and a whole host of other changes outside the cardio-respiratory system.

There is continuing controversy about the place of oxygen in palliative care. In the early palliative care literature, it is generally stated that oxygen therapy can do more harm than good if the equipment comes between patient and family in the late stages of an illness. There was, and remains, a concern that patients can become dependent on oxygen, not wishing it to be removed even when they are clearly dying and when pharmacological therapy could offer some relief in the form of sedation.

Domiciliary oxygen is expensive.\(^8\) In the Cambridgeshire area alone (population 775,000) nearly 14 million pounds was spent on oxygen concentrators in 2000, a rise from 11 million in 1996. It is important that clinicians are able to target this drug at the right patients as oxygen can have adverse effects (Appendix A) as well as benefits for patients’ and families’ quality of life.

This working party set out to examine the evidence available for the use of oxygen in the palliation of breathlessness in chronic obstructive pulmonary disease (COPD), advanced cancer and cardiac failure. We did not consider neurological disease, interstitial lung disease or acute exacerbations of heart failure or COPD. Oxygen is one part of a complete palliative care treatment strategy—other appropriate medical and surgical interventions, the management of psychological and social concerns and support of the family and other carers are also essential to produce the best symptom relief possible. These aspects of care are not further mentioned as the remit of this group was to assess the evidence available on the use of oxygen in the palliation of breathlessness and make recommendations (even where good evidence was scarce) to guide palliative care clinicians in the use of oxygen for the palliation of breathlessness.

We were asked to consider only randomised controlled trials (RCT)\(^9\) and the search strategy used is set out in each section. The evidence for each patient group is summarised and then general clinical recommendations are made from our findings and expert clinical opinion.\(^10,11\)

**Definitions**\(^10\)

*Short-burst oxygen therapy:* Intermittent use of oxygen for relief of breathlessness, before exercise or for recovery after exercise.

*Ambulatory oxygen therapy:* Provision of oxygen therapy during exercise and/or the activities of daily living.

*Long-term oxygen therapy (LTOT)*: Provision of oxygen therapy at home on a continuous and long-term basis, ideally for at least 15 h daily, including time spent asleep. In COPD, it is prescribed within specific guidelines to prolong survival.

**Background**

Participants with COPD in trials of oxygen use can be divided into four groups: those with acute exacerbations, at rest, during exercise or on long-term oxygen therapy. The British Thoracic Society (BTS) guidelines recommend the use of long-term oxygen therapy in specific patients to improve survival rather than palliation, as it reduces secondary polycythemia, prevents progression of pulmonary hypertension and improves neuropsychological health. At rest the BTS COPD guidelines\(^11\) state “Short bursts of oxygen from a cylinder via a facemask are widely prescribed to relieve breathlessness. There are no data to support or refute this practice…” The guidelines also state that good evidence to support the use of ambulatory oxygen is also lacking.

Dyspnoea is a common symptom in patients with advanced cancer and generally has a mixed aetiology.\(^12\) Oxygen is commonly used in the palliation of breathlessness without clear evidence of its efficacy.

The mechanisms behind the sensation of breathlessness in chronic heart failure (CHF) are not clear and are thought to be multifactorial. In addition to a variable amount of pulmonary oedema, there is an abnormal ventilatory response to exercise and carbon dioxide production resulting in an increased ventilatory dead space. Other factors may include increased arterial chemoreceptor sensitivity and abnormal skeletal muscle with enhanced muscle ergoreflex activity that further stimulates ventilation and sympathetic activity.
Method

Search strategies

A search was undertaken focused on Medline, EMBASE and the Cochrane Library limited to human studies from 1966 (1975 for heart failure). For subjects with COPD the keywords of oxygen, oxygen therapy, COPD, chronic obstructive airways disease, breathlessness and dyspnoea were searched in various combinations. The references of relevant papers were then hand searched together with Chest, Thorax and The American Journal of Respiratory and Critical Care Medicine from 1970. For subjects with cancer the keywords of oxygen, oxygen therapy, cancer, neoplasm and breathlessness/dyspnoea were searched in various combinations. The references of relevant papers were then hand searched. For subjects with heart failure the search words were CHF, oxygen therapy and breathlessness. All studies, which recorded when breathlessness was cited as a reason to stop an exercise regimen, were also reviewed.

Outcome measures

A reduction in breathlessness as measured with a specific tool or scale. In the studies found, these were often simple visual analogue scales (VASs) or the Borg scale.13

Results

Patients with COPD

There were no large RCTs found. The trials included in this review were small controlled trials either single or double blind. A crossover design was used in all trials except those of long-term oxygen. Many studies14 measured physiological variables and endurance whilst using oxygen but did not assess dyspnoea. The results are shown in table form divided into three categories of trial participants — at rest, exercise and long-term oxygen therapy at rest.

Oxygen therapy at rest: Only five papers were found where oxygen therapy was given to patients with COPD at rest and these are summarised in Table 1.

Oxygen therapy and exercise (ambulatory and short-burst oxygen): Exercise tests used included treadmill, cycle, 6 min or endurance walks; often two types of exercise were used in each study. Oxygen therapy is given during exercise unless

<table>
<thead>
<tr>
<th>Study</th>
<th>Methods</th>
<th>No.</th>
<th>Mean baseline oxygen levels</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcome</th>
<th>Main effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liss and Grant15</td>
<td>Single blind crossover trial</td>
<td>8</td>
<td>PaO2 7.07 kPa</td>
<td>2 and 4 l/min oxygen with or without Lidocaine</td>
<td>2 and 4 l/min compressed air all via nasal cannulae</td>
<td>Change in VAS</td>
<td>No significant difference. Lidocaine increases dyspnoea</td>
</tr>
<tr>
<td>Kollef and Johnson</td>
<td>Single blind crossover trial</td>
<td>9</td>
<td>PaO2 6.67 kPa</td>
<td>Transtracheal oxygen at 2 and 4 l/min with and without Lidocaine</td>
<td>Transtracheal air at 2 and 4 l/min</td>
<td>Change in VAS</td>
<td>Significantly more breathless on high flow oxygen and air. With Lidocaine no difference</td>
</tr>
<tr>
<td>Swinburn et al.17</td>
<td>Double blind randomised crossover trial</td>
<td>12</td>
<td>PaO2 6.7 kPa and SaO2 85%</td>
<td>28% oxygen via mask</td>
<td>Compressed air via mask</td>
<td>Change in VAS</td>
<td>Significant improvement on oxygen</td>
</tr>
<tr>
<td>O'Donnelly et al.19</td>
<td>Baseline test pre-exercise trial</td>
<td>11</td>
<td>PaO2 6.9 kPa</td>
<td>60% oxygen using mouth piece</td>
<td>21% oxygen using mouth piece</td>
<td>Change in Borg</td>
<td>No difference in reported dyspnoea</td>
</tr>
</tbody>
</table>

68 S. Booth et al.
<table>
<thead>
<tr>
<th>Study</th>
<th>Methods</th>
<th>No.</th>
<th>Mean baseline oxygen</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcome</th>
<th>Main effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Woodcock et al.</td>
<td>Double blind RCT</td>
<td>10</td>
<td>PaO₂ rest 9.65 kPa and exercise 8.19 kPa</td>
<td>Oxygen carried by subject or assistant</td>
<td>Compressed air both via nasal cannulae</td>
<td>Change in VAS</td>
<td>Slower increase in dyspnoea and increased endurance</td>
</tr>
<tr>
<td>Waterhouse and Howard</td>
<td>Single blind RCT</td>
<td>20</td>
<td>PaO₂ on exercise 8.9 kPa</td>
<td>Oxygen 2 and 4 l/min via nasal cannulae</td>
<td>Compressed air via nasal cannulae and room air</td>
<td>Change in VAS</td>
<td>Reduced dyspnoea on oxygen</td>
</tr>
<tr>
<td>Swinburn et al.</td>
<td>Double blind RCT</td>
<td>5</td>
<td>SaO₂ 93% rest and 86% on exercise</td>
<td>Oxygen 60% via mouth piece</td>
<td>Room air via mouth piece</td>
<td>Change in VAS</td>
<td>Increased endurance, same dyspnoea</td>
</tr>
<tr>
<td>Evans et al.</td>
<td>Single blind RCT</td>
<td>19</td>
<td>PaO₂ rest 8.05 kPa</td>
<td>Oxygen after exercise via mask</td>
<td>Compressed air via mask and room air</td>
<td>Change in VAS</td>
<td>Shorter recovery time with oxygen</td>
</tr>
<tr>
<td>Davidson et al.</td>
<td>Double blind RCT</td>
<td>17</td>
<td>PaO₂ 8.60 kPa, SaO₂ 94% at rest and 87.5% on exercise</td>
<td>Oxygen subjects choice of mask/nasal cannulae</td>
<td>Compressed air given as oxygen</td>
<td>Change in VAS</td>
<td>Slower increase in dyspnoea and increased endurance</td>
</tr>
<tr>
<td>Lane et al.</td>
<td>Single blind non-randomized crossover trial</td>
<td>9</td>
<td>PaO₂ 8.92 kPa at rest</td>
<td>Oxygen to maintain oxygen saturation via mouth piece</td>
<td>Room air via mouth piece</td>
<td>Change in VAS</td>
<td>Reduced dyspnoea on oxygen</td>
</tr>
<tr>
<td>McKeon et al.</td>
<td>Double blind RCT</td>
<td>21</td>
<td>PaO₂ 8.85 kPa and SaO₂ 92% rest and 83% exercise</td>
<td>Portable oxygen at 4 l/min via nasal cannulae</td>
<td>Compressed air via nasal cannulae and room air</td>
<td>Change in VAS</td>
<td>Slower increase in dyspnoea on oxygen</td>
</tr>
<tr>
<td>McKeon et al.</td>
<td>Double blind RCT</td>
<td>20</td>
<td>PaO₂ 7.73 kPa and SaO₂ 91% rest and 83% after exercise</td>
<td>Oxygen before exercise via nasal cannulae</td>
<td>Compressed air before exercise via nasal cannulae</td>
<td>Change in VAS</td>
<td>No difference</td>
</tr>
<tr>
<td>Leach et al.</td>
<td>Single blind RCT</td>
<td>20</td>
<td>PaO₂ 8.74 kPa at rest and 7.82 kPa after exercise</td>
<td>Oxygen at 2, 4 and 6 l/min via mask</td>
<td>Compressed air 4 l via mask</td>
<td>Change in VAS</td>
<td>Reduced dyspnoea on oxygen</td>
</tr>
<tr>
<td>Dean et al.</td>
<td>Double blind RCT</td>
<td>12</td>
<td>PaO₂ 9.47 kPa at rest and 8.4 kPa after exercise</td>
<td>40% oxygen via mouth piece</td>
<td>Compressed air via mouth piece</td>
<td>Change in Borg</td>
<td>Increased endurance until limited by the same dyspnoea</td>
</tr>
<tr>
<td>Dewan and Bell</td>
<td>Single blind RCT</td>
<td>10</td>
<td>SaO₂ maintained at</td>
<td>High and low flow transtracheal</td>
<td>High and low flow air through nasal</td>
<td>Change in Borg</td>
<td>High flow greater dyspnoea and increased endurance</td>
</tr>
<tr>
<td>Study</td>
<td>Methods</td>
<td>No.</td>
<td>Mean baseline oxygen</td>
<td>Intervention</td>
<td>Comparison</td>
<td>Outcome</td>
<td>Main effect</td>
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</tr>
<tr>
<td>Roberts et al. 31</td>
<td>Non-blind RCT</td>
<td>15</td>
<td>92% and 98% PaO2 6.98 kPa and lowest SaO2 74.6%</td>
<td>Oxygen therapy cannulae</td>
<td>Continuous oxygen via nasal cannulae and room air</td>
<td>Change in VAS</td>
<td>Less dyspnoea on both methods of giving oxygen</td>
</tr>
<tr>
<td>O’Donnell et al. 32</td>
<td>Double blind RCT</td>
<td>11</td>
<td>PaO2 9.87 kPa and SaO2 90%</td>
<td>Oxygen 60% via mouth piece</td>
<td>21% oxygen via mouth piece</td>
<td>Change in Borg scale</td>
<td>No change in dyspnoea but increased endurance</td>
</tr>
<tr>
<td>Marques-Magallanes et al. 33</td>
<td>Single blind RCT</td>
<td>18</td>
<td>PaO2 6.8 kPa</td>
<td>Oxygen 40% after exercise via mask</td>
<td>Compressed air via mask and room air</td>
<td>Change in VAS</td>
<td>No reduction in dyspnoea</td>
</tr>
<tr>
<td>Revill et al. 34</td>
<td>Single blind RCT</td>
<td>10</td>
<td>SaO2 92% at rest and 80% on exercise</td>
<td>Oxygen 2 l/min via nasal cannulae</td>
<td>Sham oxygen via nasal cannulae and room air</td>
<td>Change in Borg scale</td>
<td>No change in dyspnoea but increased endurance</td>
</tr>
<tr>
<td>Killen and Corris 35</td>
<td>Single blind RCT</td>
<td>18</td>
<td>SaO2 94% at rest and &lt;90% on exercise</td>
<td>Oxygen 2 l/min via face mask before and after exercise Oxygen at 4 l/min via nasal cannulae</td>
<td>Compressed air via face mask</td>
<td>Change in VAS</td>
<td>Reduced dyspnoea on oxygen</td>
</tr>
<tr>
<td>Knebel et al. 36</td>
<td>Double blind RCT</td>
<td>31</td>
<td>SaO2 97% at rest and 90% on exercise</td>
<td>Compressed air via nasal cannulae and room air</td>
<td>Compressed air via nasal cannulae</td>
<td>Change in VAS</td>
<td>No reduction in dyspnoea</td>
</tr>
<tr>
<td>Somfay et al. 37</td>
<td>Single blind RCT</td>
<td>10</td>
<td>SaO2 95.7% at rest and 92% on exercise</td>
<td>Oxygen at 30%, 50%, 75% and 100% via mouth piece</td>
<td>Compressed air via mouth piece</td>
<td>Change in modified Borg</td>
<td>Oxygen dose-dependent reduction in dyspnoea</td>
</tr>
<tr>
<td>Jolly et al. 38</td>
<td>Double blind RCT</td>
<td>20</td>
<td>PaO2 &gt; 8 kPa at rest and on exercise two groups SaO2 &lt; 90% and &gt; 90%</td>
<td>Oxygen 6, 9 and 12 l/min via nasal cannulae</td>
<td>Compressed air via nasal cannulae</td>
<td>Change in Borg scale</td>
<td>Oxygen reduced dyspnoea in desaturation and non-desaturation groups</td>
</tr>
<tr>
<td>Maltais et al. 39</td>
<td>Double blind RCT</td>
<td>14</td>
<td>PaO2 11.3 kPa at rest and 9.33 kPa on exercise</td>
<td>Oxygen via mouth piece (FiO2 = 0.75)</td>
<td>Room air via mouth piece</td>
<td>Change in Borg scale</td>
<td>Reduced dyspnoea on oxygen</td>
</tr>
<tr>
<td>O’Donnell et al. 19</td>
<td>Double blind RCT</td>
<td>11</td>
<td>PaO2 6.93 kPa at rest and 6.13 kPa after exercise</td>
<td>Oxygen 60% via mouth piece</td>
<td>Oxygen 21% via mouth piece</td>
<td>Change in Borg scale</td>
<td>Increased endurance until limited by the same dyspnoea</td>
</tr>
<tr>
<td>Eaton et al. 40</td>
<td>Double blind RCT over 12 weeks</td>
<td>50</td>
<td>At rest PaO2 9.2 kPa and SaO2 94% and</td>
<td>Oxygen 4 l/min during exercise via nasal cannulae</td>
<td>Compressed air 4 l/min during exercise via nasal cannulae</td>
<td>Change in chronic respiratory</td>
<td>Reduced dyspnoea on oxygen</td>
</tr>
</tbody>
</table>
Table 3  Summary of studies using oxygen therapy in the long term for breathlessness in patients with COPD.

<table>
<thead>
<tr>
<th>Study</th>
<th>Methods</th>
<th>No.</th>
<th>Mean baseline oxygen</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcome</th>
<th>Main effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>McDonald et al.</td>
<td>Single blind randomised crossover trial over 12 weeks</td>
<td>26</td>
<td>PaO₂ 9.2 kPa and SaO₂ 94%</td>
<td>Oxygen 4 l/min via nasal cannulae</td>
<td>Compressed air via nasal cannulae during exercise</td>
<td>Change in Borg</td>
<td>No significant change in dyspnoea</td>
</tr>
<tr>
<td>Rooyackers et al.</td>
<td>Randomised controlled trial over 10 weeks not blind</td>
<td>24</td>
<td>PaO₂ 10 kPa at rest and 7.3 kPa at peak exercise</td>
<td>Oxygen 4 l/min during exercise</td>
<td>Room air during exercise 10 weeks</td>
<td>Change in Borg and chronic respiratory disease questionnaire</td>
<td>Rehabilitation programme improved dyspnoea, no increased benefit from supplemental oxygen</td>
</tr>
<tr>
<td>Garrod et al.</td>
<td>Single blind randomised controlled trial over 6 weeks</td>
<td>22</td>
<td>At rest PaO₂ 8.5 kPa and SaO₂ 92.3%, SaO₂ 82% on exercise</td>
<td>Oxygen 4 l/min during exercise via nasal cannulae</td>
<td>Compressed air 6 weeks during exercise via nasal cannulae</td>
<td>Change in Borg</td>
<td>Small decrease in dyspnoea</td>
</tr>
<tr>
<td>Eaton et al.</td>
<td>Double blind RCT over 12 weeks</td>
<td>50</td>
<td>At rest PaO₂ 9.2 kPa and SaO₂ 94% and SaO₂ 82% after exercise</td>
<td>Oxygen 4 l/min during exercise via nasal cannulae</td>
<td>Compressed air 4 l/min during exercise via nasal cannulae</td>
<td>Change in chronic respiratory disease questionnaire</td>
<td>Small decrease in dyspnoea</td>
</tr>
</tbody>
</table>
otherwise stated. Twenty-two papers were found and the results are summarised in Table 2.

Long-term oxygen therapy (LTOT): Trials of LTOT tend to use quality of life measures as opposed to measurements of breathlessness and only three have been included using our criteria. The aim of LTOT is to prolong survival not to palliate dyspnoea but where dyspnoea was assessed it was important to see the effect. The trials are summarised in Table 3.

Patients with cancer

There were no large RCTs found. Two of the trials included in this review were small controlled trials with a crossover design and one an 'N of 1’ study. The results for patients with advanced cancer are shown in Table 4. The patients in the trials had advanced cancer with either primary or secondary disease in the thorax. Most, but not all had lung cancer.

Table 4 Summary of studies using oxygen therapy for breathlessness in patients with advanced cancer.

<table>
<thead>
<tr>
<th>Study</th>
<th>Methods</th>
<th>No.</th>
<th>Mean baseline oxygen</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcome</th>
<th>Main effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bruera et al.</td>
<td>N of 1 double blind crossover trial</td>
<td>1</td>
<td>SaO2 84%</td>
<td>Oxygen at 5 l/min for 5 min at rest via mask</td>
<td>Compressed air at 5 l/min via mask</td>
<td>Change in VAS</td>
<td>Less breathless on oxygen</td>
</tr>
<tr>
<td>Bruera et al.</td>
<td>Double blind crossover trial</td>
<td>14</td>
<td>&lt;90% SaO2</td>
<td>Oxygen at 5 l/min for 5 min at rest via mask</td>
<td>Compressed air at 5 l/min via mask</td>
<td>Change in VAS</td>
<td>Less breathless on oxygen</td>
</tr>
<tr>
<td>Booth et al.</td>
<td>Single blind crossover trial</td>
<td>38</td>
<td>Between 80% and 99% SaO2</td>
<td>Oxygen at 4 l/min for 15 min at rest via nasal cannulae</td>
<td>Compressed air at 4 l/min via nasal cannulae</td>
<td>Change in VAS and Borg scale</td>
<td>Improvement with air and oxygen and no significant difference between the two gases</td>
</tr>
</tbody>
</table>

Table 5 Summary of the available evidence on the use of oxygen in chronic heart failure.

<table>
<thead>
<tr>
<th>Study</th>
<th>Method</th>
<th>No./ NYHA grade</th>
<th>Comparison</th>
<th>Outcome</th>
<th>Main effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moore et al.</td>
<td>Double blind RT Bicycle ergometer exercise test</td>
<td>7/II 5/III</td>
<td>21%, 30% and 50% oxygen via a mouthpiece</td>
<td>Change perceived exertion (Borg scale) and dyspnoea (VAS)</td>
<td>Mean SaO2 unchanged during exercise on air Dyspnoea reduced with 50% oxygen Mean SaO2 fell on exercise on air No change in distance walked or Borg or VAS scores with oxygen</td>
</tr>
<tr>
<td>Restrick et al.</td>
<td>Double blind RT 6 min walks, oxygen carried by subject or assistant. Endurance walks, oxygen carried by subject</td>
<td>12/III</td>
<td>Air and oxygen at 2 and 4 l/min via nasal cannulae</td>
<td>Change in breathlessness as rated on a modified Borg scale and VAS</td>
<td></td>
</tr>
<tr>
<td>Russell et al.</td>
<td>Double blind RT. Bicycle ergometer exercise test</td>
<td>16/II–III</td>
<td>21% and 60% oxygen via a mouthpiece</td>
<td>Stated reason for stopping exercise</td>
<td>Mean SaO2 unchanged during exercise on air 13 subjects stopped exercising complaining of fatigue and three because of dyspnoea</td>
</tr>
</tbody>
</table>
Patients with heart failure

There were no large randomised controlled studies found. There were no studies specifically looking at the effects of oxygen on reducing the sensation of breathlessness in severe heart failure.

There were two small studies which included VAS score and/or Borg scale for breathlessness as one of the study end-points and one study recorded dyspnoea as a reason patients gave for stopping exercise schedules. The studies are discussed below and summarised in Table 5.

Moore et al.46 found that during bicycle ergometer exercise testing with oxygen-enriched air, there was a significant increase in arterial oxygen saturation. In addition, total exercise duration was prolonged, carbon dioxide production was reduced. When breathing 50% oxygen, perceived exertion rated (Borg score) was significantly reduced and subjective dyspnoea scores rated lower on a VAS. Inhaling 30% oxygen produced values intermediate between air and 50% oxygen. Restrick et al.47 and Russell et al.48 did not confirm this. Restrick, in a double-blind study of 12 subjects with heart failure (New York Heart Association (NYHA) class III) found that although 2 and 4 l/min ambulatory oxygen increased resting arterial oxygen saturation compared with air, there was no significant difference in distance walked or perceived breathlessness on a Borg or VAS. In this study, patients were required to carry their own portable oxygen cylinders: this would have increased workload in compromised patients. Russell et al. failed to show any reduction in minute ventilation or functional benefit with higher oxygen concentrations. The study unfortunately did not look at the subjective assessment of breathlessness although the authors did comment on the number of patients who stopped due to breathlessness or fatigue. All patients had the same reason for stopping during exercise tests, breathing either concentration of oxygen. In both Moore and Russell’s studies, the mean arterial oxygen saturation did not fall during exercise on air in contrast to Restrick’s study where the mean oxygen saturation fell significantly. In response to Russell’s study, Abinader and Sharif49 noted that the effect of increased oxygen concentration in patients with heart failure is variable. They commented that the concentration of 60% inspired oxygen was probably too high leading to an increase in systemic vascular resistance and also suggested that the exercise programme may have been too strenuous for those with severe heart failure. They also raised the point that none of Russell’s subjects desaturated on exercise and suggested that it is those patients with heart failure who desaturate on exercise that benefit most from oxygen.

Chua et al.50 investigated the contribution of the peripheral chemoreceptors to ventilation and also the effects of their suppression on exercise tolerance in patients with mild to moderate heart failure. In the course of this study, an increase in exercise tolerance and a decrease in dyspnoea was noted when the participants were breathing 100% oxygen—but as a descriptive study this was not included in our review of evidence.

Summary of evidence in patients with COPD

(1) There is evidence for and against using oxygen for palliation of breathlessness at rest.
(2) The majority of studies using oxygen during exercise show that patients experience less breathlessness at equivalent level of exercise when compared to air.
(3) There is no evidence that pre-oxygenation reduces breathlessness during exercise.
(4) There is recent evidence that using oxygen may speed recovery from breathlessness, given before or after exercise.35
(5) A recent study suggests that the effect of ambulatory oxygen on quality of life over a longer-term cannot be predicted from patients’ baseline characteristics or their acute/short-term response to oxygen therapy.40 Even when they experienced acute/short-term response to oxygen therapy, a significant proportion of patients will not continue to use ambulatory oxygen at home because of poor tolerability.

It is important to note that all these trials had small numbers of subjects. In most papers the investigators remark on the markedly different responses from one patient to another.

Summary of evidence in patients with cancer

Oxygen may be helpful for the palliation of breathlessness in some patients with advanced cancer but at the present time there is little evidence to enable clinicians to predict which patients will obtain benefit. Some form of formal clinical assessment like an ‘N of 1’ trial, is necessary to determine its usefulness for each individual.

Summary of evidence in patients with heart failure

There is insufficient evidence currently available for the use of oxygen for breathlessness in these patients. Most patients included in the reviewed
studies had stable mild to moderate heart failure (NYHA II–III) and it is difficult to extrapolate these results to patients with severe (NYHA IV) CHF, or to those with unstable disease.

**Conclusion**

It is clear both from the work of this group and the RCP working party,\(^{10}\) that further research is needed to enable *palliative care clinicians* to prescribe this potentially useful therapeutic tool more effectively. This paper reviews the evidence concerning oxygen treatment alone. In the trials presented here patients were stable and receiving other standard treatments. Oxygen therapy is not a complete answer to the palliation of breathlessness in these groups of patients.

When the literature as a whole is reviewed, there is evidence that oxygen can have a useful role in the palliation of this symptom\(^{18,45}\) in selected patients with advanced cancer and COPD.\(^{43}\) In CHF the absolute lack of evidence is a barrier to any certainty. The clinical recommendations for the use of oxygen in palliative care below are based on the findings of our review in conjunction with the wider body of expert clinical opinion.\(^{10,11,51}\)

**Key recommendations**

**Basic principles of oxygen therapy in palliative care**

- Oxygen therapy may be one part of the palliative or supportive care of patients with cancer, COPD and chronic cardiac failure, never a complete treatment in itself.
- The adverse effects of oxygen therapy need to be part of the assessment for oxygen therapy for each individual (set out in Appendix A).
- Oxygen therapy in palliative care is more complex than the simple correction of hypoxaemia.
- Only in exceptional circumstances should oxygen be instigated as a *long-term option for continuous use*, by a physician, without some formal assessment of its efficacy for breathlessness, or quality of life, for that patient. Such assessment is probably most usefully done in the home over a pre-determined period of time.
- The assessment method used before an individual is prescribed oxygen therapy needs to be tailored for each person and the way in which oxygen is to be used. Formal exercise testing (as set out in Appendix C) may not be the most appropriate or most accurate way of assessing the need for oxygen for a particular patient. Clinical judgement and consultation with the patient are the foundations of palliative care as improved quality of life is the central aim.
- The treatment strategy, including the use of oxygen, may change quite rapidly in advanced cancer and needs frequent reassessment and adjustment as necessary.
- LTOT for chronic respiratory illness should only be instigated by a respiratory physician.

**Recommendations for clinical practice**

**Oxygen therapy at rest**

**Patients with COPD and advanced cancer**

Oxygen therapy at rest should only be prescribed as a long-term option for use during most hours of the day after careful assessment of the severity of breathlessness and quality of life over a predetermined time by patients using simple diaries and appropriate scoring systems. An ‘n of 1’ trial, using the principles described by Bruera,\(^{44}\) may be the simplest way of doing this (see Appendix B). Patients who benefit from oxygen and compressed air should be given whichever gas is most appropriate.

**Patients with chronic heart failure**

There is no evidence to suggest that the use of oxygen therapy at rest is useful in patients with CHF. An individual trial may be indicated if the patient is hypoxaemic.

**Short-burst oxygen therapy**

Short-burst oxygen therapy and short-term oxygen therapy is *recommended* for patients with advanced cancer for the relief of breathlessness. The RCP working party stated that “despite extensive prescription of short-burst oxygen therapy, there is no adequate evidence available for firm recommendations...it may be prescribed for episodic breathlessness not relieved by other treatments in patients with severe COPD...heart failure and in palliative care”.

There is some evidence from Booth et al.\(^{18}\) that oxygen and air can help to relieve breathlessness at rest and whilst this study did not demonstrate a significant difference between oxygen and air the improvements in dyspnoea were greater with oxygen than with air. The work of Killen and
Corris\textsuperscript{35} indicates that short-burst oxygen therapy \textit{before or after exertion} in patients with COPD can reduce the severity of dyspnoea on exertion. Patients with advanced cancer, who are breathless without a remediable cause, have a short prognosis (months rather than years). Most are treated in oncology outpatients or hospice units where it may be difficult to do formal exercise testing as a routine. Whilst there is a clear need for more research evidence, it is acceptable to provide short-burst oxygen therapy for patients with breathlessness on exertion after a formal, but simple test of its efficacy in that individual.\textsuperscript{52}

**Ambulatory oxygen therapy**

**Patients with COPD and advanced cancer**

Ambulatory oxygen therapy is appropriate for many patients with COPD and breathlessness who desaturate on exercise, and this condition should be actively sought using simple exercise testing and oximetry. In the RCP report, ambulatory oxygen is recommended\textsuperscript{10} for patients who, desaturate at least 4% below 90% on a baseline walk breathing air and/or there is an improvement of 10% in walking distance or breathlessness scores with supplemental oxygen or experience a sustained improvement in their breathlessness on using it. Assessing the impact of oxygen over a period of time on a patient’s quality of life at home, by means of simple standardised tools may give a more accurate picture of its importance to an individual as a recent study by Eaton et al. demonstrated. Although some patients gained acute (measured by an exercise test) and short-term (assessed by the Chronic Respiratory questionnaire) benefit from oxygen therapy this was not necessarily sustained over a 12 week period. In addition, 14(41%) of acute or short-term responders did not want to continue oxygen after the trial—11 of these citing poor acceptability. It is not possible to determine which patients will benefit from oxygen from their baseline characteristics. Some sort of formal assessment is needed. A recent retrospective study in patients with COPD suggested that a baseline resting arterial oxygen saturation below 95% may predict the need for ambulatory oxygen\textsuperscript{53} but the results of this study need further careful prospective research. At the moment, for patients with \textit{advanced cancer} a documented improvement in breathlessness on exertion when using oxygen or a simple ‘N of 1’ trial would give sufficient evidence for the prescription of ambulatory oxygen in this group.

**Patients with chronic heart failure**

There is little evidence to support any recommendations for patients with CHF but patients who are troubled by breathlessness and who are willing to use oxygen should have a formal trial of its efficacy at rest and on exercise. The RCP report does not recommend ambulatory oxygen therapy for patients with CHF.

**Appendix A. Adverse effects of oxygen therapy**

1. Restriction of activities.
2. Oxygen apparatus is cumbersome and for an already disabled patient may act as a disincentive to going out and living as normally as possible.
3. Impaired communication between patient and family.
4. If patients become psychologically dependent on oxygen they may attend too much on the mechanics of having their oxygen therapy. Some will not even remove their mask for even a minute and conversation with is impeded. They may even become frightened when there is any interruption in the oxygen supply and refuse to go out without a continuous supply from a cylinder. This may have a deleterious impact on quality of life.
5. Fire hazard: Oxygen promotes combustion. Patients who smoke during oxygen therapy are in great danger of facial burns and some fatalities have been reported.
6. Hypercapnic respiratory failure: The dangers of oxygen therapy in those patients with Type II respiratory failure are well known.
7. Withdrawing oxygen: Once oxygen has been given to a patient it is often difficult to stop its use even when it is on longer relieving breathlessness or being used appropriately.
8. The cost of oxygen: Oxygen is not cheap and should be used appropriately rather than universally.
9. Humidification of oxygen in LTOT is usually unnecessary as this is done adequately by the patient’s own upper respiratory tract. Humidifiers tend to be noisy, bulky and often ineffective but may be necessary for a specific problem.

**Appendix B. Formal testing to assess patients for oxygen at rest**

1. At present there is no agreed testing procedure.
2. Formal assessment of fan or oxygen should include rating scales to assess breathlessness before and after the intervention.
(3) Formal assessment of oxygen therapy should include the use of oximetry to establish for each individual whether there is a link between hypoxaemia and breathlessness.

(4) Formal assessment of oxygen therapy should establish whether there is a difference for an individual between the response to oxygen at rest and on exercise.

(5) The rating scale should be appropriate both to the patient group and the parameter tested. For example, VASs are useful for breathlessness in any condition but can only assess the symptom itself at a particular period of time, rather than its impact on quality of life. It may be more appropriate to measure quality of life if assessing the benefits of oxygen for a patient at home—they can then choose to use it most appropriately for their circumstances.

(6) An 'N of 1' trial may be helpful.

Appendix C. Formal exercise testing to assess patients for ambulatory oxygen testing

(1) Choose a validated exercise test such as the shuttle walking test.

(2) The patient should have at least one formal practice test, as there is a learning effect.

(3) Just before starting the test, measure the patient’s SaO2 whilst they breathe room air and ask the patient to assess their current level of breathlessness using a VAS.

(4) Carry out the test with oxygen or air (the patient should not know which they are receiving) and measure saturation and breathlessness on a VAS as soon after the patient stops as you can. It is possible to measure saturation and pulse rate continuously with some oximeters.

(5) Repeat the test after a rest period (2 h plus) or on another day using oxygen or air from a portable cylinder carried by the patient. The oxygen and air administration should be carried out as a double-blind procedure and the patient should not be told their saturation results until after both have been completed.

References


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The use of oxygen in the palliation of breathlessness


