

# Short burst oxygen therapy in patients with COPD

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## **What is Short Burst Oxygen Therapy?**

Doctors, nurses and patients have assumed for many years that oxygen relieves breathlessness. For this reason, Short Burst Oxygen Therapy (SBOT) is in widespread use for breathless patients with Chronic Obstructive Pulmonary Disease (COPD). SBOT consists of a prescription for home oxygen therapy, usually from large volume cylinders, to be used as required at the patient's discretion. Most patients who use SBOT are not hypoxaemic at rest although some may desaturate during exertion. Some patients use SBOT before exercise (hoping to increase exercise capacity and reduce breathlessness) but most use SBOT after exertion to relieve breathlessness. Patients tend to report subjective benefit from SBOT and the National Health Service in the UK spent 17.8 million pounds (about 22 million Euros) on oxygen cylinders in 2005 [1].

## **What are the physiological causes of breathlessness?**

Breathlessness is a curious symptom which is poorly understood. Everybody is familiar with the sensation of breathlessness after vigorous exertion although the oxygen concentration of the blood in normal subjects (and in many patients with COPD) remains normal during exercise. The sensation of breathlessness is a very complex physiological phenomenon, largely attributable to the increased work of breathing during exertion and the necessity to eliminate increased amounts of carbon dioxide. The sensation is affected by many physiological systems including the peripheral chemoreceptors (carotid bodies which sense  $pO_2$ ,  $pCO_2$  and pH), central chemoreceptors which monitor  $pCO_2$  and pH but not  $pO_2$ , the respiratory centre of the brain, mechano-receptors in the lungs and chest wall and sensory fibres in the face and upper airways. Medically unexplained breathlessness associated with hypocapnia is the main symptom in the well recognised clinical syndrome of hyperventilation or dysfunctional breathing [2]. Subjects with this clinical problem report marked breathlessness at rest in the presence of normal or elevated oxygen saturation, commonly 99% or even 100% breathing air.

As most exertional breathlessness is not associated with hypoxaemia, there is little reason to suppose that oxygen would relieve post-exertional breathlessness even if the breathless person happens to have COPD.

## **Does hypoxaemia cause breathlessness?**

Many acutely ill patients are hypoxaemic and breathless but is it the hypoxaemia or the disease that causes the sensation of breathlessness? Millions of normal subjects experience modest hypoxaemia every year during air travel without any subjective sensation of breathlessness (although the respiratory rate may be increased). Commercial aircraft are pressurised to the equivalent of an altitude of about 2000-2500 meters and the mean oxygen saturation of passengers falls from 97% at sea level to 93% at cruising altitude [3]. It is common for the oxygen saturation of normal individuals to fall below 90% during travel on commercial airliners, especially whilst walking about the plane, the average nadir of oxygen saturation amongst healthy cabin crew during flight is 88.6% and some experience desaturation as low as 80% [4]. Despite these impressive falls in saturation, breathlessness is a very rare symptom amongst airline passengers, even in the case of patients with mild COPD where the mean oxygen saturation falls from 96% at sea level to 90% at cruising altitude and 87% whilst walking in the aisle of the aircraft [5].

In the more extreme example of research subjects who remove an oxygen mask at high altitude in an unpressurised aircraft or at simulated altitude in a pressure chamber, research subjects develop profound hypoxaemia which leads to a decline in mental function followed by loss of consciousness but they do not experience breathlessness [6].

It is clear from the above observations that modest hypoxaemia, or even severe hypoxaemia, in the absence of disease or exertion does not produce a sensation of breathlessness (hypoxaemia without breathlessness) and it is common for normal subjects and COPD patients to experience breathlessness without hypoxaemia. Therefore, there is very little correlation between the blood oxygen saturation of a subject and the presence or absence of breathlessness.

***Does oxygen relieve breathlessness?***

Could the popular assumption of benefit from SBOT be wrong? It is clear from the above paragraphs that most exertional breathlessness is not associated with hypoxaemia and pure hypoxaemia (in the absence of disease or exercise) does not cause breathlessness. These observations would suggest that the administration of oxygen after exercise might have little effect on the sensation of breathlessness for patients with lung disease. It has been shown that the oxygen cost of breathing ( $\text{VO}_2$ ) in patients with COPD may be approximately 50% of the whole body  $\text{VO}_2$  [8]. Therefore the administration of supplemental oxygen during exercise may reduce the work of breathing by allowing subjects to achieve a given blood oxygen saturation with less respiratory effort. Additionally, it has been suggested that oxygen therapy may allow a reduction in dynamic hyperinflation in patients with COPD [9, 10].

These mechanisms may explain the consistent but modest beneficial effect found in trials of ambulatory oxygen therapy (given during exercise) for patients with COPD. It has been shown that people with severe COPD who are hypoxaemic at rest or who desaturate on exercise can walk a greater distance with less subjective breathlessness if they are given supplemental oxygen during exertion [11]. However, the benefits of ambulatory oxygen are modest and one double blind trial showed that COPD patients who met all the agreed criteria for ambulatory oxygen (including objective benefit in the laboratory) actually used very little portable oxygen each month when they were given cylinders to use during exertion at home and there was no difference between the use of air cylinders and oxygen cylinders in this double blind trial [12].

***Are many COPD patients treated with SBOT?***

In view of the modest benefits of ambulatory oxygen which is given throughout episodes of exertion, it is perhaps surprising that so many doctors and nurses still believe that SBOT (given before or after exercise but not during exertion) might have any clinically significant benefits. The British National Health Service spends about 20 million Euros (17 million pounds) per year on short burst oxygen therapy and it is likely that other large European countries spend similar amounts of money on this treatment modality [1]. Health care systems in some other countries such as Denmark do not reimburse SBOT at all and there is no evidence that clinical outcomes in Denmark are inferior to those in countries such as the UK where SBOT is in widespread use. A six-month study of SBOT usage has shown that COPD patients tend to use SBOT very sparingly after an initial burst of enthusiasm and there is some evidence that a majority of SBOT users can be persuaded to abandon this apparently ineffective treatment modality with support and counselling [13, 14].

***What do the Guidelines say about SBOT?***

Despite the widespread use of SBOT, the words "Short Burst Oxygen Therapy" do not appear at all in the 2007 GOLD (Global initiative for Obstructive Lung Disease) COPD strategy statement and the British NICE guideline states that SBOT "*should only be considered for episodes of severe breathlessness in patients with COPD not relieved by other treatments... and only if an improvement in breathlessness following therapy has been documented*" [15, 16]. There is therefore a major discrepancy between the advice in the guidelines and actual practice in many countries. Perhaps it is time to ask if this treatment is effective.

***What is the evidence of benefit from SBOT?***

Twelve studies of SBOT before or after exercise (or at rest in one study) are summarised briefly in table 1. The early study of Woodcock and colleagues suggested that some patients could increase their exercise tolerance if pre-treated with oxygen from nasal cannulae for 5-15 minutes [17]. This strategy had some effect on dyspnoea during a brief treadmill test but not during a six minute walk. This is not surprising as pre-oxygenation can have only a very modest effect on the blood oxygen saturation of normoxaemic COPD patients (maximum 2-6% rise in saturation if the baseline saturation is 94-98%) and it can produce only a slightly greater rise in saturation (maximum 7-10% rise) in those with modest hypoxaemia at rest (resting saturation 90-93%). Patients with saturation below this level are likely to be candidates for LTOT and ambulatory oxygen rather than SBOT.

Dejours estimated that pre-oxygenation might increase the body oxygen store of a hypoxic patient by about 80 mls but this is unlikely to have much clinical benefit because the oxygen cost of exercise is about 1000 mls per minute at a normal walking pace [18]. It has been shown that pre-oxygenation increases breath-holding time (at rest) by about 30 seconds in healthy volunteers and about 13 seconds in patients with COPD [19, 20]. This is probably insufficient to deliver any clinically significant increase in exercise capacity for most patients and the majority of studies of pre-oxygenation in COPD patients have been negative [21]. Furthermore, most patients who report subjective benefit from SBOT tend to use it after exertion (to relieve breathlessness) rather than before exercise to try and increase their exercise capacity [22].

What is the evidence supporting the use of SBOT after exercise in COPD patients? It can be seen from table 1 that the methodology of exercise and of oxygen administration differed greatly in the published studies but there was little or no clinical benefit in most of the studies. Although some small studies have reported modest benefits, a meta-analysis of all studies failed to show any clinically significant effect on the speed of recov-

Table 1. - Summary of trials of Short Burst Oxygen Therapy for patients with COPD

Reference Year Number of subjects	Intervention	Main Outcomes
<b>Experimental studies</b>		
17 Woodcock 1981 n = 10	Breathing oxygen before exercise (4 l/min nasal)	Improved exercise capacity for short treadmill test and 6 minute walk but dyspnoea was reduced only for the short treadmill test
23 Evans 1986 n = 19	67% oxygen or air from face mask after exercise step test	Recovery time for breathlessness quicker on oxygen but not reproducible on a repeat test
24 Mc Keon 1988 n = 20	Air or oxygen at 2.5 l/min from nasal prongs before treadmill exercise test	No difference in distance walked, heart rate or breathlessness
25 Swinburn 1991 n = 12	28% oxygen or air from mask <i>at rest</i> in 12 COPD hospital in-patients with hypoxaemia	Air "helped breathing" on 62% of occasions and oxygen on 92% of occasions (p<0.05)
26 Marques-Magallanes 1998 n = 18	Oxygen or compressed air via mask at 10 l/min or room air after treadmill exercise	No significant differences in outcomes
27 Killen 2000 n = 18	Oxygen or air from mask at 2 l/min before and after ascending stairs	Borderline reduction in dyspnoea on oxygen
28 Nandi 2003 34 pre, 18 post	28% oxygen or air from a mask before or after 6 minute walk	No effect on walk distance or breathlessness
29 Lewis 2003 n = 22	Oxygen or air before and after 6 minute walk (2 l/min; nasal cannulae)	No important differences in walk distance or breathlessness
9 Stephenson 2004 n = 18	40% oxygen or air after exercise	Oxygen produced no reduction in dyspnoea but reduced ventilatory effort and increased inspiratory capacity
22 Quantrill 2007 n = 22	SBOT users used nasal oxygen or air after two everyday tasks	Subjective and objective recovery (pulse) slightly quicker on oxygen but only 5 of 22 patients could correctly identify oxygen versus air in a single-blind study
30 McKinlay 2007 n = 37	Oxygen or air mask at 4 l/min or cooling fan or room air after step test	No difference in breathlessness scores between the interventions in crossover study. Borderline effect on pulse recovery time
<b>Long-term home study</b>		
13 Eaton 2006 n = 78	SBOT for six months with oxygen or air from cylinder (2 l/min; nasal cannulae)	No differences between oxygen and air. High initial cylinder use and low subsequent use in both groups

ery from exercise-induced exertion although the oxygen saturation of the blood was improved [21]. Furthermore, a double-blind randomised trial of the use of oxygen cylinders or air cylinders by 78 COPD patients over a six month period showed no difference in quality of life or health care utilisation [13]. In that study, the use of SBOT (or air cylinders) was high initially but rapidly fell to very low levels.

***Many COPD patients report subjective benefit from SBOT. Is there objective evidence of benefit in these cases?***

Perhaps the most clinically relevant study of SBOT use was the recent paper by Quantrill and colleagues which recruited only patients who were already using SBOT and reporting benefit from it [22]. They asked patients to identify two daily liv-

ing activities for which they were already using SBOT for relief of breathlessness. The patients undertook each of the two chosen activities twice, at least 15 minutes apart and they received either air or oxygen from nasal cannulae after exercise. The mean subjective and objective recovery time was about 35 seconds lower using oxygen but this was not statistically significant and only 5 of 22 patients could correctly distinguish oxygen from air after both activities (the same proportion as would occur by chance). This may explain the low level of long-term usage of SBOT in the six-month study of Eaton and colleagues [13].

#### ***Why might patients report benefit from SBOT despite the negative clinical trials?***

Most doctors who work in countries where SBOT is used will have encountered patients who report benefit from this treatment. For example the patients in the study of Quantill and colleagues had all reported subjective benefit from SBOT but three quarters of them could not distinguish oxygen from air in a single-blind study [22]. Why might patients report benefit from a treatment that seems to deliver so little benefit in randomised trials?

Firstly, there may be a placebo effect. This effect was demonstrated elegantly (for a different long-term disease) in the study of Kaptchuk and colleagues who found that a placebo treatment for irritable bowel syndrome had a modest effect which was greatly enhanced if the patient-practitioner relationship was augmented by warmth, attention and confidence [31]. For this reason, it is likely that the most conscientious, sympathetic and enthusiastic practitioners will see the most marked placebo effect. It is therefore possible that the confidence of many patients in SBOT is a tribute to the enthusiasm of their doctors for this treatment!

Secondly, there is likely to be reversion to the mean. SBOT is often prescribed at a time of crisis such as a COPD exacerbation after which the patient's symptoms are likely to improve irrespective of what treatment is given. The study of Eaton and colleagues showed high initial usage of SBOT (or air cylinders) with no difference between the groups and a subsequent rapid decline in the use of SBOT (or air cylinders) after the initial burst of enthusiasm [13]. This could reflect improvement in the underlying condition or a gradual realisation by the patient that SBOT was ineffective.

Thirdly, it is possible that some patients may experience some palliation of breathlessness due to reflexes associated with the cooling effect of compressed gas flowing onto the face or airways [32, 33]. It is common for breathless patients to seek relief by opening a window to achieve a similar effect. However, this hypothesis was tested in a study at the author's hospital where patients with COPD exercised four times in random order and had four different types of intervention during the recovery period (Oxygen from mask at 4 l/min, air from mask at 4 l/min, cooling air from an electric fan or no intervention) [30]. There was no differ-

ence in breathlessness scores and no significant difference in subjective or objective recovery times between these four groups, suggesting that neither air from a mask nor air from a fan are likely to provide any significant palliation of breathlessness if given after exercise in COPD.

Fourthly, there may be a small sub-group of COPD patients who genuinely derive significant physiological benefit from SBOT but any such group is likely to be small because of the overall lack of effect in meta-analysis and the modest clinical benefits reported in the few trials that did show some benefits from SBOT. Furthermore, the study of Quantill and colleagues was performed in patients who had already reported personal benefit from SBOT but, even in this group of patients, it was difficult to demonstrate any clinically meaningful benefits from SBOT [22].

#### ***How should clinicians respond to the present state of knowledge concerning SBOT for patients with COPD?***

Clinicians should firstly assess the blood oxygen level of patients with COPD. Those with oxygen saturation below 92% should have their blood gases measured. Patients with PaO<sub>2</sub> below 7.3 kPa (55 mm Hg) when stable and a small number of patients with PaO<sub>2</sub> between 7.3 and 8.0 kPa associated with cor pulmonale will benefit prognostically from Long Term Oxygen Therapy (LTOT) [16]. Some of these patients may benefit from additional ambulatory oxygen therapy to increase their exercise tolerance and to diminish the degree of breathlessness during exertion but there is no reason to believe that SBOT would confer any additional benefit for these hypoxaemic patients.

COPD patients with blood oxygen tension above 7.3 kPa without cor pulmonale or above 8.0 kPa with cor pulmonale will not benefit from LTOT and there is little evidence of benefit from SBOT for these patients either. Faced with a patient who requests SBOT, I would recommend that the clinician should conduct a simple crossover study for the patient. Oxygen or air should be given (in random order and ideally twice for each modality) by nasal cannulae at 4 litres per minute in a single-blind manner. The use of nasal cannulae will avoid the increased resistance to breathing that a mask may produce. The intervention should be offered before or after exercise, depending on the patient's preference. Experience has shown that most patients use SBOT after rather than before exercise [22]. SBOT should be prescribed only for patients who express a clear preference for oxygen after this single-blind assessment. The SBOT prescription should only be continued for patients who actually use the treatment several times each week and who report ongoing benefit at follow-up consultations [16]. Meanwhile, academic clinicians need to devise more clinically-focused trials to identify which, if any, patients with COPD will derive objective benefit from SBOT.

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