Does home oxygen therapy (HOT) in addition to standard care reduce disease severity and improve symptoms in people with chronic heart failure? A randomised trial of home oxygen therapy for patients with chronic heart failure

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Scientific summary

The home oxygen therapy (HOT) trial

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Background

Chronic heart failure (CHF) affects at least 1% of the population and is responsible for around 4% of all admissions to hospital in the UK. The prognosis of heart failure if it is not well treated is bleak. The clinical course for most patients with heart failure tends to be one of gradual decline, often punctuated with episodes of severe deterioration resulting in hospitalisation. Towards the end of their lives, many patients with CHF become very symptomatic, with limiting breathlessness on minimal exertion and even at rest. Although standard treatment may relieve symptoms, for many the last few months and even years of life can be miserable, with persisting severe breathlessness on minimal exertion and episodic hospitalisation.

Home oxygen therapy (HOT) is commonly prescribed to patients with severely symptomatic CHF in order to alleviate suffering. However, unlike the situation for patients with chronic obstructive airways disease and severe hypoxia, in whom oxygen prolongs survival, there is no evidence to support the use of HOT in patients with CHF.

Objectives

The HOT trial was designed to address the question of whether or not there is any effect of HOT on quality of life (QoL) in patients with severely symptomatic heart failure. Secondary end points were to assess the effects of HOT on breathlessness, 6-minute walk test distance, severity of left ventricular (LV) systolic dysfunction, N-terminal B-type natriuretic hormone (NT-proBNP) level and prognosis.

The study consisted of three parts. The main study was a randomised controlled trial (RCT) designed to measure the impact of HOT on QoL in severely symptomatic patients. A qualitative substudy assessed the burden on patients and their carers, and an acute oxygen substudy assessed whether or not there was any effect of oxygen given in the same concentration as used by concentrators at home on haemodynamics.

Methods

The main study was a pragmatic, two-arm RCT, recruiting patients with severe CHF. Patients were recruited from heart failure outpatient clinics in hospital or the community, in a range of urban and rural settings. Patients had to have heart failure of any aetiology, severe symptoms (breathlessness either at rest or on minimal exertion) and at least moderate LV systolic dysfunction, and be receiving maximally tolerated medical management. Patients were excluded if they had had a cardiac resynchronisation therapy device implanted in the past 3 months, chronic obstructive pulmonary disease fulfilling the criteria for long-term oxygen therapy (LTOT), interstitial lung disease or malignant disease that would impair survival or were using a device or medication that would impede their ability to use LTOT.

Patients received best medical therapy (BMT) and were randomised to open-label LTOT, prescribed for 15 hours per day including overnight hours, or no oxygen therapy. Home oxygen was delivered by concentrators in the patients' homes. The inspired oxygen was increased from 20.9% (normal room air) to approximately 28%. There were two substudies: a linked qualitative substudy to assess the view of 25 patients and a free-standing oxygen substudy to assess the haemodynamic effects of acute oxygen administration.

Results

The HOT trial was stopped early by the funders, the Health Technology Assessment programme, because of poor patient adherence to the oxygen prescription. Between April 2012 and February 2014, 114 patients were randomised to receive either LTOT or BMT. The mean age was 72.3 years [standard deviation (SD) 11.3 years] and 70% of patients were male. Ischaemic heart disease was the cause of heart failure in 84% of patients; 95% were in New York Heart Association class III; mean left ventricular ejection fraction (LVEF) was 27.8%; and median NT-proBNP was 2203 ng/l. Arterial oxygen saturation was normal at rest and there was no significant change in arterial oxygen saturation during exercise or during recovery from exercise. There was a low prevalence of sleep-disordered breathing.

The primary analysis used a covariance pattern mixed model which included patients only if they provided data for all baseline covariates adjusted for in the model and outcome data for at least one post-randomisation time point ($n = 102$: intervention, $n = 51$; control, $n = 51$). There was no difference in Minnesota Living with Heart Failure (MLwHF) questionnaire score at 6 months between the two arms [at baseline the mean score was 54.0 (SD 18.4) for LTOT and 54.0 (SD 17.9) for BMT; at 6 months the mean score was 48.1 (SD 18.5) for LTOT and 49.0 (SD 20.2) for BMT; adjusted mean difference –0.10, 95% confidence interval (CI) –6.88 to 6.69; $p = 0.98$]. At 3 months, the adjusted mean MLwHF questionnaire score was lower in the LTOT group (adjusted mean difference –5.47, 95% CI –10.54 to –0.41; $p = 0.03$), coinciding with improvements in breathlessness scores which did not persist to 6 months. There was no effect of LTOT on any secondary measure including 6-minute walk test distance, NT-proBNP level and LVEF. There was slightly greater survival in the oxygen-treated group (unadjusted hazard ratio 2.03, 95% CI 0.76 to 5.40, for BMT relative to LTOT), but the difference was not statistically significant ($p = 0.16$).

In the haemodynamic substudy there were no deleterious effects of 28% oxygen. There was a small increase in cardiac output and a small fall in pulmonary vascular resistance.

Adherence to HOT was poor, with only 11% of patients reporting using the oxygen as prescribed. Findings from the qualitative substudy suggested that participants viewed study participation in the trial both as an altruistic act and as a way of accessing optimal clinical care. Adherence was related not specifically to the context of a clinical trial but to a deep-seated belief that oxygen was a therapy for acute deterioration or for those with end-stage disease. Thus, participants felt that the use of LTOT was counterintuitive, despite clear explanation of the trial's aim. This misunderstanding formed a poor basis for subsequent weighing up by the participants of the benefit–burden balance of the LTOT.

Conclusions

The prevalence of hypoxia in patients with severe heart failure at rest, following exercise and during an overnight sleep test is low. There is no evidence that LTOT, although safe, improves the symptoms, prognosis or severity of heart failure in patients with severe CHF at 6 months. There is no evidence to support the use of HOT in patients with heart failure.

Recommendations for future research

The trial was stopped early because of poor adherence to the prescription of 15 hours per day. However, the prescription was based on extrapolation from studies of patients with a different pathology, chronic airways disease, and who had severe hypoxia. It may be that shorter periods of exposure might have been effective, either in terms of symptom relief or in terms of preventing hospitalisation. We suggest that two further studies might be appropriate:

1. a trial of patients with severe heart failure randomised to have emergency oxygen supply in the house, supplied by cylinders rather than oxygen concentrator, powered to detect a reduction in admissions to hospital
2. a study of bed-bound patients with heart failure who are in the last few weeks of life, powered to detect changes in symptom severity.

Trial registration

This trial is registered as ISRCTN60260702.

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