Abstract:

Aims.

To review current guidelines and studies available to health care professionals in the United Kingdom and explore the literature to identify reasons for the prescription of palliative oxygen therapy in non-hypoxaemic patients.

Background.

Oxygen therapy is often associated with the palliative treatment for breathlessness. Although prescription guidelines are available and risks of oxygen therapy are known the therapy is still prescribed for non-hypoxaemic patients.

Design.

A literature search was conducted using relevant databases. Cited evidence from published guidelines was also consulted.

Results.

The findings suggests that oxygen is no more effective than room air for treating dyspnoea for non-hypoxaemic patients although two small studies of self-reported benefits from patients and carers indicate different perceptions of need.

Conclusion.

The findings suggest a knowledge gap with regards understanding the reasons for the prescription of oxygen therapy in non-hypoxaemic patients.

Key Phrases:

- The majority of research available regarding oxygen prescribing focuses on the physiological benefit of oxygen predominantly for hypoxaemic patients. However, its use is widespread in breathlessness management for palliative patients.
- Oxygen therapy is not a benign intervention and therefore inappropriate prescribing may cause harm hence a need to understand reasons for prescriptions.
- Findings suggest that oxygen therapy may relieve breathlessness for non-hypoxaemic patients but not significantly better than the administration of room air.
- The presence of a caregiver may increase the likelihood of receiving oxygen therapy suggesting treatment decisions are not based solely on prescription criteria.

MESH Keywords: Oxygen, Palliative Care, Inappropriate Prescribing, Primary Health Care, Secondary Care

Conflict of interest:

No conflict of interest has been declared by the author.

The clinical benefits and reasons for prescription of palliative oxygen therapy in non-hypoxaemic patients: a literature review

Introduction

Oxygen, when prescribed as clinical therapy, should be considered to be a drug (Joint Formulary Committee 2017); documented risks of oxygen therapy include increased damage to lung function, which is potentially fatal in susceptible patients, and discomfort (Uronis et al. 2008, Clemens et al. 2009, Jaturapatporn et al. 2010, Uronis et al. 2014), psychological dependency, anxiety and altered self-image (Uronis et al. 2008) and reduced mobility and participation in social activities (Uronis et al. 2008, Jaturapatporn et al. 2010, Breaden et al. 2013, Collier et al. 2017). However in the United Kingdom (UK), although oxygen has to be prescribed for home use, there is no national requirement for this to be undertaken by a qualified prescriber or specialist; it can be initiated by non-specialist health care professionals, as agreed by local protocol, and can be initiated in both primary and secondary care (Wedzicha & Calverley 2006) with follow-up and review services managed locally, although recommendations for this process are available (NHS Primary Care Commissioning 2011). There are published guidelines and prescription criteria for both emergency oxygen (O'Driscoll *et al*. 2017) and home oxygen (Hardinge *et al*. 2015) but these primarily focus on its use for treatment and symptom management in hypoxaemic patients, that is patients with a resting PaO2 ≤7.3 kPa or ≤8.0 kPa with other complications (Hardinge et al. 2015); the guidelines are less clear for non-hypoxaemic palliative patients. This open approach to home oxygen prescription in conjunction with lack of clarity for its use in palliative care may potentially lead to inappropriate prescriptions.

The majority of research available in the field of oxygen prescribing focuses on the physiological benefit of oxygen predominantly for hypoxaemic patients and is based on two randomised controlled trials undertaken in the 1980s (Nocturnal Oxygen Therapy Trial Group 1980, Medical Research Council Working Party 1981). The literature to be discussed in this review suggests numerous proposed explanations for inappropriate oxygen prescription for patients including for those receiving palliative care but there is little understanding of healthcare professionals' reasons for prescribing oxygen for non-hypoxaemic patients. This suggests there is a need to explore the literature further to explore the rationale for prescribing oxygen in palliative care (Ben-Aharon *et al*. 2012). Available research from outside the UK has been included in this review but it should be noted that home oxygen therapy for all patient groups in the UK is funded by the National Health Service (NHS) which is not the case with other countries which may lead to differences in prescription patterns when making international comparisons.

Literature Review

A comprehensive literature search was undertaken to include papers from 2006 until 2017; literature published since the establishment of NHS Home Oxygen Services. The strategy included searching databases and inspecting the bibliographies of located articles. The following search terms and Boolean operators were utilised: 'domiciliary oxygen' or 'home oxygen' or 'long term oxygen' and palliat* or 'end of life' or 'terminal' or 'breathless* using databases such as CINAHL Plus, Medline and PsycINFO.

Inclusion criteria: all original studies written or translated into English language; the vast majority of articles were excluded after initial review of abstracts. Articles were deemed ineligible if the article

did not specifically relate to the use of home oxygen therapy for palliative non-hypoxaemic adult patients; the majority of studies were focussed solely on oxygen as a treatment of hypoxaemia and were excluded. Full-text analyses were conducted for included studies. There were neither geographical limitations on the search criteria nor restrictions on methodological approaches used by different studies

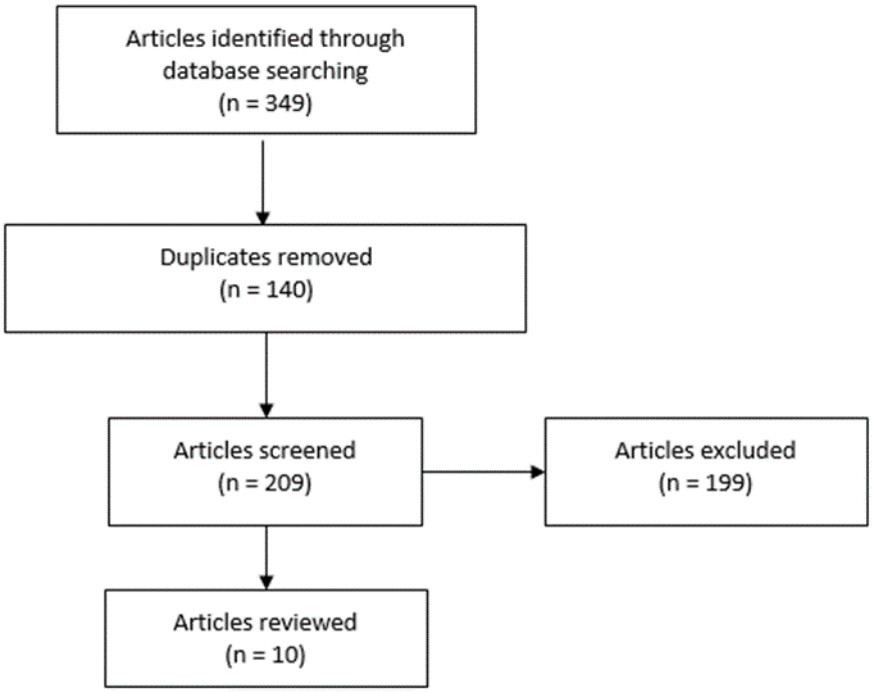

Figure 1 Flow diagram of article selection.

Results

Seven studies (Philip *et al.* 2006, Clemens *et al.* 2008, Currow *et al.* 2009, Abernathy *et al.* 2010, Jaturapatporn *et al.* 2010, Campbell *et al.* 2013, Clark *et al.* 2015) were located assessing the clinical and reported benefits of home oxygen therapy for non-hypoxaemic palliative care patients. Three studies have focussed on other proposed reasons for clinicians prescribing home oxygen for this patient group; one study (Breaden *et al.* 2013) explored nurses' rationale for oxygen prescriptions and two studies (Currow *et al.* 2008, Collier *et al.* 2017) researched the benefits from the caregiver perspective and the impact of their presence on the decision to prescribe oxygen.

Table 1 Summary of included studies.

Study	Focus of study	Sample size	Design	Primary method of data collection	Brief summary of findings
Abernathy *et al.* (2010) USA/UK/ Australia	To measure the effectiveness of oxygen compared with room air	239 participants (patients)	International multicentre double blind RCT	Numerical Rating Scale 0-10	No significant difference in breathlessness or side effects
Breaden *et al.* (2013) Australia	To understand the factors that most influence palliative care nurses' initiation of home oxygen	51 nurses	Qualitative study - symbolic interactionism	Focus groups	Two emerging themes – Theme A – health service issues including Oxygen often to 'treat caregiver anxiety'. Theme B – clinical issues including once oxygen placed in home, the security it provided made it difficult to remove
Campbell *et al.* (2012) USA	To determine the benefit of administering oxygen to patients who are near death	32 patients	Double blind repeated measure study	Respiratory Distress Observation Scale	91% showed no change in respiratory comfort or distress with change of protocol
Clark *et al.* (2015) UK	To determine the effect of home oxygen therapy on quality of life for patients with severely symptomatic heart failure	102 patients	RCT	Minnesota Living with Heart Failure questionnaire	No difference in scores between intervention and control groups
Clemens *et al.* (2008) Germany	To compare effects of oxygen and opioid treatment in hypoxic and non-hypoxic palliative care patients	46 patients	Prospective non-randomised	Numerical Rating Scale Oxygen saturation recordings	Opioid application significantly decreased intensity of dyspnoea and respiratory rate, not the case with oxygen. Oxygen saturation and dyspnoea not strongly correlated.

Table 1 (*Continued*).

Collier *et al.* (2017) Australia	To understand caregiver factors associated with caring for someone with long-term oxygen therapy	20 participants (caregivers)	Constructivist grounded theory	Semi-structured interviews	Caregivers see home oxygen as both a constant reminder of death yet also see it as life sustaining - they may see these perspectives simultaneously. Clinicians, like caregivers, tend to over-estimate the benefit and under-estimate the potential harms.
Currow *et al.* (2008) Australia	To determine if palliative oxygen less likely to be prescribed when a person lives alone at the end of life	5203 patients	Univariate analyses	Demographic data	Presence of a caregiver in the home is associated with palliative oxygen prescription.
Currow *et al.* (2009) Australia	To assess the symptomatic relief of breathless from oxygen therapy for palliative care patients	1239 patients	Consecutive cohort study	Symptom Assessment Scale Demographic data	Did not reveal any groups where symptomatic response rates differed markedly after oxygen was introduced.
Jaturapatporn *et al.* (2010) Canada	To report the prevalence and experience of palliative care patients receiving home oxygen	22 patients	Qualitative interviews and thematic analysis	Structured interviews	Patients identified more advantages of home oxygen therapy than disadvantages.
Philip *et al.* (2006) Australia	To determine the effect of oxygen versus air on the relief of dyspnoea in patients with advanced cancer	51 patients	Randomised double blind crossover trial	Visual Analogue Scale Dyspnoea Assessment Questionnaire Oxygen saturation recordings	Dyspnoea improved significantly with air and oxygen via nasal prongs, no differences between the treatments.

Oxygen versus room air

Four studies (Philip *et al.* 2006, Clemens *et al.* 2008, Abernathy *et al.* 2010, Campbell *et al.* 2013) compared the clinical benefits, which is the improvement of breathlessness with or without an improvement in oxygen saturation levels, of oxygen therapy versus the administration of room air.

The first study conducted by Philip *et al*. (2006) was a randomised double blind crossover trial of 51 non-hypoxaemic patients with advanced cancer and considered both reduction in breathlessness intensity and improvement in oxygen saturation levels as potential clinical benefits. The participants were randomised to either receive nasal oxygen or room air for 15 minutes followed by a crossover to receive the other treatment after a 30 minute interval. There was no significant difference between the mean changes in self-reported scores for either gas using a visual analogue scale (VAS) (p=0.622) or a questionnaire (p=0.767). Pulse oximetry showed a significant difference between the two gas types but there was no correlation between VAS score and oxygen saturation.

Abernathy et al. (2010) undertook randomised control trials over nine sites in three countries. The 239 participants, non-hypoxaemic individuals with life-limiting illness, were recruited to either nasally administered oxygen therapy or room air via a concentrator machine for at least 15 hours a day over a 7 day period. Self-reported findings from a numerical rating scale (NRS) of 0-10 showed that mean morning breathlessness improved for both gases in the morning (p=0.504) and in the evenings (p=0.554); there was no statistically significant difference in benefits for either group. However, as with the study by Philip *et al*. (2006) there appears to be some improvement in breathlessness for both the 'control' (room air) and the intervention (oxygen therapy) which may suggest that this be viewed as a comparative study of two interventions without a true control.

Clemens *et al*. (2009) compared oxygen therapy and room air with the addition of opioid administration as a further intervention for palliative care patients not divided by disease diagnosis. They used a prospective non-randomised method to study the differences in effects on breathlessness between oxygen therapy and opioid use, and for opioid use alone. 46 participants were studied at baseline and then after oxygen use and opioid use. There was no significant difference in self-reported breathlessness scores using a NRS for non-hypoxaemic patients as a result of oxygen therapy (p=0.096) but there was a significant change in reported breathlessness after opioid administration.

Campbell *et al*. (2013) utilised a double blind repeated measure study of 32 end-of-life patients; nasal room air, nasal oxygen and no flow were alternated randomly every 10 minutes. The primary measure in absence of self-reported breathlessness was via a Respiratory Distress Observation Scale (RDOS) completed by the patient's registered nurse; this included monitoring movement and facial expressions in addition to measurement of vital signs. The average RDOS score did not differ from baseline during the study with either of the three flows given (p=0.74). It is questionable whether this is a blinded study as 'no flow' would not produce the same sound as both the medical air and oxygen groups.

Oxygen versus no gas administration

Clark *et al.* (2015) recruited 114 non-hypoxaemic patients with a diagnosis of congestive heart failure (CHF); they were randomised to either best medical therapy (BMT), that is maximally tolerated medicinal management, alone or in conjunction with long-term oxygen therapy for at least

15 hours per day in the home, including overnight hours. The primary measure was the Minnesota Living with Heart Failure (MLwHF) quality of life questionnaire. The adjusted mean difference suggested no significant difference between the two groups (p=0.98) and it was concluded that oxygen therapy has no impact on quality of life, although there was recognition that the study was significantly underpowered. It should be noted that BMT was not defined in the paper; it may be that patients had different treatment regimens, which questions the reliability of the findings.

The effect of long term oxygen on breathlessness

The study by Currow *et al*. (2009) was a consecutive cohort study of community palliative care services over a 4 year period; of this cohort 1239 palliative non-hypoxaemic patients received oxygen therapy and were included. Benefits were measured using a symptom assessment scale (SAS). The change in mean SAS score was insignificantly different after one week of treatment (P=0.28) and after a fortnight (p=0.35).

Jaturapatporn *et al.* (2010) interviewed a purposive sample of 22 non-hypoxaemic palliative care patients prescribed home oxygen therapy. Data was analysed using a thematic approach. Four of the eight patients reported that their shortness of breath continued but had improved. For the other four, they reported that their shortness of breath had completely reversed as an outcome of oxygen therapy.

Other reasons for clinician prescription

Two studies focussed on the reasons for palliative home oxygen prescription in addition to, or instead of, the potential clinical benefit of improving breathlessness or oxygen saturation levels.

Currow *et al.* (2008) summarised from their research that home oxygen is often prescribed for palliative non-hypoxaemic patients even when published criteria are not met; they proposed one reason for these prescriptions is the presence of a caregiver. They collected data from a community palliative care programme to identify demographics and characteristics of patients with a prescription for home oxygen therapy. Not having a caregiver significantly reduced the likelihood ($p<0.001$) and therefore concluded that the caregiver presence is associated with an increased likelihood for a prescription of palliative home oxygen therapy.

Breadon *et al*. (2013) facilitated focus groups for a purposive sample of 51 palliative care nurses. Two major themes emerged from this study. The first, ‘assessing the patient’s need for home oxygen’ suggested that nurses often have to manage the expectations of relatives, carers and other clinical staff as these groups often request oxygen when patients are actively dying; it was commented that oxygen may be prescribed to 'treat caregiver anxiety'. The second theme ‘monitoring home oxygen’ raised the issue that once oxygen is installed in the home, it is difficult to remove even if unneeded.

Discussion

The purpose of establishing UK Home Oxygen Services was to identify patients who no longer require home oxygen, help address a patient's perceived need for the therapy when there is no clinical need and reduce inappropriate oxygen prescriptions (DH 2008). NHS guidance supported this

by stating oxygen may be of value for palliation in end of life (EOL) care however palliative patients should have evidence of hypoxaemia (NHS Medical Directorate 2012); the original wording in NHS guidance may have led to an increase of oxygen prescriptions at the time of cancer diagnosis but this was clarified in later publications (NHS Primary Care Commissioning 2011).

The British Thoracic Society (BTS) guidelines for home oxygen prescription (Hardinge *et al*. 2015) may appear contradictory at first reading. The palliative oxygen therapy guidelines states that patients at EOL experiencing chronic breathlessness should not receive oxygen therapy if non-hypoxaemic; instead it is suggested they receive a trial of opioids and other treatment such as fan therapy. Clinicians are subsequently advised in the BTS guidelines that oxygen therapy may be considered by specialist teams for patients unresponsive to other treatments suggesting that hypoxaemia is not necessarily a requirement for prescription.

Current guidelines for prescribing and funding home oxygen are predominantly derived from survival data in patients with COPD; guidelines based on this patient group may not be generalisable to palliative care patients (Abernathy *et al*. 2005, Breaden *et al*. 2013). If there is a lack of evidence and subsequent guidelines available to clinicians regarding symptom management for patients at the latter stages of disease then this has the potential to lead to inconsistent access and variable practice (Ambrosino & Simonds 2007, Uronis *et al.* 2008, Abernathy *et al*. 2010).

Ben-Aharon *et al.* (2012) suggests there is widespread prescription of oxygen therapy for dyspnoeic EOL patients yet there is a paucity of evidence for clinical benefit documented in published randomised control trials; this lack of supporting evidence for its widespread use is supported by findings from the studies reviewed in this paper. A number of the studies did find that the presence of a caregiver increases the likeliness of the therapy being prescribed (Currow *et al*. 2008, Breadon *et al*. 2013). However, it may be that there are patients living alone without a caregiver that do require oxygen therapy but have no advocate to request an assessment; the causal nature of these variables should not be assumed. Regardless, it is reported that clinicians are subjected to considerable pressure from carers to prescribe oxygen (Clark *et al*. 2011) and oxygen may be prescribed for the psychological benefit of the caregiver in some instances rather than to treat the patient (Collier *et al*. 2017). Other proposed reasons for palliative oxygen prescriptions include clinicians' belief in its efficacy for reducing breathlessness (Abernathy *et al*. 2005), the perceived need for clinicians to 'do something' (Currow *et al*. 2009, Campbell *et al*. 2013), to fulfil patients' requests (Abernathy *et al.* 2010, Clemens *et al*. 2009) and to reduce re-admission rates (Mukherjee *et al* 2011).

Although the two studies using patient reported symptoms to compare oxygen therapy versus room air suggested that oxygen therapy did not relieve breathlessness significantly better than room air (Philip *et al.* 2006; Abernathy *et al*. 2010), they did suggest that administration of both gases resulted in some perceived benefit for the participants. The literature offers two potential reasons for the apparent success of room air in reducing breathlessness. The first of these is simply the placebo affect (Bruera *et al*. 2003; Philip *et al*. 2006) or even the presence of a researcher at stages of the study leading to reduced anxiety and consequently decreasing the feeling of breathlessness (Philip *et al*. 2006). The second is due to the mechanisms of action of gas administration. It has been proposed that the flow of cool air on oral mucosa and facial nerves has an inhibitory effect and reduces the sensation of breathlessness (Bruera *et al*. 2003; Philip *et al*. 2006). This suggests the small amount of research that is available may be deemed of poor quality as the often utilised 'control' that is room air may indeed be viewed as an intervention due to its potential beneficial effect on breathlessness; these studies should be viewed as comparative rather than controlled.

Fardy (2016) acknowledges the concern relating to a lack of prescriptive criteria for home oxygen therapy but argues that, regardless of this, prescribers will and should continue to make individualised decisions mindful of published guidelines but determined by what interventions relieve the patient's symptoms most effectively. The BTS guidelines (Hardinge *et al*. 2015) state that an individual formal assessment and evaluation of the efficacy of oxygen therapy for improving chronic breathlessness and the associated impacts on quality of life should be assessed for each patient between 24 hours and 3 days of commencement. It is not clear from policy literature whether this has been included in the provision of local assessment and review services; it is likely that this would require further long-term financial investment in chronic disease and palliative care services.

The findings in this review should be considered with some caution due to the limited number of available studies, a lack of understanding of an appropriate control group for comparing interventions, and the reasons for clinician prescribing of oxygen therapy in this patient group being under-researched when compared with studies reviewing the efficacy of home oxygen therapy for hypoxaemic patients with COPD.

Conclusion

To summarise, oxygen therapy is not a benign intervention (Uronis *et al*. 2008) and the appropriateness of prescription should be considered by clinicians; the risks to patient safety alone supports the needs for further research in this field. However, some published studies suggest that oxygen administration may relieve breathlessness in non-hypoxaemic palliative patients, although perhaps no more successfully than the administration of room air. Currently there are no available studies comparing oxygen therapy with fan therapy, which may have similar mechanisms of action (Hardinge *et al*. 2015).

Some areas for future research have been considered including the comparison of oxygen therapy with a true control, and the comparison of oxygen versus other treatments with similar mechanisms of action such as fan therapy or even room air via a concentrator device. In addition, there is a need for future studies that focus on the rationale behind the widespread use of domiciliary oxygen therapy in EOL patients exploring the reasons, beliefs and practices that lead to prescription for this patient group (Currow et al. 2008, Currow et al. 2009, Ben-Aharon et al. 2012). This review suggests that a greater understanding of clinicians' reasons for palliative oxygen prescription is required to provide safe, research-based practice to palliative patients in the future. This paper has highlighted the implications for clinical practice for potential oxygen prescribers; in the absence of robust guidelines, individualised patient assessment and evaluation of oxygen therapy is therefore recommended (Abernathy *et al.* 2005, Uronis *et al*. 2008, Uronis *et al*. 2014).

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