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Palliative Care for People with Non-Malignant Lung Disease: summary of current evidence and future direction

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What is known

Background

Palliative care has predominately focussed on management of patients with *cancer* at the *end-of-life* (EOL). The End-of-Life Care Strategy (1) and other National Institute for Health and Care Excellence (NICE) guidance has demanded that Palliative Care embrace *all* patients with life-limiting disease, irrespective of diagnosis. In addition focus of care should not be limited to the last days or weeks of life but should extend earlier in the patient pathway.

Non-malignant lung disease has a high mortality and symptom burden and encompasses various pathologies including chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), cystic fibrosis (CF), pulmonary hypertension, neuromuscular disorders and infections. The physical and psychosocial needs of patients with these chronic lung diseases at end-of-life are comparable to those with lung cancer (2). This article will focus on COPD (which encompasses a range of primarily bronchial obstructive disorders, e.g. chronic bronchitis and emphysema), ILD (a large group of progressive disorders causing lung parenchymal fibrosis which include idiopathic pulmonary fibrosis, connective tissue disease and asbestosis) and CF (an autosomal recessive genetic disorder affecting chloride ion transportation).

COPD, ILD and CF are life-limiting, non-curable illnesses. Treatments for these conditions may be primarily aimed at disease modification (slowing or halting progression of disease) or purely at palliation with improvement of symptoms and quality of life (QoL). Current research has principally evaluated treatments aimed at disease modification. Lung transplantation is increasingly an option for some patients within these groups and this unique situation highlights the dichotomy of palliation and preparation for death, balanced with active management and potential 'cure' (3). Despite the considerable symptom burden and life-limiting nature of these diseases, uncertainty in predicting prognosis can lead to poor communication about palliative and end-of-life care and often limited access to specialist palliative care services (4).

COPD is the leading cause of death worldwide with over 25,000 people dying each year in the UK. Local palliative care services might expect to be involved for a significant proportion of these patients. In contrast, there are about 2,000 deaths from ILD and around 100 deaths from CF each year (with the majority being adults). Many of these patients are cared for and die in secondary or tertiary referral centres. As palliative care expands to encompass these diseases, more referrals will be made for symptom management and end of life care requesting local palliative care at various points in the patient's illness.

It is vital that palliative and respiratory services develop models of care that promote joint working between teams. Palliative care specialists may need to be involved at an early stage to enhance symptom management and jointly support advance care planning, alongside disease-directed therapy led by the respiratory team. When symptoms improve, the patient does not need continuous specialist palliative care input, but might dip in and out of the service. For example patients can experience severe nausea and breathlessness associated with antibiotic management of infective exacerbations. At the end stage of their disease, which can be difficult to define, increased patient and family support from the Specialist Palliative Care Team (SPCT) may be required with on-going input from respiratory physicians. It is important to ensure access to appropriate expertise to guide care and also to acknowledge where teams have been involved in caring for patients over a prolonged period of time (years). Joint working enables the patients to move within the services as

their needs dictate and has the advantage that as patients approach EOL they already have a relationship and trust the palliative care service. Joint working across hospital and community services is vital to facilitate real choice regarding place of care for these patients at EOL (5).

Prognosis, prognostication

Although COPD, ILD and CF have different aetiologies, affect people of different ages and can have differing disease trajectories, they tend to be slowly progressive illness, punctuated by infective exacerbations. Patients have often coped with their illness for many years. In COPD, for example, attempts to prognosticate and identify patients in last year of life based on disease parameters have been largely unsuccessful (6, 7). In practice patient-related factors such as increasing breathlessness between exacerbations, weight loss, and increasing anxiety are often associated with EOL. Table 1 lists the Gold Standards Framework (GSF) Prognostic Indicator Guidance for COPD, although it has not been formally validated in these patient groups, on-going use implies semi-validation in clinical practice.

In view of the progressive nature of these illnesses, and the difficulty with prognostication, it is important a care strategy is implemented early and is adaptable throughout the course of the illness. Treatment discussions and advance care planning are vital. Patients may require invasive/non-invasive ventilation at different time points and/or be assessed for lung transplantation, although, even if accepted many become ineligible or die whilst awaiting a suitable transplant. Appropriate escalation of treatment may be successful earlier in the patient's illness but become less effective and increasingly burdensome as disease progresses. Initially the best form of symptom management is disease-modifying therapies. A combination of disease and symptom-directed treatment will be needed during the course of the patient's illness shifting to a primary focus of symptom management. The difficulty in distinguishing between a severe exacerbation and dying presents palliative physicians, especially in the hospice setting, with both a dilemma regarding how "active" to be in managing exacerbations and the need to have clearly defined admission and onward referral criteria with on-going support from respiratory physicians.

Table 1: Gold Standards Framework (GSF) Prognostic Indicator Guidance for COPD (8)

Chronic Obstructive Pulmonary Disease (COPD).
At least two of the indicators below:
Disease assessed to be severe (e.g. FEV1 <30% predicted)
Recurrent hospital admissions (at least 3 in last 12 months due to COPD)
Fulfils long term oxygen therapy criteria
MRC grade 4/5 – shortness of breath after 100 metres on the level of confined to house
Signs and symptoms of right heart failure
Combination of other factors – i.e. anorexia, previous ITU/NIV, resistant organisms
More than 6 weeks of systemic steroids for COPD in preceding 6 months.

What are the supportive and palliative care needs of people with non-malignant lung disease?

Despite medical therapy, around 75% of individuals with moderate to severe COPD experienced dyspnoea (9), with most not achieving relief from dyspnoea in the last 6 months of life. Dyspnoea causes social isolation, difficulty performing activities of daily living and impairs QoL. Prevalence of anxiety and depression in these patients may reach 80% (10). Pain, breathlessness, and fatigue are frequent and comparable to cancer and heart disease cohorts (11). In addition the information needs of these patients are great (4, 12). One qualitative study showed that patients' understanding of COPD was poor, with a lack of awareness of both the progressive nature of their disease and that they might die of COPD. Despite this the patients were concerned that their disease might progress and were frightened that they would die of breathlessness or suffocation. None of the patients in this study had discussed these fears with any health care professional (13). Not only does COPD affect the patient, but it also has been shown to impact on the carer, with loss of personal liberty and dignity, the need to adapt to the effects of the disease and with the carer taking on multiple roles, they also experienced some of the same losses as the patient and appeared enmeshed with the illness (14).

In their last year of life, most patients with ILD experienced severe breathlessness, cough, fatigue, depression, anxiety, chest pain and an impaired QoL (15, 16). Qualitative research describes how dyspnoea and cough impact on every part of the lives of ILD patients and carers, and patients expressed frustration and anger at their limited independence and the impact of illness on family relationships. ILD patients and carers report a lack of information sharing and although they may know that the disease is terminal they have a poor understanding of prognosis or what might occur at end-of-life (17, 18).

Symptoms are also frequent in patients with CF, as 84% had pain, 83% cough and 64% breathlessness (19). Qualitative interviews describe similar themes regarding lack of information and the challenge of maintaining hope whilst planning for death (20). Although CF caregivers identified many symptoms, they did not think they could be controlled and were concerned about the role of opioids such as morphine and their potential for hastening death (21).

Despite the poor prognosis and symptom burden of non-malignant lung disease, there is inequitable access to specialist palliative care services, often with no formal process for identifying patients at end of life (22).

Evidence base for specific symptom interventions

Although there is a range of symptoms experienced by patients with non-malignant lung disease, we have focused on management of dyspnoea. A combination of non-pharmacological and pharmacological interventions is needed and it is important that self-help strategies are taught early and reinforced. The mainstay of treatment is physiotherapy (which may need to be intensive and sustained) and psychology. Even in advanced disease, evidence for the most cost-effective care in COPD remains that for pulmonary rehabilitation and stopping smoking, with targeted vaccinations (23).

A Cochrane review of non-pharmacological measures for dyspnoea in advanced disease, showed breathing training, walking aids, neuro-electrical muscle stimulation and chest wall vibration to be effective (24) with no evidence for distractive auditory stimulation, relaxation, fan, counselling and support with breathing-relaxation training, case management and psychotherapy. One recent study supports handheld fan therapy to reduce the sensation of breathlessness (25).

Evidence increasingly supports the benefits of short –term opioids in treating breathlessness in COPD patients (26-28). Data on longer term efficacy and safety, and data for COPD patients with type 2 respiratory failure are lacking. Given the prognostic uncertainties our view is that it is prudent to use opioids in patients who: are breathless at rest; have otherwise severe breathlessness unresponsive to other interventions; or are clearly at EOL (29). Views vary as to the best way of initiating and titrating opioids for these patients (26,29).

A recent Cochrane systematic review found no evidence that benzodiazepines relieved dyspnoea in patients with COPD. They caused more drowsiness than placebo, but less than morphine. When opioids and non-pharmacological measures are ineffective, benzodiazepines are often trialled especially if anxiety is problematic (30).

Oxygen is beneficial in hypoxaemic COPD patients and Long term Oxygen Therapy (LTOT) reduces the risk of developing cor pulmonale. Oxygen may relieve dyspnoea in patients with COPD who are mildly or non-hypoxaemic, but this should be individualised (31) as there are no predictive factors to determine who will benefit. In a recent international study, palliative oxygen and medical air both relieved dyspnoea and improved QoL to a similar, albeit small degree (32). Thus a 3–4 day trial of oxygen or medical air could be used to assess patients who would benefit.

These review findings are supported by the Canadian Thoracic Society clinical practice guideline for managing dyspnoea in patients with advanced COPD (33). In a recent hospital based study, dyspnoea was improved after a palliative care consultation, with opioids ± benzodiazepines associated with improvement in dyspnoea (34).

The use of bi-level non-invasive ventilation (NIV) in COPD at EOL is controversial. Opinions vary as to whether NIV is helpful in managing distressing symptoms at EOL or unhelpful, being a significant barrier to communication (35, 36). Goals of care need to be proactively established with a clear management plan, especially if patients are admitted to a hospice (36).

For patients with ILD, the evidence base for symptom management is poor. A recent systematic review shows strong evidence for the use of pulmonary rehabilitation and pirfenidone to improve functional outcomes and moderate evidence for both sildenafil and pulmonary rehabilitation in improving QoL. (37).

What is unknown?

Although limited aspects of assessment, management and prognostication are known and described above, there is much that remains unknown and these need to be explored further, especially in individual diseases. The optimal model(s) of service delivery remain unknown and although several different models are being trialled in clinical practice, these need formal evaluation.

How to deliver the service

Service delivery models currently in use include ring-fencing some time in an already established multidisciplinary team (MDT), setting up a new subspecialised MDT or a subspecialised clinic. Negotiating that part of an existing respiratory MDT meeting is focussed towards palliative issues with the SPCT attending for this section is probably the most manageable first step. Both inpatients and outpatients with palliative care needs can be discussed, direct referrals can be made and patients known to the SPCT can be brought back to the MDT. Attending the whole of the MDT, may be needed in the first instance whilst teams are getting to know each other's remit, role and what the SPCT can offer, but once this is established supporting some of the MDT is a better use of limited resources. Initial joint review of inpatients by both teams, with the SPCT seen as part of the wider MDT has also been important, together with opportunities to meet patients early when symptoms are problematic, to develop rapport for increased input at later stage. This is a model used in establishing SPCT input for CF patients in the Royal Brompton Hospital, UK. Another MDT model is to set up a new fortnightly MDT, specifically for a group of patients, such as very severe COPD. This could bring together respiratory, palliative and microbiology consultants to optimise the disease-directed and symptom management plans. This is a model that was used in establishing joint working between the palliative care and respiratory teams in Barnsley, UK (38).

St Joseph's Hospice, UK has set up a clinic specifically to meet needs for COPD patients - liaising with their local respiratory clinicians. A 'Hospital-to-Home' case-conference model of care for patients no longer having disease modifying treatment, with a focus on ascertaining preferred place of care and death and facilitating transition of care from tertiary referral to community setting, is currently being evaluated for patients with ILD at the Royal Brompton Hospital. This may help in information sharing between professionals.

The model used, would depend on patient numbers, their needs and the resources available. By integrating the service with the respiratory team, there can be joint learning as palliative care physicians will not be experts in non-malignant lung disease and respiratory physicians will often benefit from better understanding of what modern palliative care is and what it can offer. By developing the teams in tandem, trust and knowledge is gained and the patients benefit, by seeing the most appropriate clinician for them at that time.

Implications for clinical practice

We need to develop effective working between the hospital, hospice and community SPCTs, with respiratory services backup, to ensure seamless delivery of care in patients with life-limiting non-malignant lung disease. This may involve a shift in traditional working practice as patients are often very actively treated right up to death, including with NIV and being considered for transplant which represents the potential for 'curative' treatment. Furthermore, the physiology of the underlying diseases is different and may require changes to type/dose of medication for symptom control. As access to palliative care is variable and underutilised for this cohort of patients, a better understanding of and subsequent reduction in the barriers to referral is vital. This can be improved

by increasing access to the SPCT by increasing visibility on the wards, informal routes of access to advice and a timely response to referrals (39).

Comprehensive supportive care is needed for these patients, with maximal pharmacotherapy directed at the underlying disease, pulmonary rehabilitation, occupational therapy, psychosocial supports, nutritional support, as well as consideration of specific palliative pharmacotherapy such as the use of opioids, benzodiazepines and potentially oxygen.

Implication for future research

Although there are studies focused on the palliative care of non-malignant lung disease there is still a lack of large high quality trials of pharmacological (opioids and benzodiazepines) and non-pharmacological interventions and their combinations. Recent articles have highlighted some key areas for further research (40-42), which are highlighted in table 2. Evaluation of these alongside the efficacy and cost-effectiveness of models of care are needed.

Table 2: Key areas for further research.

Key areas for further research
Appropriately designed and powered studies to evaluate pharmacological and non-pharmacological therapies in these disease groups
Is there a class effect from opioids
What is the role of rapid-onset opioids
Is there a subgroup of people who gain net benefit from oxygen therapy
Oxygen for breathlessness during or after movement
What is the role of combination therapies, e.g. oxygen alongside opioids and/or benzodiazepines
Develop a consensus on the use of validated outcome scales and use of primary endpoints related to symptom control and quality of life
Develop staging instruments to identify ILD patients in the last year of life
Evaluate the most cost-effective model of care for non-malignant lung disease patients towards the end of life
Explore the perceived barriers to joint working between non-malignant lung disease and palliative care services
Explore the involvement of palliative care early in the patients' disease to support symptom management

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