Liverpool Heart and Chest Hospital NHS
NHS Foundation Trust

Drug Management of Breathlessness

e-LfH e-Learning for Healthcare

NHS Health Education England

Inspected and rated Outstanding ☆ Care Quality Commission

Learning Objectives

By the end of this session you will be able to:

- Describe the appropriate disease modifying treatments for the relevant cause of breathlessness in patients approaching end of life
- Explain how to prescribe and safely administer oxygen for patients with breathlessness in end of life care
- List the main drug options used to alleviate the symptom of breathlessness in end of life including use of low dose opioids

Introduction

Symptom management of breathlessness starts with an assessment and diagnosis, based on the understanding of the underlying mechanisms producing the sensation of breathlessness. This may have more than one physiological cause, which may be malignant, non-cancer related or due to treatment. Often the most effective symptom control measure is that aimed at removing or treating the underlying cause, e.g. diuretics for heart failure. This is also known as disease modification.

Treatment often starts with disease-modifying therapy to improve the symptoms, but if this does not work alone then symptomatic drug treatment is added. In later stages of disease it may be that symptomatic treatment alone is used. The role of non-drug management is described in the session – Symptom Management / Non-drug Management of Breathlessness.

Patients with very advanced disease may well have a clear and settled view about how intensively they would like to be treated (e.g. about non-invasive ventilation) and which interventions they would wish not to receive. This is sometimes known as 'ceiling of care'. Additionally, they may have decided about where they would like their care to take place, especially if it is likely that they are dying (e.g. home, hospital or hospice). This is known as 'preferred place of care'.

Overview

This session describes the main drugs used to manage breathlessness in end of life care, their modes of action and how the drugs are matched to the underlying pathology and the patient's emotional state.

The use of oxygen for managing breathlessness is also considered.

Finally, the appropriateness of interventions, depending upon the stage of illness is explained.

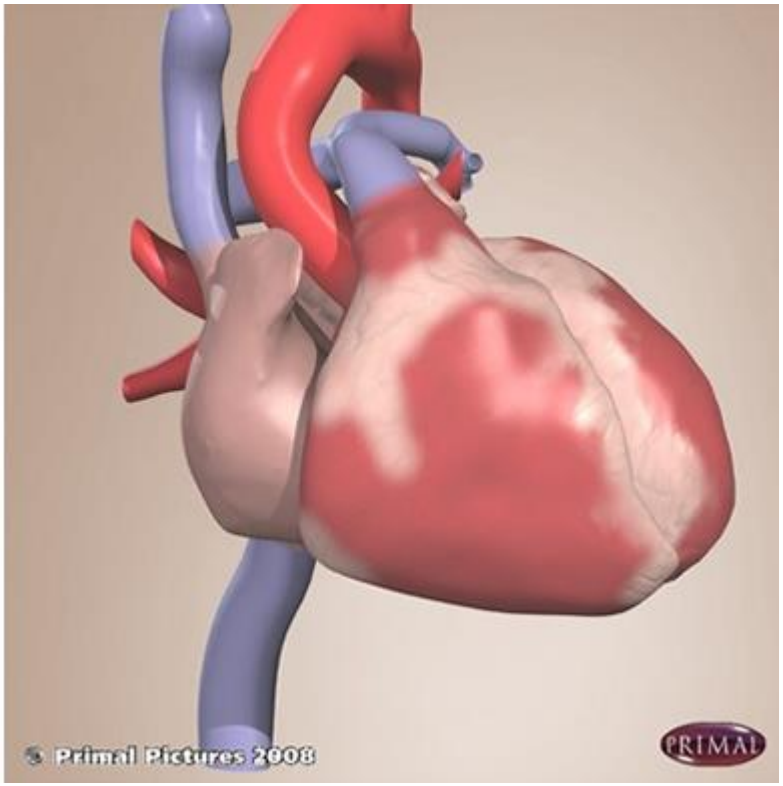
Disease Modifying Treatments
Cardiovascular Causes

Symptom Management / Assessment of Breathlessness you learnt that the most common cardiovascular causes of breathlessness (dyspnoea) are atrial fibrillation, heart failure and pulmonary embolism. What do you think are the treatment options for each of these causes?

Atrial fibrillation

Heart failure

Pulmonary embolism



Atrial Fibrillation

Atrial fibrillation in advanced disease is largely managed by heart rate control. Treatment options include digoxin, beta blockers and amiodarone, aiming for a ventricular rate of less than 100. Anticoagulants may be considered to reduce the risk of stroke, although this would need to be balanced with potential side effects and anticipated duration of survival.

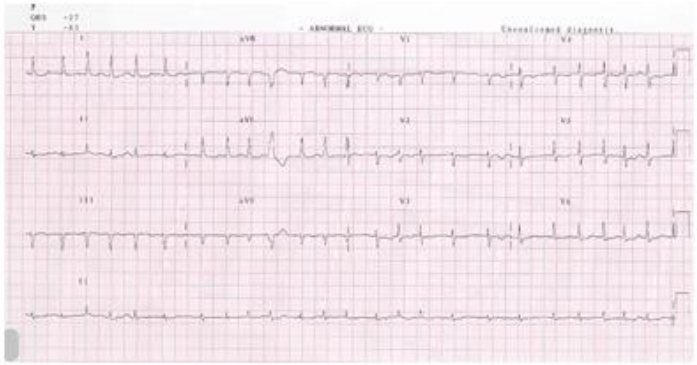


Image: ECG of atrial fibrillation with a fast ventricular response

Heart Failure

Is managed with:

Loop diuretics (e.g. furosemide)

ACE inhibitors (e.g. lisinopril), or

Angiotensin receptor blockers (ARB's) (e.g. candesartan)

And sometimes spironolactone

Care needs to be taken as side effects induce hypotension, renal failure, dehydration and hyperkalaemia. Other drugs used are beta blockers.

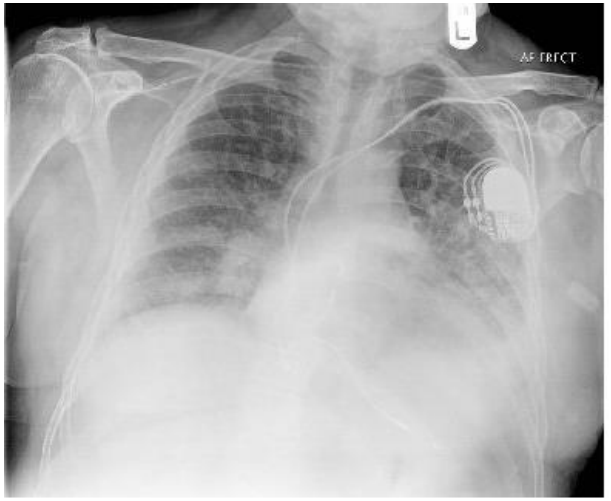


Image: X-ray of patient with LVF showing showing plethoric (blood vessels engorged) lung fields due to pulmonary oedema (also a pacemaker)

Pulmonary Embolism

Anticoagulants are one of the mainstays of the management of pulmonary embolic disease. This occurs commonly in advanced disease of any cause, but particularly malignancy. If anticoagulation is felt necessary and appropriate in the context of end of life care, it is usual to use subcutaneous low molecular weight heparin. This is because of difficulties in anticoagulant control with warfarin, due to drug interactions.

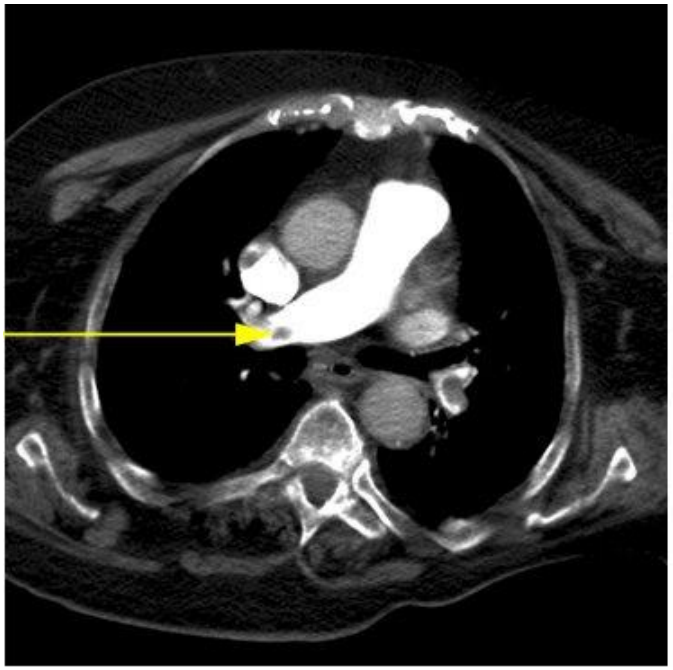


Image: CT image showing pulmonary embolism

Disease Modifying Treatments
Depression and Anxiety

Depression and anxiety are common at the end of life. Breathlessness of any cause can be associated with changes of mood, particularly anxiety and panic. It is sometimes difficult to separate the two.

Question: What do you think are the drug options for the treatment of depression?

Answer:

Tricyclic antidepressants such as amitriptyline. Sedation is a side effect which may be desired

SSRI's (selective serotonin re-uptake inhibitors) such as citalopram, paroxetine

Receptor antagonists, e.g. mirtazapine

Anxiolytics are referred to later. More information about anti-depressants and anxiolytics can be found in the session Symptom Management / Management of Depression.

Question

Breathlessness may also be caused by cancer within the chest. How may drug treatment modify this process?

Feedback

Chemotherapy

Different tumours have different responses to chemotherapy. For example, small cell lung cancer is often very chemo-sensitive and palliative chemotherapy is widely used to improve symptoms and survival. Non-small cell lung cancer is less sensitive but chemotherapy may still have a role.

Hormones

Some cancers are hormone sensitive and can regress with appropriate hormone suppression – for example metastatic breast cancer.

Learning Objectives

Oxygen and Carbon Dioxide

This section discusses the use of oxygen for managing breathlessness in end of life care.

Oxygen (O2) is needed for all tissues for metabolism. The by-product of this is carbon dioxide (CO2). O2 is delivered to the tissues almost entirely bound to haemoglobin (Hb) in the red blood cells, with a small amount dissolved in the plasma. The amount bound to Hb is measured by pulse oximetry and is expressed as oxygen saturation (SpO2). CO2 is carried dissolved in the plasma.

Image 1 Pulse oximetry

The dissolved O2 and CO2 are measured by testing arterial blood gases (a relatively invasive blood test). These are expressed as partial pressure of O2 and CO2 – i.e. pO2 and pCO2. There is a direct relationship between the pO2 and SpO2. The normal SpO2 at sea level is 95-98%.

You may remember from the session Symptom Management / Assessment of Breathlessness that breathing is controlled in part by rising levels of CO2 and falling pH as well as falling O2. In patients with chronic respiratory failure (e.g. in some with COPD) the drive to breathe from rising CO2 and falling pH is lost and the only chemical stimulus is the O2 level. Giving these patients high flow O2 can be risky as it will stop the drive to breath altogether. This is sometimes known as type 2 respiratory failure and the patients known as ‘blue bloaters’.

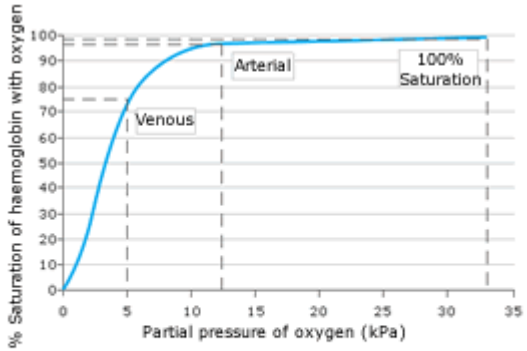


Image 2 The oxygen dissociation curve describes the relationship between SpO_2 (vertical axis) and pO_2 (horizontal axis)

The other group of patients have an exaggerated response to all of these stimuli and are generally very breathless but well oxygenated. This is sometimes known as type 1 respiratory failure and the patients known as ‘pink puffers’.

Oxygen Prescription

Home oxygen is prescribed by completing a Home Oxygen Order Form Part A (HOOF). This can be completed by any qualified and registered practitioner – medical or nursing, from primary or secondary healthcare. There may be a specific end of life pathway for oxygen prescribing in your area which provides specific guidance.

The details that need to be completed on the HOOF include:

Indication: there are 22 clinical codes in section 14, one of which is palliative care (08)

Order (section 7):

litres/min

hours/day

Equipment (section 8):

static concentrator (>4hr/day use)

static cylinder (<4hr/day use)

Consumables (section 9):

nasal cannulae

mask% and type

Ambulatory oxygen can only be arranged by referral to Home oxygen services.

Oxygen Safety

Question: Is it possible that too much oxygen could be harmful?

Answer: Yes.

Question: And in what circumstances?

Answer: In patients with chronic respiratory failure the normal response to rising CO2 levels is lost and the main stimulus to breathe is hypoxia. If too much oxygen (either flow rate or % O2) is administered, the stimulus to breathe is lost and the resulting underventilation could result in worsening acidosis, coma or even death.

Image Sources of oxygen

Conditions that predispose to this are COPD with chronic (type 2) respiratory failure and hypoventilation due to neuromuscular disease (e.g. motor neurone disease – MND).

Strategies to prevent this include:

- Lower target oxygen saturation
- Controlled oxygen therapy
- Non-invasive ventilation

Oxygen Administration

Target Oxygen Saturation

National guidelines on oxygen therapy recommend two levels of target oxygen saturation: 94+% for most patients and 88-92% for patients with chronic (type 2) respiratory failure. This is because these people will have a lower resting SpO2 and it will prevent oxygen induced hypoventilation.

There are two main options for oxygen administration:

Controlled Oxygen

Oxygen can be administered by nasal cannulae (1-6 litres/min), Venturi mask (24%, 28%, 35%, 40% and 60%) and a variety of other masks in an uncontrolled fashion.

Oxygen given by the Venturi mask can be titrated accurately to achieve the desired target oxygen saturation. The disadvantage is that people tend to take off oxygen masks to eat, talk and sleep. A reasonable compromise is to use nasal cannulae titration in a similar fashion. The main complications of nasal cannulae are nasal dryness, discomfort and nose bleeds.

Image 1 Venturi mask and oxygen flow regulators

Non-invasive Ventilation (NIV)

This is a recognised treatment for type 2 respiratory failure. It is rarely used as a palliative intervention in COPD, but is being used increasingly to improve respiratory symptoms in neuromuscular diseases, such as end stage Motor Neurone Disease (MND). This is covered in more detail in the session Symptom Management / Non-drug Management of Breathlessness.

Image 2 BIPAP (non-invasive ventilation) machine

Symptomatic Treatment of Dyspnoea
Introduction

In this section we will consider the drugs that can be used to reduce the unpleasant perception of breathlessness in advanced disease, when disease modifying treatment is either ineffective or inappropriate. These drugs may be used in conjunction with the non-drug options (described in session – Symptom Management / Non-drug Management of Breathlessness), or as death approaches, be the only treatment.

The main drugs used for symptomatic treatment in dyspnoea are:

- Benzodiazepines
- Opioids

Of these two options opioids would usually be the first choice.

Here we will look at benzodiazepines first.

Symptomatic Treatment of Dyspnoea
Benzodiazepines in Breathlessness

Benzodiazepines, also known as anxiolytics, are used for short term and sometimes long term management of anxiety states, for sedation in medical procedures and in epilepsy.

They also have a role in the symptomatic management of dyspnoea as the links below indicate:

- Oral
- Sublingual
- Subcutaneous

Oral

Oral diazepam (starting at 1–2mg OD) has been used for the chronic distress and anxiety of dyspnoea with COPD and type 1 respiratory failure (‘pink puffers’).

Sublingual

Where breathlessness and its distressing emotional concomitants are more acute in onset, a faster acting preparation is needed, such as lorazepam 500 micrograms–1mg sublingually.

Subcutaneous

At the end of life, subcutaneous midazolam may be used as in other causes of distress and agitation.

Unfortunately, none of these is accompanied by evidence from a randomised controlled trial (RCT).

Neither subcutaneous midazolam or sublingual lorazepam are licensed for the palliation of dyspnoea, though both are recognised practice in specialist palliative care.

Symptomatic Treatment of Dyspnoea
Opioids 1

Bert has severe COPD with emphysema. He is on full inhaler therapy and has completed pulmonary rehabilitation twice. His exercise capacity is to his back door, which he frequently visits to 'get enough cool air in'. He has never had ankle swelling. He is afraid of going to sleep in case he does not wake up. His SpO2 at rest is 93%. Apart from inhalers and antidepressants he is on no drugs.

Question: Do you think opioids may be a treatment option for Bert's condition?

Answer: Yes. It is safe to use opioids in COPD, particularly in those with predominant emphysema (type 1 respiratory failure).

It is important, particularly in the opioid naïve, to start at low dose and titrate up appropriately.

Question: Is Bert right to worry that he will never wake up again?

Answer: No. Morphine (or indeed any other drug treatment) is extremely unlikely to cause his sudden death. It is recognised that patients with advanced emphysema can survive for years with a severe symptom burden.

Symptomatic Treatment of Dyspnoea
Opioids 2

Bert is (just) ambulatory, not in respiratory failure.
Treatment options would be:

Codeine phosphate starting at 15mg bd and escalating at most weekly, by 30–50% increments towards 30mg QDS

Morphine sulphate IR suspension (Oramorph) – 1-2mg bd and similar escalation

Morphine sulphate MR tablets (MST) 5mg od (given in the morning as most breathlessness is in the waking hours)

As a general principle it is recommended to start with a low dose and slowly escalate to limit the likelihood of adverse side effects, such as respiratory depression, nausea and drowsiness. All may result in constipation, nausea and drowsiness.

Nebulised morphine was thought to be effective, and with a lower side effect profile than oral or injected morphine, but no trial has shown it to be more effective than placebo, so its use is not recommended.

Symptomatic Treatment of Cough

Cough commonly accompanies dyspnoea at the end of life. The management depends on whether the cough is productive or dry:

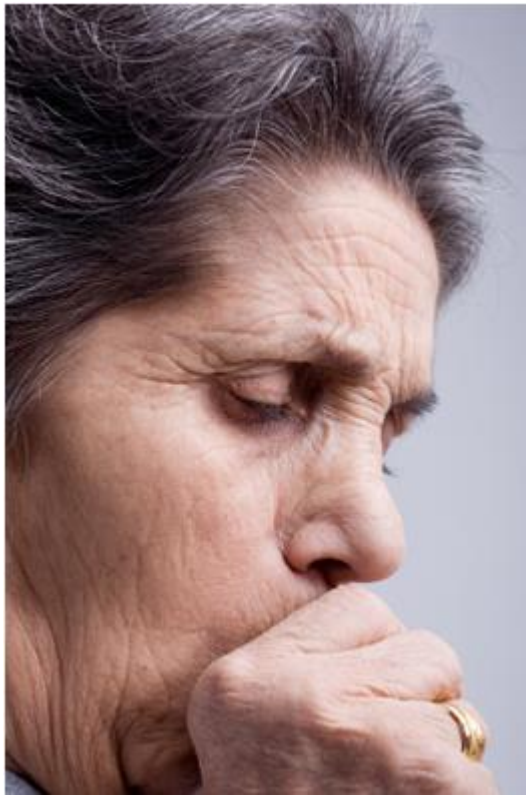
1) Dry cough

This is usually managed with an opioid cough suppressant. Options include codeine linctus 15mg (5ml) 6hrly, methadone 2mg 12hrly or morphine IR suspension 5mg (2.5ml) 4hrly prn.

2) Productive cough

The options are to liquefy the sputum to facilitate clearance, with or without physiotherapy, or to attempt to dry it up with antimuscarinic drugs such as hyoscine hydrobromide, hyoscine butylbromide or glycopyrrolate.

Sputum can be loosened up with 5ml nebulised saline, either 0.9% or preferably 1.8% (hypertonic). An alternative is oral carbocysteine capsules or suspension 750mg tds.



End of Life Care in COPD Case Study Question 1

Alice is 73 and has COPD with cor-pulmonale (see Symptom Management / Assessment of Breathlessness) and chronic respiratory failure. She has long term oxygen therapy (LTOT).

During the last year, she has had three admissions to hospital with exacerbations requiring non-invasive ventilation (NIV). She has found the experience increasingly distressing and following the last admission, she told her daughters that she didn't want NIV again. She is well supported at home by her three daughters and their families.

Her GP is called to see Alice at home when she has again become more breathless, distressed and frightened. What are the two issues that would need to be addressed immediately?

Feedback

The issues are:

- **Ceiling of care** - this would be decisions about disease modifying interventions, such as antibiotics, controlled oxygen, physiotherapy, ventilation (non-invasive or invasive) and cardiopulmonary resuscitation. Most of the life prolonging interventions could only be administered in hospital
- **Place of care** - whether she wants to be managed at home and whether appropriate support can be provided, or be admitted to hospital or hospice

Alice may already have expressed her preferences for future care in the event of her deterioration.

Session Key Points

- The symptom of breathlessness, a subjective experience with an emotional component, can be difficult to manage
- Where possible, the most effective management for breathlessness is to treat or remove the underlying cause
- There are a limited number of drug options to alleviate the symptom of breathlessness
- Starting opioids at a low dose and titrating carefully should not cause respiratory depression in patients with cancer, airways obstruction or heart failure
- Drugs are only one part of an integrated approach to management of breathlessness