*ABC of palliative care***Breathlessness, cough, and other respiratory problems**

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Respiratory problems are common in patients with advanced incurable disease. This article describes palliation of adult patients with malignant disease, but the principles can be applied to many types of non-malignant disease.

A detailed history, examination, and appropriate investigations are needed to establish the most likely cause of any symptom. The history should cover factors that influence the severity of the symptom, including pre-existing diseases (such as chronic obstructive pulmonary disease, which is relatively common in patients with lung cancer), exacerbating factors (such as anaemia, ascites, or profound anxiety), and additional factors (such as pulmonary embolism, infection, or left ventricular failure). All of these will influence management.

Breathlessness

Breathlessness has non-physical as well as physical aspects and, like pain, can be defined by what a patient says it is. It is an unpleasant sensation of being unable to breathe easily. It is relatively common during the terminal stages of cancer: in one survey 70% of 1700 patients with cancer suffered breathlessness during their last six weeks of life. It is a particularly distressing and frightening symptom, not only for patients but also for carers. Activity, levels of anxiety, speed of onset, and previous experience may influence patients' perception of breathlessness and its severity.

While there is often an obvious cause (such as pleural effusion or extrinsic bronchial compression), in some patients no cause is found despite thorough assessment. Little is known about the effects of cachexia on respiratory muscle function, and hyperventilation may account for breathlessness in some cases.

Management

Management of a breathless patient should be individualised, but some general principles apply in all cases. Many members of an interdisciplinary team can contribute. As well as nursing and medical input, physiotherapy is often helpful, particularly for advice on positioning patients in bed, percussion, huffing, control of hyperventilation, and relaxation methods. Practical aids for daily activities are essential.

In selected patients specific treatment such as anticancer therapy can improve symptom control and quality of life. The appropriateness of various strategies varies with time, but, for many patients, the disadvantages of travelling to a distant or regional centre may be justified when weighed against symptomatic relief from radiotherapy, laser therapy, or stenting of an endobronchial tumour. Surgical pleurodesis with insufflated talc should be considered early rather than after repeated pleural aspirations.

Oxygen

Oxygen is usually seen as a non-specific treatment for breathlessness. Patients can become highly dependent on oxygen therapy, and many see it as their lifeline. In patients with chronic lung and heart disease, however, there is good evidence that oxygen therapy is only of benefit in specific situations such as hypoxia or pulmonary hypertension. Randomised controlled

Radiograph of patient with malignant pericardial effusion and secondary pleural effusion causing breathlessness

General principles of managing breathlessness

- Reassurance to patient, family, non-professional and professional carers
- Explanation
- Advice on positioning patient in bed
- Stream of air—Such as fan, open window
- Distraction and relaxation techniques
- Consider blood transfusion if patient anaemic
- Encourage adaptations in activities of daily living, lifestyle, expectations

Therapeutic options for specific situations**Pleural effusion**

- Pleural aspiration, with or without pleurodesis
- Pleuroperitoneal shunt

Pericardial effusion

- Aspiration, with or without fenestration

Hypoxia

- Oxygen

Lymphangitis

- High dose corticosteroids

Endobronchial disease

- High dose corticosteroids
- Laser therapy
- Cryotherapy
- Stenting

trials in breathless patients with malignancy are difficult to conduct, and treatment is often based on observational studies and clinical experience. Further research is needed to identify which patients are most likely to benefit from oxygen.

Meanwhile, the pros and cons of oxygen therapy should be considered on an individual basis. The use of nasal speculae rather than a mask can avoid some of the potential problems. The gas can be humidified, but this is noisy. A 24 hour trial of continuous or intermittent oxygen therapy may be appropriate, and it should be accompanied by some form of subjective assessment by patients, with intermittent oximetry if possible. If such a trial of oxygen is successful and relatively long term use is appropriate and anticipated, then an oxygen concentrator rather than cylinders should be considered for patients at home.

Only a small number of patients should require continuous oxygen. For others, explanation combined with non-specific drug measures, especially anxiolytics, and possibly a bedside or hand held fan can have dramatic effects, sometimes removing the need for oxygen therapy even in patients apparently "glued" to their masks.

Benzodiazepines

Anxiolytics, particularly benzodiazepines, have a place in managing breathlessness even in patients who do not have prominent anxiety or panic attacks. Low doses of benzodiazepines can cause substantial improvement in some patients, and concern about possible respiratory depression is usually unfounded—any such concern should be weighed against the potential benefit of treatment. Benzodiazepines probably relieve breathlessness through anxiolytic and sedative effects and, possibly, muscle relaxation.

The vicious cycle in which anxiety aggravates breathlessness and breathlessness in turn creates further anxiety is experienced to some degree by most breathless patients, regardless of the cause of the symptom. Some patients may experience a severe panic attack and become convinced that they are about to die. Such attacks are more common than is acknowledged. Patients should be advised of measures that they can initiate and which allow them to regain control. These have been summarised as "Stop, purse lips, drop (shoulders), and flop."

Opioids

The relation between opioids and respiration is not simple; if used inappropriately, opioids can induce respiratory depression, which is determined by pathophysiology, prior exposure to opioids, rate and route of dose titration, and coexisting pathology. However, low dose oral opioids can improve breathlessness, sometimes dramatically, although the precise mechanism of action is unknown.

The dose of opioid can be titrated in the same way as when used for pain control, but lower doses and smaller increments should be used. In patients not previously exposed to opioids, as little as 2.5 mg of morphine elixir every 4 hours may be sufficient. If a patient is already receiving controlled release morphine, it is usual to convert to a quick release preparation and allow for a dose increment. For patients unable to swallow, subcutaneous diamorphine can be used. In almost all cases concurrent laxatives should be prescribed.

Trials of nebulised morphine have been conducted in healthy volunteers and in patients with chronic obstructive pulmonary disease and with breathlessness due to malignant disease. The current evidence does not support their use. In any case, bronchospasm, particularly at higher doses, can be a problem, and there is no consensus on the optimal drug, dose, schedule of administration, or method of dose titration.

Pros and cons of oxygen therapy

Potential advantages

- Reverses hypoxia
- Improved wellbeing in some patients
- Placebo effect
  - Patient
  - Relatives
  - Professionals

Potential disadvantages

- Ties patient to oxygen source
- Potential loss of respiratory drive
- Claustrophobia
- Difficulty in talking
- Distancing
- Dry mouth
- Cost

Choices of anxiolytic drug for treating breathlessness

Lorazepam (0.5-2 mg) can be taken sublingually and is rapidly absorbed with a rapid onset of action and a short half life. It is particularly useful for self administration during an episode of acute breathlessness

Diazepam (starting dose usually 5 mg daily) is preferred if a regular anxiolytic is required. Some patients require much higher doses. With a half life of 30-60 hours, it can be administered as a single bedtime dose, orally or rectally

Midazolam—If parenteral administration is required, midazolam can be given by subcutaneous injection (initially 2.5-5 mg) or by infusion (starting dose 10 mg/24 hours, increasing as necessary), often in combination with low dose diamorphine

Methotrimeprazine, a phenothiazine with profound sedating properties at higher doses (and antiemetic properties), is occasionally used as an alternative to midazolam

Cycle of increasing panic and breathlessness

Advice to patient about "panic attacks"

- Try to stay calm
- Purse your lips
- Relax shoulders, back, neck, and arms
- Concentrate on breathing out slowly (if breathing in seems difficult)

The opium poppy, *Papaver somniferum*

Other drugs

Traditionally, other drugs are more commonly administered via nebulisers. If a trial of such a drug is thought appropriate, then nebulised normal saline should be used in the first instance. Inhaled bronchodilators should be reserved for patients with reversible airways obstruction. Other nebulised drugs should be regarded as experimental in this population of patients.

Cough

Cough is a normal but complex physiological mechanism that protects the airways and lungs by removing mucus and foreign matter from the larynx, trachea, and bronchi and is under both voluntary and involuntary control. Pathological cough is common in malignant and non-malignant disease. Cough can be classified in various ways, and several causes may coexist in one patient.

Management

Management should be determined by the type and the cause of the cough as well as the patient's general condition and likely prognosis. When possible, the main aim should be to reverse or ameliorate the cause, combined with appropriate symptomatic measures. Exacerbating factors should be defined, and simple measures such as a change in posture, particularly at night, can be very helpful.

Breathlessness can trigger cough, and vice versa. Persistent cough can also precipitate vomiting, exhaustion, chest or abdominal pain, rib fracture, syncope, and insomnia, and these problems may need to be addressed.

Cough suppressants are usually used to manage dry, but not productive, cough, except in irritant nocturnal cough and cough in dying patients. The most effective antitussive agents are the opioids. Codeine linctus is a mild antitussive while the strong opioids have a more pronounced effect. Methadone linctus can be particularly effective at night, because it has a long half life, but the risk of accumulation exists.

Mucolytic treatments such as simple linctus or nebulised saline may benefit patients with wet unproductive cough. Use of nebulised saline can result in the production of copious liquid sputum, and this makes it unsuitable for those who are unable to expectorate.

Nebulised local anaesthetics can relieve intractable and unproductive cough for which no other treatment has been found. Bronchospasm can occur and not necessarily only with the first dose—nebulised bronchodilators should therefore be available, at least when treatment is initiated. Both lignocaine (up to 5 ml of 2% solution every 6 hours) and bupivacaine (up to 5 ml of 0.25% solution every 8 hours) have been used. The relative efficacy and toxicity of these agents have not been established, and treatment reduces the sensitivity of the gag reflex and causes a transitory hoarse voice. Patients should not eat or drink for an hour after nebulisation.

Antibiotics can be used, even in dying patients, to relieve a productive cough that is causing pain, insomnia, or distress. The decision on whether to treat an infection with antibiotics may raise ethical dilemmas and needs careful consideration and discussion. Appropriate chest physiotherapy should be considered in all patients including those close to death.

Antimuscarinics—In some patients it is more appropriate to reduce salivary secretions. Hyoscine hydrobromide can be given as a subcutaneous injection (0.2–0.4 mg, repeated as necessary) or by subcutaneous infusion over 24 hours (1.2–2.4 mg). It has central side effects, causing sedation and occasionally dysphoria. If these are problematic, glycopyrronium bromide is an alternative option.

Common causes of cough

Non-malignant

Acute infection

- Upper respiratory viral infection
- Bronchopneumonia

Airway disease

- Asthma
- Chronic obstructive pulmonary disease

Irritant

- Foreign body
- Cigarette smoke
- Oesophageal reflux

Cardiovascular causes

- Left ventricular failure

Malignant

Airway obstruction

- Endobronchial disease

Pleural disease

- Pleural effusion
- Mesothelioma

Chronic infection

- Cystic fibrosis
- Bronchiectasis
- Postnasal drip

Parenchymal disease

- Interstitial fibrosis

Recurrent aspiration

- Motor neurone disease
- Multiple sclerosis

Drug induced

- Angiotensin converting enzyme inhibitors
- Inhaled drugs

Interstitial disease

- Lymphangitis
- Multiple pulmonary metastases
- Radiation pneumonitis

Vocal cord palsy

- Hilar tumour or lymphadenopathy

Classification of types of cough

- Productive cough, patient able to cough effectively
- Productive cough, patient not able to cough effectively
- Non-productive cough

Pharmacological agents that inhibit cough

Opioids and opioid derivatives

- Codeine phosphate
- Dextromethorphan
- Pholcodine
- Methadone
- Morphine

Local anaesthetics

Lozenges

- Benzocaine
- Lignocaine
- For laryngeal, pharyngeal, or tracheal irritation

Nebulised

- Lignocaine
- Bupivacaine
- Useful for intractable, unproductive cough (with care)

Corticosteroids

- Prednisolone
- Dexamethasone
- Often used to relieve cough related to endobronchial tumour, lymphangitis, or radiation pneumonitis

Bronchodilators

- Salbutamol
- Ipratropium
- Can relieve cough associated with chronic obstructive pulmonary disease

Therapeutic options in managing productive cough

Tenacious sputum

- Steam inhalation
- Nebulised saline
- Simple linctus
- Physiotherapy
- (Cough suppression)

Heart failure

- Diuretics

Purulent sputum

- Antibiotics
- Postural drainage
- Physiotherapy
- Cough suppression

Loose secretions but unable to cough

- Positioning
- Hyoscine hydrobromide
- Glycopyrronium bromide
- Suction

Haemoptysis

In many studies of patients with haemoptysis a definite cause is established in only half of cases. Even in patients with a proved malignancy, haemoptysis can be due to other causes. While lung cancer is the commonest cause of massive haemoptysis (>200 ml/24 hours), non-malignant disorders such as acute bronchitis, bronchiectasis, and pulmonary embolism can cause mild to moderate haemoptysis.

Management

It is important to establish that the blood or blood stained material has come from the chest and not the nose, upper respiratory tract, or gastrointestinal tract. Management depends on the cause and prognosis. Radiotherapy (endobronchial or external beam) and laser therapy are particularly effective in controlling bleeding from endobronchial tumour.

Massive haemoptysis should be regarded as an emergency whether or not resuscitation is appropriate. Patients bleeding as a result of a non-malignant cause such as aspergilloma, lung abscess, or bronchiectasis may warrant active management, but this is rarely the case in patients with haemoptysis and lung malignancy receiving palliative care.

Palliative management should be aimed at reducing awareness and fear. A combination of a parenterally administered strong opioid and a benzodiazepine is usually required. The intravenous route should be used if there is peripheral vascular shutdown. It is often possible to predict the likelihood of a massive bleed and to plan for such a crisis in several ways, including establishing an emergency supply of appropriate drugs in the patient's home. Careful judgment is required in deciding whether to discuss the risk of massive haemoptysis with a patient and relatives.

Stridor

A harsh inspiratory wheezing sound results from obstruction of the larynx or major airways. Treatment with corticosteroids (such as dexamethasone 16 mg daily) can provide rapid relief. Explanation should always be given, together with advice about sitting or lying as upright as possible and measures to relieve anxiety. Radiotherapy or endoscopic insertion of a tracheal or bronchial stent should be considered but are not always appropriate. Inhalation of a mixture of helium and oxygen (in a ratio of 4:1) is used in some centres.

Pleural and chest wall pain

Pleural and chest wall pain may exacerbate breathlessness and may be difficult to manage. Analgesics should be prescribed in a step-wise fashion as detailed in the first article in this series. If a patient also has a cough then cough suppression will help. Radiotherapy should be considered if the pain is caused by bone or soft tissue metastases. An intercostal nerve block may alleviate pain from rib metastases or fracture.

Conclusion

Patients and their lay and professional carers need to acknowledge that respiratory problems, particularly breathlessness, can be difficult to palliate. A patient centred, problem orientated approach is required. Professionals from many different specialties and disciplines have a potential role. Few of the management strategies discussed above have been submitted to adequate scientific scrutiny, and there is urgent need for further research.

Therapeutic options for haemoptysis

Minor bleed

Caused by lung tumour

- Oral haemostatic drug—Such as tranexamic acid or ethamsylate
- Radiotherapy—External beam or endobronchial

Caused by pulmonary embolism

- Laser therapy
- Anticoagulation

Any cause

- Treat coagulation disorder if present
- Cough suppressant

Major bleed

Resuscitation appropriate

- Establish intravenous access
- Transfusion
- Bronchoscopy and endoscopic measures
- Bronchial artery embolisation
- Open surgery

Resuscitation inappropriate

- Intravenous opioid and benzodiazepine

Both situations

- Nurse patient lying on his or her side, on the side of the tumour
- Mask evidence of bleed—Such as with red or green towels
- Calm witnesses—Patient, family, staff, other patients

Radiograph showing bilateral bronchial stents in patient with obstructive lesion

The picture of the opium poppy is reproduced courtesy of the Royal Botanical Gardens, Kew.

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