10. GUIDELINES FOR THE MANAGEMENT OF INTRACTABLE BREATHLESSNESS IN PATIENTS WITH MALIGNANT DISEASE

10.1 GENERAL PRINCIPLES

- Breathlessness is a common symptom in patients with advanced malignancy. Approximately 70% of patients experience breathlessness during the last six weeks of life. ¹
- Breathlessness in the patient with advanced cancer is usually multifactorial. It is important to consider potentially reversible causes of breathlessness and treat where appropriate (see Guidelines on Antibiotics, Ascites, Blood Transfusions, Corticosteroids, Fatigue, Pleural Effusions). Table 10.1 includes some of the common causes of breathlessness in patients with advanced cancer. ²

| Table 10.1 Common causes of breathlessness in patients with advanced cancer ² |
|---------------------------------|---------------------------------|---------------------------------|
| Anaemia                         | Iatrogenic e.g. chemotherapy    | Pericardial effusion            |
| Anxiety                         | Infection                       | Pleural effusion                |
| Ascites                         | Intrathoracic malignancy        | Pneumothorax                    |
| Bronchospasm                    | Ischaemic heart disease         | Pulmonary embolism              |
| Chronic obstructive pulmonary disease | Lymphangitis carcinomatosis    | Pulmonary fibrosis              |
| Congestive cardiac failure      | Neuromuscular disorders         | Stridor                         |
| Fatigue / cachexia              | Pain                            | Superior vena cava obstruction  |

- Intractable breathlessness can be defined as breathlessness where active management of the cause is no longer possible and / or appropriate. ¹
- The mechanisms involved in the sensation of breathlessness are poorly understood. Physical, psychological, social and spiritual factors may all contribute to the experience of breathlessness. It is important to adopt a multi-disciplinary approach to the management of this difficult symptom. ³
- Management approaches will include both pharmacological and non-pharmacological measures. ³, ⁴
- Benzodiazepines, opioids and oxygen are the mainstay of medical management for intractable breathlessness. Therapeutic trials of medications, either singly or in combination, may be necessary to determine an effective management strategy for an individual patient. ³

10.2 GUIDELINES

10.2.1 Non-pharmacological options

- These are important and should not be overlooked. They may be used alone or in conjunction with medication. ⁵, ⁶, ⁷ [Level 4]

- They include:
  - Reassurance and explanation.
  - Use of a fan or cool air across the face.
  - Adequate positioning of the patient to aid breathing.
  - Breathing exercises and relaxation training.
  - Advice on modifying lifestyle.
10.2.2 Pharmacological options

Benzodiazepines [Level 3]

- Benzodiazepines may be useful especially if there is coexisting anxiety and / or fear.\(^8\)
- Lorazepam is suggested for episodes of paroxysmal breathlessness. Dose: 0.5mg-1mg sublingually as required (maximum dose is 4mg daily). \(^9\)
- In patients unable to tolerate oral medication or those in the dying phase, subcutaneous midazolam 2.5mg-5mg as required may be appropriate. \(^2\) If effective, this can then be incorporated into a 24 hour subcutaneous infusion via a syringe driver.

Nebulised medication [Level 4] / [Level 1-]

NB: The first administration of any nebulised medication, including saline, must be monitored for adverse effects such as bronchospasm. \(^9\)

- Nebulised non-opioids
  - Nebulised sodium chloride 0.9% may help as a mucolytic. Consider a trial for 24 hours. Dose: 5ml via a nebuliser 4 hourly or as required. \(^10\) [Level 4]
  - A trial of a nebulised bronchodilator should be considered if there is evidence of airways obstruction. \(^11\) [Level 4] Commonly prescribed bronchodilators are Salbutamol and Ipratropium Bromide.
    Dose: Salbutamol 2.5mg-5mg up to 4 times in 24 hours. \(^9\)
    Dose: Ipratropium bromide 500microgrammes up to 4 times in 24 hours. \(^9\)
  - There is no current evidence to support the use of nebulised lignocaine in the management of intractable breathlessness and therefore it is not recommended for use at present. \(^12\) 20 [Level 4]
- Nebulised opioids
  - Current evidence does not support the use of nebulised opioids in the management of intractable breathlessness. \(^13\) [Level 1-]

Systemic opioids [Level 1]

- Morphine is the most commonly prescribed oral opioid in the management of intractable breathlessness. \(^13\)
- The prescribing of oral opioids on an “as required basis” may be appropriate for paroxysmal breathlessness. \(^13\)
- A trial of morphine sulphate solution should be considered for patients who are opioid naïve. Dose: Morphine Sulphate solution 2.5mg-5mg every four hours, or as required. \(^13\)
- There is some evidence that the use of a short-acting opioid is more effective at relieving breathlessness. It may be necessary to prescribe on a regular basis in addition to any long-acting opioid that the patient may be taking. If a patient is already established on opioids it may be appropriate to increase the dose of the long acting opioid by 25-50%. This would not be appropriate if the patient is experiencing intermittent periods of breathlessness as they may then get an increase in side-effects \(^14\), \(^15\), \(^16\).
- Diamorphine / morphine are the strong opioids of choice in patients who are unable to swallow. Dose: Diamorphine 1.25mg-5mg as required subcutaneously if the patient is opioid naïve. If diamorphine is unavailable then morphine may be used as an alternative. Dose: Morphine 2.5mg-10mg as required subcutaneously. If effective, the appropriate dose can be incorporated into a 24 hour infusion via a syringe driver. \(^13\), \(^16\)

- Acupuncture, aromatherapy and reflexology.
Oxygen [Level 3]

- The evidence for efficacy is limited. 2,17
- A trial of oxygen should be considered in patients known to be hypoxaemic (i.e. oxygen saturation less than 90%). Care is required in patients with known COPD and Type 2 respiratory failure.
  - Dose: Oxygen 24-28% in patients with known COPD.
  - Oxygen 24-60% for other patients. 17
- The use of continuous oxygen should be avoided if possible as this may lead to patient dependence, reduced mobility and give limited benefit. Intermittent use is the preferred mode of administration. 2
- Oxygen administered via a mask may be claustrophobic, cause a barrier between the patient and family and result in dryness of the mouth. Nasal prongs are often better tolerated than masks. Humidified oxygen may be more comfortable for the patient. 2

Corticosteroids [Level 3]

- Corticosteroids may help in patients with tumour compression or lymphangitis carcinomatosis.
- They are also used in exacerbations of obstructive airways disease. There is no evidence of their benefit in non-specific dyspnoea. If there is no improvement, they should be discontinued (see Guidelines on the Use of Corticosteroids). 2,3
  - Dose: Dexamethasone 4mg-8mg daily administered before 2pm. Occasionally higher doses (8mg-16mg) are used e.g. lymphangitis, superior vena cava obstruction.

Anti-cholinergic medications [Level 4]

- Anti-cholinergic medications are the drugs of choice in the management of respiratory secretions in the dying phase. Hyoscine hydrobromide and glycopyrronium are the two most commonly used drugs. 18
  - Hyoscine hydrobromide: 400micrograms subcutaneously as required. Prescribe 1.2mg-2.4mg subcutaneously via a syringe driver over 24 hours. 21
  - Glycopyrronium: 200micrograms subcutaneously as required. Prescribe 600micrograms - 2.4mg subcutaneously via a syringe driver over 24 hours. 22

Other medications [Level 4]

- There is anecdotal evidence that phenothiazines, antihistamines, cannabinoids and nebulised furosemide may be useful in the management of intractable breathlessness. 2 [Level 4]

10.3 STANDARDS

1. Reversible causes of breathlessness should be identified and treated where appropriate. 2 [Grade D]
2. Patients with anxiety should be considered for a trial of relaxation therapy and / or anxiolytics. 18 [Grade C]
3. All patients with breathlessness should have access to non-pharmacological interventions. 6,7. 19 [Grade C]
4. Breathlessness should be controlled in all dying patients. 20 [Grade D]
5. All patients prescribed nebulised medication should first receive a test dose. 10 [Grade D]
6. Any adverse reactions to nebulised medication should be clearly documented in the clinical notes. 20 [Grade D]
7. Diamorphine / morphine are the opioids of choice if patients are unable to swallow. 13 [Grade A]
8. Midazolam is the benzodiazepine of choice in patients who are unable to swallow. ² [Grade D]
9. Nebulised opioids should not be used in the management of intractable breathlessness. ¹⁴ [Grade C]

10.4 REFERENCES


10.5 CONTRIBUTORS

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