Opioids for Breathlessness in Advanced Disease

This guideline is intended to be used to aid primary and secondary care healthcare professionals primarily in the early management of the use of opioids for adult patients with breathlessness in advanced disease.

Background

- The effectiveness of opioids in relieving breathlessness has been studied among people with cancer, COPD and chronic heart failure.[1] Most evidence is in people with COPD.[2] Most data available is considered low certainty.
- Not all opioids show reduction in breathlessness. Data from larger RCTs supports **morphine but not oxycodone**.[7,17]
- The recent MABEL trial suggested that morphine did not improve breathlessness but had a potential benefit on physical activity levels and cough.[19]
- Most experience is with morphine. [1] There is insufficient evidence as to whether the synthetic opioids (e.g. fentanyl, buprenorphine) are effective in breathlessness. There is preliminary evidence to support prophylaxis for exertion-induced breathlessness for morphine and fentanyl but risk-benefit balance is not known.[2]
- Modified release preparations are preferred over immediate release in the majority of patients [8,9]
- Systematic reviews and RCT meta-analyses support use of opioids by **oral and parenteral** but not nebulized route.[10,11]
- Morphine and other opioids reduce the ventilatory response to hypercapnia, hypoxia and exercise, decreasing respiratory effort and breathlessness.[3] Improvements are seen at doses that do not cause respiratory depression.[4-5]
- In the largest cohort study (of patients with severe COPD), there were no excess deaths or hospitalizations reported with lower opioid doses equivalent to morphine ≤30mg/24h PO.[17] A small number of patients with Type 2 respiratory failure may be sensitive to opioids, and a joint management plan for these individuals should be made with the Respiratory specialists. Caution is advised when patients are on other respiratory depressant medications e.g. benzodiazepines.
- European Respiratory Society guidelines suggest opioids should not be routinely used for the treatment of breathlessness due to low certainty of evidence, and if used should be following optimal management of underlying disease process and non-pharmacological methods of breathlessness management.[18]

Produced in partnership with The Leeds Teaching Hospitals Trust, Leeds Community Healthcare NHS Trust, St Gemma's Hospice and Wheatfields Hospice. Sue Ryder

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Management

Non Pharmacological Management

Refer to A practical guide to coping with breathlessness: Information for patients

Pharmacological Management

Consider the use of opioids for breathlessness if:

- Breathlessness persists despite optimal treatment of the underlying cause.
- Non-pharmacological methods (relevant to the performance status and prognosis of the patient) have been implemented and moderate to severe breathlessness persists.
- The patient has, and is using a breathlessness crisis plan (Appendix 1), with information in a format they can access.

Opioids should only be used in the management of breathlessness in advanced disease as part of a breathlessness management plan, and not as the sole intervention/management. It cannot be assumed morphine will be beneficial in all diseases, so carefully monitoring is needed. De-prescribing should be routine in the absence of benefit in either subjective breathlessness or performance status.

Caution: Short term opioid related adverse effects are generally mild and include constipation and nausea. It is important to provide appropriate explanation, laxatives (1st line would be senna, if no contraindications), and antiemetic (PRN) and monitoring.[1] All patients who are prescribed opioids for breathlessness in advanced disease should also be given patient information on use and side effects. In LTHT we recommend the My Opioid Prescription leaflet.
Opioids can cause a range of adverse effects on immune and endocrine function, and these are likely to become more clinically relevant with long term use, so careful thought should be given to longer term opioid prescribing (e.g. >12 months).

Starting morphine for breathlessness in opioid- naïve patients with normal renal function

Modified -release (MR) approach

Week1
- Morphine Sulfate MR 5mg b.d

week2
- If no benefit
- Increase to Morphine Sulfate MR 10mg b.d.

week3
- If no benefit
- Increase to Morphine Sulfate MR 15mg b.d.

Week 4
- If no benefit
- Stop medication

Immediate-release (IR) approach

MR morphine sulfate should be the standard approach. For the small group of patients who don't wish to take MR opioids, IR could be considered. Starting doses can be as little as 500 micrograms morphine sulfate b.d., titrated gradually weekly up to 5mg q.d.s., if necessary. When dose is unchanged for 2 weeks, consider switching to MR formulation.[1]

If already taking an opioid

In patients on <30mg/24h oral morphine (or oral morphine equivalent) for pain, the dose can be increased in appropriate increments up to 30mg total daily dose. In patients taking doses > 30mg/24h oral morphine (or oral morphine equivalent) for other indications, there is unlikely to be any benefit to starting additional opioids for breathlessness.

For patients on buprenorphine or methadone maintenance for opioid addiction, specialist advice should be sought and the decision should be made in conjunction with Forward Leeds, specialist palliative care and/or respiratory specialists.

Renal impairment

Due to the lack of evidence for oxycodone continue to use Morphine between a GFR of <50 and >20 but titrate more slowly and monitor closely for side effects. If GFR <20, a trial of low dose buprenorphine may be considered. If concerns seek specialist advice.

Breathlessness in the last days and hours of life

The recommended daily limits to opioid dose may not apply in the last days of life. For LTHT patients: See LTHT Care of the Dying Person - (Breathlessness) or seek SPCT advice. For Hospice, Community Patients Care of Dying Person -Breathlessness

Key Points

- There is evidence that opioids are safe in breathless patients when used appropriately, and at low doses.
- Morphine is the opioid with the best evidence for breathlessness, although all evidence is low certainty.
- Use MR preparations where possible.
- Use the lowest effective dose and stop medication if no improvement in symptoms or performance status.
- Use more sparingly in patients with longer prognoses due to accumulation of increasing adverse effects over time
- Avoid complicated regimes of differing opioids/doses for different indications, but consider the whole clinical picture.
- Medication alone is unlikely to be effective for breathlessness and should be one part of a multi-faceted approach.

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Provenance:

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Clinical Condition - Breathlessness
Target Patient Group - Adults with advanced disease
Target Professional Group - Primary& Secondary Care Healthcare Professionals

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