Review: oral or parenteral opioids alleviate dyspnoea


QUESTION: Are opioids effective in the treatment of dyspnoea?

Data sources
Studies were identified by searching Medline (1966–99), EMBASE/Excerpta Medica (1980–99), CANCERLIT (1988–99), CINAHL (1982–99), the Cochrane Library, Dissertation Abstracts, and SIGLE; reviewing the reference lists of relevant studies, reviews, and book chapters; and contacting authors, other experts in the field, and palliative care organisations.

Study selection
Studies were selected if they were randomised, double blind, placebo controlled trials of any opioid to alleviate breathlessness in patients with dyspnoea caused by any disease.

Data extraction
Data were extracted by 2 independent reviewers on disease causing dyspnoea, intervention (opioid used and dosage), study methodology, and results. Study quality was assessed using the 5 point Jadad scale and the Cochrane Collaboration criteria for concealment. Main outcome measure was a subjective assessment of dyspnoea. In studies of patients at rest, the breathlessness measurement nearest to 1 hour after opioid administration was used; in studies with exercise tests, the breathlessness measurement relating to the exercise test was used. Dyspnoea measurements recorded at a fixed point during exercise or after a fixed length of exercise were used for meta-analysis.

Main results
18 crossover trials met the inclusion criteria, 9 trials involved oral (8 trials) or parenteral (1 trial) opioids (116 patients), and 9 involved nebulised opioids (177 patients). 9 trials of oral or parenteral opioids and 3 trials of nebulised opioids were included in a meta-analysis. Overall, opioids had a positive effect on the sensation of breathlessness (table 1). When trials of oral or parenteral opioids and nebulised opioids were analysed separately, only oral or parenteral opioids showed a positive effect (table 1). Opioids had no significant effect on either arterial blood gas (4 trials) or oxygen saturation (9 trials). Side effects were those typical of opioid use (nausea and vomiting, drowsiness, and constipation).

Conclusions
Oral and parenteral opioids are effective in the treatment of dyspnoea. Nebulised opioids have no beneficial effects.

Oro or parenteral and nebulised opioids v placebo for subjective assessment of dyspnoea*  

<table>
<thead>
<tr>
<th>Trial in meta-analysis</th>
<th>Number of trials</th>
<th>Standardised mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All trials</td>
<td>12</td>
<td>−0.31 (−0.50 to −0.13)</td>
</tr>
<tr>
<td>Oral or parenteral opioids</td>
<td>9</td>
<td>−0.40 (−0.63 to −0.17)</td>
</tr>
<tr>
<td>Nebulised opioids</td>
<td>3</td>
<td>−0.11 (−0.32 to 0.10)†</td>
</tr>
</tbody>
</table>

*All trials were crossover trials. Follow up not reported. CI defined in glossary. A random effects model was used.
†Not significant.

COMMENTARY

In palliative care, opioids are recommended for the management of breathlessness in patients with advanced cancer. Opioid treatment is also recommended for breathlessness in end stage pulmonary disease and congestive heart failure, although in practice it is less commonly used, perhaps because of a reluctance to acknowledge that these patients are in the terminal phase of their illness. The systematic review by Jennings et al is therefore an important analysis of available data on the effectiveness of opioid treatment.

The 18 studies included in the review evaluated the effects of opioid treatment in various contexts and diseases. It is comforting that the review concludes that patients’ subjective assessments of breathlessness showed significant improvement from baseline, because this finding confirms current practice. The review also confirms that the nebulised route of administration is ineffective. However, it is unclear whether opioids help to improve breathlessness triggered by exertion, as the trials of non-nebulised opioids showed modest but non-significant increases in exercise tolerance.

The review warrants closer scrutiny in some respects. The authors rightly point out that all of the studies were small, with studies of oral and parenteral opioids including a total of only 116 patients. Furthermore, only 2 of the studies were of patients with cancer, and yet opioids are most commonly used in this group. The authors provided little critical commentary on the paucity of data available for meta-analysis or how this limits the conclusions that can be drawn.

Importantly, however, the review confirms that current practice should at least proceed. More research is needed, particularly to investigate the effectiveness of opioids in different disease groups and compare them with alternative or adjuvant treatments. Non-pharmacological interventions might be an interesting place to start because the relative value of opioids used in conjunction with self management interventions is yet to be determined.

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