Hyoscine vs glycopyrronium for drying respiratory secretions in dying patients

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CRD summary
The author of this review concluded that there was no clear evidence to support the choice of hyoscine over glycopyrronium for drying up the secretions that cause the 'death rattle'. A thorough search identified only two relevant studies with conflicting results. The author's interpretation of the evidence was appropriate and the conclusion is likely to be reliable.

Authors' objectives
To determine if hyoscine hydrobromide is more effective than glycopyrronium for drying respiratory secretions in dying patients.

Searching
MEDLINE (1996 to 2004), EMBASE (1980 to 2004), CINAHL (1982 to 2004), the Cochrane Library and Pharm-line were searched. Additional studies were sought through searches of the meta-Register of Controlled Trials and the UK National Research Register, reference list checks, and contact with palliative care colleagues via an Internet bulletin board. The search strategy was reported in full.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were initially eligible for inclusion. Having failed to identify relevant RCTs, the author broadened the inclusion criteria to relevant prospective studies in which the treatment and control groups were treated equally apart from the intervention of interest, with explicit definition of the method used to assess the outcome and more than 80% follow-up. The studies also had to provide some interpretative description of the results.

Specific interventions included in the review
Studies that compared hyoscine hydrobromide with glycopyrronium were eligible for inclusion. The studies did not have to specify administration of hyoscine by injection to be included. Hyoscine could be given as a single injection or as a continuous subcutaneous infusion. One included study used a six-step protocol for drug administration, according to which both groups received glycopyrronium as steps four to six.

Participants included in the review
Studies in terminally ill patients were eligible for inclusion. In the included studies, treatment was administered to hospice patients who had a 'death rattle'.

Outcomes assessed in the review
The eligible outcome was assessment of respiratory secretions. The included studies used either a point scoring system or subjective observer rating (mild, moderate, severe) to record respiratory noise volume. Measurements were recorded before treatment and 30 minutes after any administration of treatment, and change was assessed as better, same or worse. One study took observations every 4 hours until death. The results were expressed as response to treatment.

How were decisions on the relevance of primary studies made?
The author did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The author did not state how the validity assessment was performed. The included studies were appraised on whether the setting was the same for both treatment groups, doses clearly identified, clear assessment of the level of respiratory secretions, whether single or multiple outcomes were assessed, and if statistical analysis was used.
Data extraction
The author did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The data extracted were as reported in the original studies, and included the proportion of patients with the outcome of interest and p-values obtained from tests of statistical significance.

Methods of synthesis
How were the studies combined?
A narrative synthesis was performed.

How were differences between studies investigated?
Differences in study design, population, intervention and outcome measures were discussed in the text and summarised in a table.

Results of the review
Two non-randomised studies with a control group were included. The total number of participants was 265. One study was a two-phase group comparison with 191 participants, while the other was a prospective comparative audit of 74 participants who received the drugs of interest.

Both study reports lacked quantitative data on the drugs actually given (rather than intended). In one included study the participants in each treatment group were in separate palliative care units. The other study was conducted in two phases in the same unit: participants in the first 11-month phase were given hyoscine and those in the second 9-month phase were given glycopyrronium. One study did not report levels of statistical significance for treatment differences.

In the two-phase study, patients treated with hyoscine were significantly more likely to respond to the first drug dose than patients in the glycopyrronium group (56% versus 27%, p=0.002) and significantly less likely to require a second injection (33% versus 50%, p=0.03). There was no significant difference in the proportion of patients in each treatment group who had relief from respiratory secretions at death.

In the audit study, patients treated with hyoscine were less likely to respond after the first drug dose than patients in the glycopyrronium group (35% versus 46%) and less likely to remain settled within three doses (32% versus 49%). Statistical significance was not reported. The number of patients whose secretions were relieved at death for hyoscine compared with glycopyrronium could not be established because glycopyrronium was recommended in both treatment protocols after step three.

Authors' conclusions
There was no clear evidence of a reduction in respiratory symptoms to support the choice of hyoscine over glycopyrronium in terminally ill patients.

CRD commentary
The review addressed a clear question and clearly defined the inclusion criteria. The search to identify relevant studies was thorough and well reported, although one aspect that was not mentioned was the eligibility of foreign language studies. The review was conducted by a single author and did not report methods to minimise bias and errors in the study selection, appraisal or data extraction. Given the evident extensive effort made to identify relevant studies and the precision of the inclusion criteria, on balance it was likely that the most relevant studies were identified. The included studies were well described (as far as the original reports allowed) and appropriately appraised, and a proper narrative synthesis was conducted and clearly reported. The author's conclusion is an appropriate interpretation of the evidence reviewed and is likely to be reliable.

Implications of the review for practice and research
Practice: The author stated that the choice of drug to relieve respiratory symptoms in terminally ill patients remains with the individual practitioner, as there is no clear evidence to recommend hyoscine over glycopyrronium.

Research: One ongoing study and one anticipated RCT in the UK were mentioned in the report. The author suggested that a study of highly matched patients could overcome some of the difficulties inherent in conducting clinical trials in terminally ill patients.

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