Sedation during mechanical ventilation: a systematic review  
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Authors' objectives  
To determine the most effective sedation agent used in adult patients with respiratory failure who require mechanical ventilation in the intensive care unit (ICU).

Searching  
The authors searched MEDLINE (from 1966 to August 1998) and the reference lists of retrieved articles for English language articles. The full search strategy was provided in the paper.

Study selection  
Study designs of evaluations included in the review  
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review  
Studies of any sedation agent were eligible for inclusion. The sedation agents evaluated in the included studies were propofol, midazolam, alfentanil, papaveretum, isoflurane and lorazepam. The dosages of sedative and cointerventions used varied between the studies.

Participants included in the review  
Studies of adult patients with respiratory failure, who required mechanical ventilation in the ICU, were eligible for inclusion. The characteristics of the participants in each of the included studies were not provided.

Outcomes assessed in the review  
Studies that determined the success of sedation were eligible for inclusion. The evaluation of success varied considerably between the studies and included: the effectiveness of sedation, the time to adequate sedation, time to recovery and the quality of sedation.

How were decisions on the relevance of primary studies made?  
Two reviewers assessed the validity of the included studies. Any disagreements were resolved by consensus.

Assessment of study quality  
The authors assessed validity using the following criteria: use of concealed allocation, use of intention-to-treat analyses, completeness of follow-up, use of objective criteria for outcomes, and whether the cointervention was standardised.

OThe results from the included studies were tabulated. One reviewer extracted the data and a second reviewer

Data extraction  
The authors did not state how the data were extracted for the review, or many reviewers performed the data extraction. Details of the data extracted from each individual study were not reported.

Methods of synthesis  
How were the studies combined?  
The results were presented in a narrative discussion.

How were differences between studies investigated?  
The studies were analysed separately according to the drugs evaluated in the included studies. Clinical heterogeneity precluded statistical pooling of the results.
Results of the review

Fifteen RCTs (n=996) were included in the review.

Quality assessment.

The quality of each of the included studies was low. None of the included studies stated that the allocation of treatment was concealed, only one study stated that intention-to-treat analysis was used, and most studies did not use standardised cointerventions. However, most of the studies employed a complete follow-up and used objective outcome criteria.

Propofol compared with midazolam (9 RCTs, n=690).

The time taken to recover from sedation was faster in patients treated with propofol than with midazolam (7 RCTs; data not given). Five of the studies demonstrated that propofol was a more effective sedative than midazolam, while two found equal effectiveness (data not provided).

Propofol compared with alfentanil (1 RCT, n=44).

The time taken to awaken was 5, 11 and 18 minutes, respectively, for patients receiving low, moderate and high doses of alfentanil; the time taken to breath spontaneously was 8, 22 and 27 minutes, respectively. No data were provided for those patients receiving propofol.

Propofol compared with papaveretum (1 RCT, n=27).

No difference was found in the number of patients who were able to follow commands or spontaneously breath prior to stopping the infusions (data not provided).

Isoflurane compared with midazolam (2 RCTs, n=120).

The proportions of patients adequately sedated following treatment with isoflurane were 70.7 and 86%, compared with 67.4 and 64% of patients receiving midazolam. However, this difference was only significant in the latter study (P=0.0005). Both studies found that the time to extubation was significantly shorter for patients receiving isoflurane than those receiving midazolam (data not provided).

Lorazepam compared with midazolam (2 RCTs, n=115).

One study (n=20) found that there was no significant difference in the time to reach adequate sedation, or the return to baseline mental status, following sedation with lorazepam or midazolam (data not provided). The second study (n=95) found that there was no significant difference in the quality of sedation between lorazepam and midazolam. However, less lorazepam was required to achieve the same level of sedation attained through treatment with midazolam (data not provided).

Cost information

None. However, it was highlighted that four of the included studies recorded the cost as an outcome.

Authors' conclusions

Further research is required to determine the most effective sedative agent for adult patients receiving mechanical ventilation in the ICU.

CRD commentary

The review addressed a clear question and used explicit inclusion criteria. However, since the inclusion criteria used for the outcome were not defined clearly, its appropriateness was unclear. The search for relevant studies was not extensive and there was no attempt to identify unpublished studies; the potential for publication and language bias cannot be ruled...
The authors used procedures to minimise bias when selecting the studies for inclusion, but there is a potential for observer bias in the data extraction process. The validity of the included studies was assessed systematically, highlighting their low quality.

The results were presented in a narrative summary, which was appropriate given the heterogeneity of the included studies. However, there was considerable variation in defining the success of sedation between the studies, and there appears to have been selective reporting of the outcomes used in each of the included studies. The review would have benefited from additional data and results from each of the included studies, to allow for a more objective assessment of both the interpretation of the extracted data and reliability of the review's conclusions. Consequently, based on the evidence presented, the authors' recommendation for further high-quality RCTs was appropriate.

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: The authors stated that large and methodologically robust RCTs are required to evaluate the effectiveness of sedative agents used in adult patients who require mechanical ventilation in the ICU.

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