Daily sedative interruption in mechanically ventilated patients: limited data, numerous concerns
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CRD summary
The authors concluded that daily interruption of sedation in mechanically ventilated critically-ill patients may be a promising treatment, but concerns about safety remain and further research is required. Although the authors’ cautious conclusions appear to reflect the limited evidence, the limited search, poor reporting of review methods and lack of an adequate quality assessment undermine the robustness of the conclusions.

Authors’ objectives
To evaluate the effects of daily interruption of sedation in mechanically ventilated patients on clinical outcomes.

Searching
MEDLINE was searched from inception to February 2006 using the reported search terms. In addition, reference lists in identified reports were screened. Only studies published in English were eligible.

Study selection

Study designs of evaluations included in the review
No restrictions were applied to study design.

Specific interventions included in the review
Studies that evaluated daily interruption of sedative infusions were eligible for inclusion. The included study compared daily interruption of continuous intravenous (IV) sedation and analgesia until patients awakened (able to follow commands or became agitated and required sedation) versus continuous IV sedation interrupted only by the intensive care team. All patients received continuous morphine infusion; some patients also received midazolam and some received propofol.

Participants included in the review
Studies of mechanically ventilated critically-ill patients were eligible for inclusion. The included study was in intubated medical intensive care unit (ICU) patients who needed continuous IV sedation.

Outcomes assessed in the review
Studies that reported clinical outcomes were eligible for inclusion. The included study and associated analyses assessed days of ventilation, discontinuation, length of stay (LOS) in the ICU and hospital, percentage of days awake, adverse events, need for re-intubation or tracheostomy, percentage of patients discharged home, mortality, specified complications (ventilator-associated pneumonia, upper gastrointestinal haemorrhage, bacteraemia, barotrauma requiring insertion of chest tube, venous thromboembolism, and cholestasis or sinusitis requiring surgery) and a variety of psychological measures (assessed using self-report and structured interview at least 6 months after discharge from the hospital).

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

Assessment of study quality
The authors did not state that they formally assessed validity. However, they did comment on blinding and the similarity of treatment groups at baseline.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.
Methods of synthesis
How were the studies combined?
The single identified study was described in the text together with the subsequent related post-hoc analyses.

How were differences between studies investigated?
Only one study was identified.

Results of the review
One randomised controlled trial (RCT; n=128) and two post-hoc analyses that included patients in the original trial were included in the review. The post-hoc analyses comprised a retrospective chart review (126 of the original patients) and a non-randomised comparison (32 patients who survived and were discharged: 18 patients from the original RCT and 14 non-randomised contemporaneous patients) of 13 patients in the intervention group versus 19 patients in a control group.

The RCT was single-blinded. The review authors stated that the baseline characteristics of the treatment groups were similar. Researchers who conducted the retrospective chart review were blinded and were not the original researchers. The non-randomised comparative analysis was conducted by researchers blinded to the treatment group.

The RCT reported that patients allocated to daily interruption of sedative required significantly fewer days of ventilation (4.9 versus 7.3 days, p<0.05), had significantly earlier discontinuation (p<0.05), spent significantly fewer days in the ICU (6.4 versus 9.9, p<0.05), and were awake for a greater percentage of days (85.5% versus 9%) compared with patients allocated to control. There was no difference between treatment groups in adverse events, need for reintubation or tracheostomy, hospital LOS, percentage of patients discharged home or mortality.

The retrospective chart review (n=126) reported that complications were significantly more common in the control group than in the intervention group (26 versus 13, p<0.05). Apart from gastrointestinal haemorrhage, specified complications (ventilator-associated pneumonia, bacteremia, barotrauma requiring insertion of chest tube, venous thromboembolism, and cholestasis or sinusitis requiring surgery) were lower in the intervention group than in the control group, but the statistical significance of the difference was not reported.

The non-randomised comparison reported no statistically significant difference between patients in the intervention (n=13) and control (n=19) groups in various psychological measures.

Authors' conclusions
Daily interruption of sedation in mechanically ventilated critically-ill patients may be a promising treatment, but concerns remain about its safety and further research is required.

CRD commentary
The review addressed a clear question in terms of the participants and intervention. Inclusion criteria for the outcomes and study design were broad, which seems appropriate in view of the limited evidence identified. Limiting the search to one database and reference lists might have increased the potential for publication bias. The methods used to select studies and extract the data were not described, so it is not known whether any efforts were made to reduce reviewer error and bias. The validity assessment appears limited, thus the results from the included study and post-hoc analyses may not be reliable. In addition, since there was little information about the participants in the RCT, the generalisability of the results cannot be judged. Although the authors' cautious conclusions appear to reflect the evidence, the limited search, lack of reporting of review methods and lack of an adequate quality assessment undermine the robustness of the conclusions.

Implications of the review for practice and research
Practice: The authors stated that further research is required before the widespread use of daily interruption of sedation in ventilated ICU patients.

Research: The authors stated the need for further research evaluating daily interruption of sedation in ventilated ICU
patients. The intervention should be evaluated using different analgesic and sedative agents (continuous infusion lorazepam, hydromorphone and fentanyl) and in other groups of patients (those under 40 years of age, surgical trauma ICU patients and patients with a history of alcohol or illicit drug abuse). Studies should assess acute withdrawal, measures of haemodynamic instability and pharmacoeconomic measures.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.