The effectiveness of propofol versus midazolam for the sedation of adult ventilated patients in intensive care units (ICUs)

Authors' objectives
To examine the effectiveness of midazolam versus propofol for sedation and whether treatment should be administered by bolus or continuous infusion.

Searching
The search was conducted in a number of databases, which included MEDLINE, CINAHL, Current Contents and the Cochrane Library. The search terms and a full list of the sources searched are reported in the review. In addition, the reference lists and bibliographies of the relevant articles were examined and experts were contacted for unpublished research. Non-English articles were excluded from the searches.

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

Specific interventions included in the review
Studies that investigated the effectiveness of midazolam and propofol for sedation, with or without concurrent administration of narcotics, were eligible. Studies of continuous infusions versus intermittent bolus infusion were also eligible.

Participants included in the review
Studies that investigated adult ventilated patients in intensive care units (ICUs) were eligible. Studies conducted during anaesthesia were excluded, as were those conducted in patients in recovery or cardiac units and who were not artificially ventilated.

Outcomes assessed in the review
The following outcome measures were selected to evaluate sedation: the ability to achieve the desired sedation level (as measured by sedation scale or expert observation); the length of recovery time; the duration of admission in the ICU; and the incidence of haemodynamic complications.

How were decisions on the relevance of primary studies made?
The author does not state how the papers were selected for the review; one reviewer performed the selection.

Assessment of study quality
The methodological quality of the included studies was assessed using a checklist based on the work of the Cochrane Collaboration and the Centre for Reviews and Dissemination. The articles were assessed by one reviewer. Several articles (number not reported) were also appraised by an expert in systematic reviews.

Data extraction
The data were extracted using a form developed for the review. This form was presented in the appendices. One reviewer performed the data extraction.

Methods of synthesis
How were the studies combined?
Weighted mean differences (WMD) and 95% confidence intervals (CIs) were calculated, where appropriate. The studies were combined using a fixed-effect model. Studies not included in the meta-analysis were discussed in a narrative manner.

How were differences between studies investigated?
The studies were grouped according to the status of the patient and/or whether the intervention was administered as a bolus or continuous infusion. The author state that the homogeneity of the included studies was evaluated by examining the 95% CIs, and statistically using the chi-squared test. Possible reasons for heterogeneity were investigated through an examination of the types of participants, interventions and outcome measures.

Results of the review
Thirty-seven studies were included; 18 of these were pooled in a meta-analysis.

Quality of sedation.
The majority of the data were unsuitable for meta-analysis. For critically ill patients the results were equivocal; two studies reported that propofol produced significantly better quality sedation, another that midazolam produced better sedation, and a fourth found no difference between the two interventions. None of the studies that compared infusions of midazolam with propofol in post-cardiac surgery patients reported a significant difference in the quality of sedation. Two studies comparing propofol infusions with boluses of midazolam in post-cardiac patients reported that propofol infusions provided better quality sedation.

Conflicting results were reported in two studies that compared propofol infusions with midazolam infusions in post-operative patients: one study reported that propofol provided better tolerance of the ICU, while the other reported that both drugs provided similar quality sedation. A single study that compared the efficacy of propofol infusions with midazolam infusions in surgical and medical patients found both regimes to be equally effective.

Time from cessation of sedation until extubation.
Results from three studies (n=184) that compared infusions of propofol with midazolam in general ICU, critically ill patients were combined in a meta-analysis. The WMD was -5.523 (95% CI: -5.967, -5.080), demonstrating that patients in the propofol group took less time to wean from ventilation. However, there was evidence of significant heterogeneity between the studies (chi-squared 67.86, d.f. = 2). The author suggests that the variation in the diagnoses of patients between and within the studies, and the differences in procedures, was likely to be the source of heterogeneity.

Five studies (n=161) compared infusions of propofol with midazolam in post-cardiac surgery patients. Results from four studies were combined in a meta-analysis. The fourth study had short sedation times and inclusion of the trial in the meta-analysis revealed heterogeneity. Combining three studies only gave a WMD of -1.458 (95% CI: -1.712, -1.205; chi-squared 1.51, d.f. = 2), which represented shorter extubation times for the patients sedated with propofol infusions.

The results from two studies (n=160) that compared propofol infusions with midazolam boluses for post-cardiac surgery patients gave a WMD of -2.268 (95% CI: -2.378, -2.158) in favour of propofol. However, there was significant heterogeneity between the studies (chi-squared 116.87, d.f. = 1). Possible reasons for this, as listed by the author, were differences in inclusion criteria and differences in the sedative dosage used.

Time to cessation of sedation until recovery.
Four studies (n=199) compared propofol infusions with midazolam infusions in critically ill, general ICU patients. A meta-analysis of three studies gave a WMD of -1.676 (95% CI: -1.858, -1.493), demonstrating that patients treated with propofol infusions had shorter recovery times. However, there was evidence of significant heterogeneity between the studies (chi-squared 527.88, d.f. = 2). Three studies (n=122) compared propofol infusions with midazolam infusions in post-cardiac surgery patients. The WMD was -1.000 (95% CI: -1.359, -0.642) in favour of shorter recovery times in the propofol group. However, the results were not homogeneous (chi-squared = 26.20, d.f. = 2). There were no studies in surgical patients that reported recovery times.
Duration of admission to the ICU.

One study reported the duration of admission. Patients sedated with propofol had a shorter length of stay.

Haemodynamic complications.

Several studies reported that in critically ill, general ICU patients, propofol was more likely to cause a decrease in heart rate. However, the author states that cardiovascular depression was not clinically significant. One study reported that propofol caused a greater decrease in the mean arterial pressure (MAP) and systolic blood-pressure (BP), which necessitated fluid loading in significantly more patients. Four studies in post-cardiac surgery patients reported a significant decrease in systolic BP and MAP following induction of sedation with propofol. However, midazolam was also reported to cause a significant decrease in MAP and/or systolic BP in two studies. Two studies reported that there was no significant difference in the BP and heart rate in patients receiving propofol, compared with those receiving boluses of midazolam.

For general post-operative patients, one study reported that there was no statistically-significant difference between the groups in terms of systolic BP, but patients in the propofol group experienced a significant decrease from baseline. The study also reported that patients in the propofol group experienced a decrease in MAP in the first 5 minutes after administration, and a decrease in the heart rate. In one study in patients with medical and surgical patients, more patients receiving propofol than those receiving midazolam required adjustments to infusion rates, due to hypotension.

Administration of narcotics.

Most studies that compared propofol infusions with midazolam infusions in post-cardiac surgery patients reported no difference between the groups in the routine administration of analgesia. One study reported a significant difference in the morphine requested (33% of patients in the propofol group versus 53% in the midazolam group), although the mean dose administered was similar between the groups. In three studies that compared propofol infusions with midazolam boluses, patients sedated with midazolam required more analgesia. In two studies that investigated sedation in surgical patients, no difference was found between patients sedated with propofol or midazolam in terms of analgesia administration.

Authors' conclusions

Both propofol and midazolam infusions appear to provide similar quality sedation. The author also states that extubation and recovery time for patients sedated with propofol is reduced, and that haemodynamic responses with both drugs are not generally clinically significant.

CRD commentary

On the whole, the methodological quality of the review was good. However, as only one reviewer was involved in the review process there is a greater risk of errors of judgement. The search for studies was comprehensive, and included handsearches and contact with experts. The study selection and data extraction processes were described and the author assessed methodological quality using appropriate checklists. Details of the studies were adequately presented in a series of tables throughout the report. The results of the review were well presented; the studies were combined where appropriate and heterogeneity was investigated, and where indicated possible reasons were suggested. The pooled results reported are unlikely to be reliable, given the degree of heterogeneity identified in most cases. The author's conclusions follow from the data presented.

Implications of the review for practice and research

Practice: The author states that if the major clinical consideration is the quality of the sedation, either propofol or midazolam may be administered. However, if it is important that recovery and extubation is rapid, propofol should be chosen.

Research: The author states that future research could be directed at using a combination of agents.
Bibliographic details
Magarey J. The effectiveness of propofol versus midazolam for the sedation of adult ventilated patients in intensive care units (ICUs) Adelaide, S. Australia, Australia: Joanna Briggs Institute for Evidence Based Nursing and Midwifery. Systematic Review; 11. 2000

Other publications of related interest
Magarey JM. Propofol or midazolam - which is best for the sedation of adult ventilated patients in intensive care units? A systematic review. Aust Crit Care 2001;14:147-54.

Indexing Status
Subject indexing assigned by CRD

MeSH
Critical Care; Hypnotics and Sedatives /therapeutic use; Intensive Care Units; Midazolam /therapeutic use; Nursing Care; Propofol /therapeutic use; Respiration, Artificial

AccessionNumber
12003008043

Date bibliographic record published
31/10/2003

Date abstract record published
31/10/2003

Record Status
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.