Safety and clinical effectiveness of midazolam versus propofol for procedural sedation in the emergency department: a systematic review

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CRD summary
This review concluded that midazolam and propofol were equally safe and effective for procedural sedation of adults in the emergency department, and that use of one agent over the other should be guided by resource utilisation and treatment costs. The authors’ conclusions appeared to reflect the evidence, but the limitations with the included studies should be borne in mind.

Authors’ objectives
To compare the safety and effectiveness of midazolam and/or propofol for procedural sedation in adults in the emergency department.

Searching
PubMed (from 1949), EMBASE (from 1980), CINAHL (from 1982), the Cochrane Database of Systematic Reviews, and the Central Register of Controlled Trials (CENTRAL) were searched up to March 2007 for relevant articles. Search terms were reported. Three journals and three conference proceedings were handsearched up to 2007. Bibliographic databases and reference lists of retrieved articles were manually searched. The 2006 Canadian Compendium of Pharmaceuticals and Specialties, and the Canadian Adverse Drug Reaction Newsletters (1991 to 2007) were also searched. Manufacturers were contacted for unpublished data.

Study selection
Randomised controlled trials (RCTs) and observational studies that compared the safety and effectiveness of midazolam and/or propofol for procedural sedation in adults in the emergency department were eligible for inclusion. The primary outcome of interest was major and minor adverse events (ie. any untoward health events perceived by the research assistant and/or physician administering the procedural sedation to be related to the use of midazolam or propofol). The secondary outcome was successful procedural sedation (defined as the ability to sedate the patient to the target level of sedation defined a priori by the study authors and the ability to perform the indicating medical procedure without deviating from the study protocol).

Most of the included studies were conducted in North America. Some trials included co-administration of narcotics, and study medication regimens varied. Indications for procedural sedation were mainly orthopaedic reductions and cardioversion, but also included incision and drainage, and chest tube insertions. Further study characteristics were given in a separate online table (supplementary Table S1).

One reviewer screened studies for inclusion.

Assessment of study quality
Two reviewers independently assessed the quality of RCTs according to the Jadad scale, including criteria on randomisation, double blinding, allocation concealment, and reporting of withdrawals. Studies receiving a score of 3 or more were considered high quality. Disagreements were resolved by consensus.

Data extraction
One reviewer extracted in duplicate data on the proportion of adverse events and successful procedures to calculate the mean difference between patients receiving midazolam versus propofol. Discrepancies in data extractions were resolved by reviewing the article a third time and by contacting primary study authors for clarification.

Methods of synthesis
Where there was no evidence of heterogeneity, the proportion of adverse events was pooled to calculate the probability
of major or minor adverse events. For the proportion of successful procedures, a Bayesian random-effects model was used to calculate weighted mean differences and 95% confidence intervals (CIs).

Sensitivity analysis was performed by removing one RCT at a time and by removing low quality studies. Publication bias was assessed through visual inspection of a funnel plot.

**Results of the review**

Twenty-eight studies were included in the review (13 RCTs and 15 observational studies). The number of patients could not be calculated, as the online supplementary material could not be located. Two RCTs reporting the secondary outcome scored 2 on quality and two RCTs scored 3. Three RCTs reported adequate methods for randomisation, none were double-blinded, none adequately described allocation concealment, and three reported withdrawals.

Studies reporting minor adverse events were clinically heterogeneous and the results could not be pooled. There were no statistically significant differences in the proportion of major adverse events between patients receiving propofol and those receiving midazolam (nine RCTs and 15 observational studies).

There was no statistically significant difference in the success rate for midazolam and propofol (four RCTs).

Sensitivity analyses did not significantly alter the results.

**Authors’ conclusions**

Midazolam and propofol were equally safe and effective for procedural sedation of adults in the emergency department; use of one agent over the other should be guided by resource utilisation and treatment costs.

**CRD commentary**

The review question was clear and was supported by appropriate inclusion criteria. A comprehensive search of the literature was undertaken and attempts were made to locate unpublished data. It was unclear whether any language restrictions were applied. The authors undertook quality assessment in duplicate, but study selection and data extraction were undertaken by only one reviewer, so reviewer error and bias could not be ruled out.

The authors assessed the quality of the RCTs, with two reported to be of good quality. Clinical heterogeneity was assessed and appropriate methods were used to combine the data and further explore heterogeneity. The authors acknowledged the small number of included RCTs and the potential for reporting bias.

The authors’ conclusions appeared to reflect the evidence available, but the limitations with the included studies should be borne in mind.

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

**Practice:** The authors stated that the included studies mainly used procedural sedation for cardioversion and orthopaedic reductions, and that the relative safety and effectiveness of midazolam and propofol should be restricted to these indications.

**Research:** The authors stated that further large comparative studies are needed to validate outcome measures for procedural sedation, to capture further patient outcomes, and assess the cost-effectiveness of propofol and midazolam.

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**Bibliographic details**

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.