Low-dose ketamine in addition to propofol for procedural sedation and analgesia in the emergency department

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CRD summary
This review concluded that there is insufficient evidence to recommend the routine use of low-dose ketamine combined with propofol for procedural sedation in the emergency department setting. Although the review has a number of weaknesses, this conclusion is appropriate.

Authors' objectives
To evaluate the safety and efficacy of low-dose intravenous ketamine with intravenous propofol for sedation and analgesia during emergency department procedures.

Searching
MEDLINE, EMBASE, BioMed Central, the Cochrane Library, International Pharmaceutical Abstracts and Google Scholar were searched from inception to February 2007; key search terms were reported. The reference lists of all retrieved articles were screened. Only English language publications, or those with an English language abstract, were eligible for inclusion in the review.

Study selection
Prospective controlled studies that compared ketamine and propofol with an appropriate comparator regimen for procedural sedation were eligible for inclusion. The primary outcomes of interest were: frequency of significant haemodynamic and respiratory compromise requiring active medical intervention; ketamine-specific adverse effects; sedation satisfaction scores; time until discharge criteria were met; time until discharge. The included studies were of children and adults undergoing a wide variety of procedures.

Studies of healthy volunteers and those that involved general anaesthesia were excluded from the review.

Two reviewers selected studies for inclusion in the review. Any disagreements were resolved by discussion, with reference to the retrieved article.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Data were extracted on the following outcomes: requirement for additional pain relief or sedation; changes in infusion rates; recovery; awakening; ambulation and discharge times; patient preference scores.

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
The studies were combined narratively, with studies of adult and child patients discussed separately.

Results of the review
Eleven studies (n=957) were included in the review, ten (n=897) of which were randomised controlled trials (RCTs).

Seven of the RCTs were double-blind; the remaining three were not blinded.

Children (five studies, of which four were RCTs, n=329).
Hypotension appeared less pronounced in children receiving ketamine-propofol than comparators, but the number of cases requiring medical intervention was not reported. Few cases of ketamine-specific adverse effects were reported, although the authors acknowledged that adverse effects were not consistently reported in all of the included studies. Recovery time following the procedure was not statistically significantly different between the groups in two studies. In three studies children in the ketamine-propofol group were statistically significantly less likely to need additional sedation.

Adults (six RCTs, n=628).

One RCT found no difference between groups in the need for medical intervention for haemodynamic or respiratory compromise, and another favoured the ketamine-propofol group for this outcome. One RCT reported a higher incidence of post-operative nausea and emergent reaction in patients receiving the highest doses of ketamine (36% and 16%, respectively) than in patients receiving propofol alone (4% and 0%), with a longer time to discharge in the ketamine groups. In two RCTs, satisfaction scores were lower in the ketamine-propofol group than in the comparator groups. Discharge time was significantly shorter in the ketamine-propofol group in one RCT, significantly longer in two RCTs and not significantly different in another two RCTs. Fewer patients in the ketamine-propofol groups than in the comparator groups required additional sedation, but total cumulative doses were rarely reported.

Cost information
The authors stated that the cost of a 2.5 mg/kg propofol - 0.5 mg/kg ketamine regimen in a 70-kg patient would be Canadian dollars (CAD) 6.25 (US$5.56) as opposed to CAD 4.45 (US$3.78) for propofol alone.

Authors’ conclusions
There is insufficient evidence to recommend the routine use of low-dose ketamine with propofol for procedural sedation in the emergency department setting.

CRD commentary
This review set out to answer a clear research question with explicit inclusion and exclusion criteria. The authors searched several electronic databases and listed key search terms. The searches were restricted to publications in English, or those with an English abstract, and no specific attempts were made to locate unpublished studies, which might have led to some relevant studies being missed. Steps were taken to reduce bias and error in the study selection procedure, with two reviewers selecting studies for inclusion, but it is not clear whether similar steps were applied in the data extraction process; this may raise the potential for errors. The validity of the included studies does not seem to have been assessed formally, although the authors did report whether the included studies were randomised and/or blinded. The lack of a formal validity assessment and limited reporting of study details make it unclear how much confidence the reader should have in the findings of the included studies. A meta-analysis was not undertaken, which seems appropriate given the variation in procedures and outcomes in the included studies. The authors' stated objective was to evaluate the efficacy and safety of ketamine and propofol in the emergency department setting, however, most of the included studies were conducted in non-emergency department settings. The authors also noted that most of the included studies had small sample sizes and were not consistent in reporting outcomes. The authors' conclusions are appropriate.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further RCTs of the safety and efficacy of ketamine combined with propofol for sedation and analgesia in emergency department procedures are needed. These RCTs should use clinically relevant end points, such as interventions required to manage haemodynamic and respiratory compromise and standardised patient satisfaction scores. The trials should compare ketamine-propofol with an equivalent dose of propofol alone.

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