Safe and effective procedural sedation for gastrointestinal endoscopy in children

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CRD summary
The review concluded that propofol-based therapy was the most effective regimen for procedural sedation during gastrointestinal endoscopy in children. Given the potential for bias in the review process, limitations in quality assessments, and variation in study outcomes, the authors’ conclusions may not be reliable.

Authors' objectives
To assess the safety and effectiveness of procedural sedation in children undergoing gastrointestinal endoscopy.

Searching
MEDLINE, EMBASE and The Cochrane Library were searched for published studies from January 1995 up to January 2011; search terms were reported. Reference lists of retrieved articles, reviews, editorials and guidelines were also searched.

Study selection
Studies that reported specifically on safety (incidence of adverse events) and/or effectiveness (time characteristics, need for supplemental sedation, need for restraint, procedural success, provider satisfaction, and patient comfort) of procedural sedation for gastrointestinal endoscopy in children (younger than 18 years) were eligible for inclusion in the review. Reviews, editorials, policy statements, guidelines and case reports were excluded.

Some of the included studies were limited to children younger than 12 years. Oesophagogastroduodenoscopy was the most frequent gastrointestinal endoscopic procedure. Studies used either propofol-based sedation, opioid and benzodiazepine combination, ketamine-based sedation, midazolam alone, sevoflurane inhalation, or premedication (with midazolam or atropine).

Two reviewers selected studies for the review independently but not blindly; disagreements were resolved by discussion.

Assessment of study quality
Randomised controlled trials (RCTs) appear to have been assessed for quality based on criteria including power calculation for sample size, randomisation method, and blinding.

The authors did not report how many reviewers assessed studies for quality.

Data extraction
Data were extracted on safety and efficacy outcomes as they were measured in the individual studies.

The authors did not report how many reviewers extracted data.

Methods of synthesis
Studies were synthesized in a narrative format by different categories of type of procedural sedation.

Results of the review
Twenty-six studies (25 papers) were included in the review. Eleven studies were RCTs (965 patients) and 15 were non RCTs (7,368 patients). All RCTs were reported as underpowered to detect adverse events. Five RCTs were reported as having an unclear randomisation method. Three RCTs were reported as not having blinding. Two of the non RCTs were prospective studies and six were retrospective comparative studies. Seven non RCTs were non comparative studies.

Propofol-based sedation (six RCTs): In all cases of propofol sedation, the incidence of major respiratory complications was 0.3%. Minor respiratory events occurred more frequently (up to 24% in one study), particularly in very young children. One RCT that compared propofol with general anaesthesia found that propofol provided an equivalent alternative to general anaesthesia. One RCT found that the addition of fentanyl or midazolam to propofol significantly

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lowered the propofol dose required, with no increase in adverse events. One RCT found that propofol was associated with significantly higher levels of effectiveness and patient comfort, with fewer adverse events when compared with midazolam and meperidine. One RCT found that ketamine premedication and propofol were significantly more effective in reducing propofol infusion pain than lidocaine-propofol mixture without premedication.

**Opioid and benzodiazepine-based sedation** (three RCTs): In all of the opioid plus benzodiazepine-based regimens, the incidence of major respiratory complications was 0.2%. One RCT found that use of meperidine and midazolam compared with propofol, with or without premedication midazolam, was associated with significantly higher need for supplemental oxygen, equally high procedural success rate, but it took a significantly longer time to achieve adequate sedation, mean procedure time and recovery time. One RCT reported that fentanyl plus midazolam and meperidine plus midazolam were equally safe and effective. One RCT found that intravenous meperidine plus midazolam and intranasal midazolam plus intravenous meperidine were equally safe, without major adverse events, but children receiving intranasal midazolam premedication had less intense negative behaviour than other groups.

**Midazolam alone** (one RCT): One RCT reported procedural success rates of approximately 100% with oral and intravenous midazolam but insufficient data on effectiveness. There were no major adverse events.

**Premedication** (four RCTs): Two RCTs found that premedication with midazolam prior to a propofol or opioid-based sedation regimen significantly improved the ease and comfort of both intravenous catheter placement and separating the child from the parents, and increased the level of patient comfort. One RCT found that intranasal midazolam premedication significantly reduced the intensity of negative behaviours, but not the total incidence of these behaviours. One RCT that compared atropine premedication with placebo in children sedated with other regimens had limited data to assess outcomes.

Details of the findings of non RCTs were reported in the paper.

**Authors’ conclusions**
Propofol-based therapy was the most effective regimen for procedural sedation during gastrointestinal endoscopy in children. The addition of midazolam, fentanyl or remifentanil to propofol may increase the effectiveness, without creating more adverse events.

**CRD commentary**
The review addressed a clear research question, supported by appropriate but broad inclusion criteria that included non randomised studies. A limited number of relevant databases were searched for studies, along efforts to find studies in reference lists, but no specific attempts were made to find unpublished studies, so it was possible that some studies could have been missed. Selection of studies was undertaken by two reviewers, but the authors did not state how many reviewers assessed studies for quality or extracted data for the review, so reviewer error and bias could not be ruled out.

The authors did not report whether a valid tool was used for quality assessment, but incomplete details on the power, randomisation methods and blinding were reported for some RCTs. The studies were synthesized in narrative format according to broad categories of type of sedation regimen. However, due to the different outcome measures used in the studies and limited numbers of studies that assessed some therapies, solid conclusions on the comparative effectiveness and safety of sedation regimens was not possible.

Given the potential for bias in the review process, limitations in quality assessments, and variation in study outcomes, the authors’ conclusions may not be reliable.

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

**Practice:** The authors stated that there was considerable risk that deep sedation with propofol may result in an unconscious state for a limited period of time; parents and children should be warned that this may happen.

**Research:** The authors suggested that well-designed procedure-specific large RCTs comparing validated outcome measures on effectiveness and safety were needed but may not be ethically justifiable.

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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.