Greater incidence of emergence agitation in children after sevoflurane anesthesia as compared with halothane: a meta-analysis of randomized controlled trials

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CRD summary
This review assessed the incidence of emergence agitation in children anaesthetised with either sevoflurane or halothane. The authors concluded that sevoflurane exhibited a significantly greater incidence of emergence agitation. The authors’ conclusions from this well-conducted review reflected the evidence presented and were likely to be reliable.

Authors' objectives
To compare the incidence of emergence agitation in children anaesthetised with either sevoflurane or halothane.

Searching
MEDLINE, EMBASE, American College of Physicians Journal Club database, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials and DARE were searched to April 2007. Search terms were reported. The reference lists of all included papers were manually searched to identify additional articles. The search was restricted to English-language studies.

Study selection
Randomised controlled trials (RCTs) that compared the incidence of emergence agitation in children less than 12 years anaesthetised with sevoflurane versus halothane were eligible for inclusion. Studies involving neurologically impaired patients were excluded. Many studies included premedication/analgesics and some included regional block. Included studies were in children aged three months to 12 years of age undergoing various types of minor surgical or diagnostic procedures. The primary outcome was the incidence of emergence agitation.

Two reviewers independently selected studies for inclusion in the review. Any disagreements were resolved by consensus.

Assessment of study quality
Two independent reviewers assessed the studies for quality based on: randomisation; standardised anesthesia protocol; blinding for outcomes measurement; comparability; withdrawals; and definition of emergence agitation. The maximum quality score was 6. Disagreements were resolved through consensus.

Data extraction
Data were extracted in order to calculate odds ratios (ORs), with 95% confidence intervals (CIs) calculated for dichotomous data. Authors were contacted for missing data.

Two reviewers independently performed the data extraction and any disagreements were resolved by consensus.

Methods of synthesis
The studies were combined using the Mantel-Haenszel model to calculate an OR with 95% CI. The fixed-effects model was used in the absence of heterogeneity. Heterogeneity was assessed using the $X^2$ ($p<0.10$) and $I^2$ tests (with a 50% threshold). Subgroup analyses were undertaken for: patients younger than seven years of age; study protocols including routine premedication with benzodiazepines; patients anaesthetised for myringotomy insertion; and patients anaesthetised for minor inguinal or urologic surgery. Sensitivity analysis was undertaken for studies with a quality rating >4. Publication bias was assessed by visual inspection of funnel plots and by using Egger's test.

Results of the review
Twenty-three studies were included (n=1,252 sevoflurane and n=1,111 halothane), most of which were of high quality
(median score 5, range 2-6). There was no significant heterogeneity between studies and no evidence of publication bias.

The pooled OR (23 studies) of emergence agitation with sevoflurane was 2.21 (95% CI: 1.77, 2.77, p<0.0001), indicating that sevoflurane anaesthesia more often resulted in emergence agitation than halothane.

Sensitivity analysis using only high-quality studies (14 studies) yielded an OR of emergence agitation with sevoflurane of 1.82 (95% CI: 1.37, 2.41, p<0.0001).

Subgroup analyses for patients younger than seven years of age (11 studies) gave an OR of 1.88 (95% CI: 1.39, 2.54, p=0.0001). For those where the study protocol included routine premedication (12 studies) the OR was 1.77 (95% CI: 1.26, 2.47, p=0.0009). For myringotomy insertion studies (six studies) the OR was 1.79 (95% CI: 1.26, 2.53, p=0.001). For those with pain-treated inguinal surgery (five studies) the OR was 3.20 (95% CI: 1.65, 6.22, p=0.0006).

Authors’ conclusions
Children anaesthetised with sevoflurane exhibited a greater incidence of emergence agitation than those anaesthetised with halothane.

CRD commentary
The review addressed a clear question and consulted a wide range of sources for studies with clear inclusion criteria. The literature search was restricted to publications in English and there was no apparent search for unpublished studies, so some studies may have been missed. Both publication and language bias could have been present, as acknowledged by the authors, but a formal assessment of publication bias did not detect its presence. Appropriate methods were used to minimise reviewer error and bias during the review process, which was undertaken in duplicate. Only RCTs were included the majority of which were of high methodological quality. Suitable methods were used for the meta-analysis. Heterogeneity was assessed and none was found. The review was well conducted and clearly reported. Both sensitivity and subgroup analyses were conducted, all of which were in accordance with the finding for all studies combined. The authors’ conclusions reflected the evidence presented and were likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that paediatric anesthesiologists should consider methods to reduce the risks of emergence agitation after sevoflurane anesthesia.

Research: The authors did not state any implications for research.

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