A meta-analysis of nausea and vomiting following maintenance of anaesthesia with propofol or inhalational agents

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Authors' objectives
To investigate the incidence of post-operative nausea and vomiting following maintenance of anaesthesia with propofol, compared with inhalational agents.

Searching
The MEDLEY database, which contains published literature on Zeneca's pharmaceutical products, was searched. Propofol was used as a major descriptor with the subheadings 'induction' or 'maintenance'; or with 'inhalational anaesthetics' as a major descriptor, with the subheadings 'induction' or 'maintenance' together with 'comparison', 'nausea' and 'vomiting'. Studies reported in any language were considered.

Study selection
Study designs of evaluations included in the review
The included studies were prospective randomised controlled trials (RCTs) of the maintenance of anaesthesia with propofol or an inhalational agent, for which results for nausea, vomiting or 'nausea and vomiting' were available. Duplicates were excluded.

Specific interventions included in the review
The interventions included the following agents used in anaesthetic regimes:

- maintenance of anaesthesia with propofol and inhalational agents such as isoflurane, desflurane, enflurane, halothane and sevoflurane;
- induction agents such as propofol, etomidate, methohexitone, thiopentone, and sufentanil analgesia including opiate narcotics;
- and nitrous oxide.

Some comparator groups used propofol as an induction agent.

Participants included in the review
The participants included adults and children undergoing the following types of surgery under general anaesthesia:
- arthroscopy or minor orthopaedic; breast; eye; facial, oral or dental; ear, nose and throat; gynaecological laparoscopy; other gynaecological; squint; and other or unspecified surgery.

Outcomes assessed in the review
The outcomes assessed were nausea, vomiting, and nausea and vomiting combined.

How were decisions on the relevance of primary studies made?
The publications were examined individually by two independent authors.

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

Data extraction
The following data were extracted by two authors, independently of Zeneca: induction agent; maintenance agent;
analgesia; presence or absence of nitrous oxide; age (child or adult); type of surgery; period of assessment of post-operative nausea and vomiting; and the number of patients with nausea, vomiting, or nausea and vomiting. In studies with more than 2 treatment arms, the two most appropriately-matched treatment arms were selected for comparison. The log odds ratios (ORs) were calculated for each data set, and for the subsets of the vomiting data set.

Methods of synthesis
How were the studies combined?
The common OR was estimated by combining the log ORs using the fixed-effect and random-effects approaches described by Whitehead and Whitehead (see Other Publications of Related Interest). The number-needed-to-treat (NNT) was calculated by performing an additional meta-analysis using the probability difference approach, which employs a random-effects model. The fail-safe N was also calculated.

How were differences between studies investigated?
Heterogeneity was assessed statistically. In the case of significant heterogeneity, the influence of the following covariates was evaluated: surgery type, comparator anaesthetic, observation period, opiate narcotic drug usage, and the patient's age.

Results of the review
Seventy RCTs recorded vomiting (4,074 patients), 61 RCTs recorded nausea (3,516 patients), and 17 RCTs recorded nausea and vomiting (742 patients).

The random-effects model produced only marginally wider confidence limits than the fixed-effect model, with similar mean OR estimates. Only the results from the fixed-effect models were reported. It was not possible to subsequently determine the distribution across time of different patients' post-operative nausea and vomiting, due to insufficient clarity in the reporting of the results. For studies reporting more than one time interval, only the first was included in the analysis.

The OR observations for induction and maintenance with propofol, compared with other agents, were as follows for the defined subsets.

Vomiting data set.
Full data set: the OR was 0.267 (95% confidence interval, CI: 0.220, 0.325, P<0.0001), and the heterogeneity P was 0.045. Box plots suggested that all the comparator anaesthetics produced similar ORs in favour of propofol. Surgery type, opiate narcotic use, patient's age and nitrous oxide did not appear to influence the OR. The NNT was 7.1 (95% CI: 5.6, 9.7) and the fail-safe N was 3,090 trials.

Full data set, excluding the 0 to 24 hour follow-up trials (66 RCTs): the OR was 0.240 (95% CI: 0.198, 0.295, P<0.0001) and the heterogeneity P was 0.57.

Adults subset (57 RCTs): the OR was 0.288 (95% CI: 0.232, 0.357, P<0.0001) and the heterogeneity P was 0.16.

Children (13 studies): the OR was 0.174 (95% CI: 0.104, 0.289, P<0.0001) and the heterogeneity P was 0.06.

Comparator of isoflurane as maintenance (42 RCTs): the OR was 0.267 (95% CI: 0.205, 0.347, P<0.0001) and the heterogeneity P was 0.12.

Comparator of isoflurane as maintenance and propofol as induction (16 RCTs): the OR was 0.391 (95% CI: 0.247, 0.621, P<0.0001) and the heterogeneity P was 0.01.

Comparator of desflurane or sevoflurane as maintenance (6 RCTs): the OR was 0.430 (95% CI: 0.244, 0.757, P=0.003) and the heterogeneity P was 0.17.

Opiate narcotic (45 RCTs): the OR was 0.275 (95% CI: 0.218, 0.348, P<0.0001) and the heterogeneity P was 0.09.
Nitrous oxide (51 RCTs): the OR was 0.250 (95% CI: 0.202, 0.309, P<0.0001) and the heterogeneity P was 0.12.

Nausea data set.

The common OR was 0.377 (95% CI: 0.316, 0.450, P<0.0001) and the heterogeneity P was 0.02. The NNT was 8.1 (95% CI: 6.3, 11.1) and the fail-safe N was 1,804 trials.

Nausea and vomiting data set.

The common OR was 0.374 (95% CI: 0.262, 0.535) and the heterogeneity P was 0.44. The NNT was 6.6 (95% CI: 4.6, 11.9) and the fail-safe N was 112 trials.

**Authors' conclusions**
Patients who received maintenance of anaesthesia with propofol had a significantly lower incidence of post-operative nausea and vomiting in comparison with inhalational agents. This lower incidence was regardless of induction agent, the choice of inhalational agent, the presence or absence of nitrous oxide, patient's age, or use of opiate.

**CRD commentary**
This clearly written and presented review included a statistical assessment of the heterogeneity among studies; heterogeneity was also investigated by considering several potential covariates. Although the authors only used the database provided by a pharmaceutical company, efforts were made to minimise bias in selecting the studies for inclusion, and also in extracting the data. Studies reported in seven languages were identified. The methods used to select the studies and extract the data were described.

The authors assert that the database used was comprehensive, but it is not possible to comment on the probability any relevant studies being omitted. It was unclear whether the inclusion criteria were defined prospectively or retrospectively. The validity of the primary studies was not assessed. Information on the included studies was limited. Two of the authors were employees of Zeneca.

The authors' conclusions would have been strengthened by including an assessment of the validity of the primary studies.

**Implications of the review for practice and research**
The authors did not state any implications for clinical practice or research.

**Bibliographic details**

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**Other publications of related interest**

**Indexing Status**
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**MeSH**
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Incidence; Isoflurane /adverse effects /analog & derivatives; Methyl Ethers /adverse effects; Narcotics /adverse effects; Nausea /chemically induced; Nitrous Oxide /adverse effects; Odds Ratio; Postoperative Complications /chemically induced; Propofol /adverse effects; Prospective Studies; Randomized Controlled Trials as Topic; Risk Factors; Vomiting /chemically induced

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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.