Omission of nitrous oxide during anesthesia reduces the incidence of postoperative nausea and vomiting: a meta-analysis

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Authors' objectives
To perform a meta-analysis in order to determine the impact of nitrous oxide on post-operative nausea and vomiting (PONV).

Searching
MEDLINE was searched from January 1966 to December 1994 using the following terms: 'anesthetic', 'gases', 'nitrous oxide', 'postoperative complications', 'nausea' and 'vomiting'. Additional articles were obtained by a manual search of cross-references from original articles, review articles, correspondence, and abstracts. Only English language articles were included. The search was repeated and no further articles were identified.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were included.

Specific interventions included in the review
Anaesthetic agents: nitrous oxide, ketamine, fentanyl, nitrogen, enflurane, morphine, isoflurane, sufentanil, propofol and halothane,

Participants included in the review
Adults and children undergoing a variety of surgical procedures were included.

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

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not report the criteria used to assess validity, or how the validity assessment was performed.

Data extraction
The data were abstracted independently by two of the authors. No differences in the data abstracted were observed.

Methods of synthesis
How were the studies combined?
The odds ratio (OR) of individual trials, pooled ORs, and 95% confidence intervals (CIs) were calculated using a fixed-effect model (see Other Publications of Related Interest no.1). The relative risk was obtained from the pooled ORs, and the risk reduction was calculated.

How were differences between studies investigated?
A chi-squared test of heterogeneity was calculated. Subgroup analysis was carried out on the following groups:

- studies confined to adult women;
paediatric patients;

isoflurane or enflurane anaesthetics;

intravenous anaesthesia, with nitrous oxide being used in the nitrous oxide group and no other anaesthetic gas or vapour being used in the comparison group;

studies performed exclusively on patients having laparoscopic surgery;

studies on patients having intra-abdominal surgery; and

studies performed on adult patients having dental, general surgical, neurosurgical and miscellaneous procedures.

**Results of the review**

Twenty-six RCTs (n=2,756) were included. These were reported in 24 articles.

The overall pooled OR was 0.63 (95% CI: 0.53, 0.75, p<0.0001), and the reduction of the odds of PONV was 37 plus or minus 7% in the non-nitrous oxide group. This implies that the omission of nitrous oxide significantly reduces PONV.

The test for heterogeneity was negative.

Subgroup analysis revealed the greatest beneficial effect of omission of nitrous oxide was to be observed in female patients.

**Authors' conclusions**

The omission of nitrous oxide reduced the odds of PONV by 37%, a reduction in risk of 28%. Further studies and RCTs are needed to: elucidate the emetogenic mechanism of nitrous oxide; determine prospectively the subgroups that would have the greatest clinical benefit from omission of nitrous oxide; and determine the incidence of adverse outcomes (such as awareness) after omission of nitrous oxide during general anaesthesia.

**CRD commentary**

It may be helpful to note that the overall incidence of PONV was 32.4 and 25.5% in the nitrous oxide and non-nitrous oxide groups, respectively. The method the authors chose to report in their conclusions may be interpreted incorrectly to overestimate the associations between nitrous oxide and post-operative emesis. The review may suffer from publication bias as no attempt was made to locate unpublished literature, although this issue is addressed by the authors in their discussion. Limiting the search to English language articles only may also introduce bias. The review presented clear inclusion criteria, but no details of how these criteria were applied were given. Likewise, no information on the validity of the primary studies was presented.

The authors provide a useful discussion on this and other reviews of nitrous oxide and PONV.

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Other publications of related interest

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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.