Omitting antagonism of neuromuscular block. Effect on postoperative nausea and vomiting and risk of residual paralysis: a systematic review

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Authors' objectives
To test the evidence that antagonism of the neuromuscular block at the end of surgery influences the incidence of postoperative nausea and vomiting, and to evaluate the likelihood of harm when antagonism is omitted.

Searching
MEDLINE from 1966, Biological Abstracts from 1966, EMBASE from 1980, and the Cochrane Library (Issue 1, up to March 20 1998), were searched using combinations of the following free text terms: 'nausea', 'vomiting', 'emesis', 'neostigmine', 'prostigmine', 'edrophonium', 'antagonism' and 'neuromuscular block'. The reference lists of retrieved reports and review articles were examined, and locally available anaesthesia journals were handsearched. Studies reported in any language were considered, abstracts were not included, and the authors of the primary studies were contacted where there was ambiguity about the data.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs), which reported dichotomous data on outcomes of interest, were included.

Specific interventions included in the review
Antagonism with different doses of neostigmine (1.5 to 2.5 mg; 60 to 70 microg/kg) or edrophonium (50 microg/kg to 1 mg/kg) combined with different doses of atropine (10 to 20 microg/kg; 0.5 to 1.2 mg) or glycopyrrolate (0.4 to 0.5 mg; 10 microg/kg) was compared with spontaneous recovery (placebo or no treatment) after general anaesthesia. The anaesthetics used were: propofol, nitrous oxide (N2O), fentanyl, thiopental, halothane-N2O, midazolam, isoflurane-N2O, pethidine, methohexital, morphine and atropine. The neuromuscular blocking agents used were: pancuronium, tubocurarine, vecuronium and mivacurium.

Participants included in the review
Adults and children undergoing surgical procedures.

Outcomes assessed in the review
The cumulative incidence of early (0 to 6 hours) and late (0 to 27 hours) nausea and vomiting was presented in the paper as incidence rate and as cumulative prevention (actually, cumulative non-incidence). The adverse event of 'insufficient muscle power on awakening requiring rescue antagonism' was also reported.

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
Each report was assessed on the adequacy of randomisation and blinding, and the description of withdrawals using the 5-point Oxford score of Jadad et al. (see Other Publications of Related Interest). Each retrieved report was read by both authors independently to assess validity, and any differences were resolved by discussion.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.
Methods of synthesis
How were the studies combined?
A random-effects model was used to calculate the relative risk of omitting antagonism with respect to anti-emetic effects. The numbers-needed-to-treat were calculated, and the numbers-needed-to-harm were calculated for adverse events.

How were differences between studies investigated?
The authors do not state how differences between the trials were investigated.

Results of the review
Eight RCTs (1,134 participants) were included.

Neostigmine: for all outcomes (i.e. nausea or vomiting separately, both early or late), neostigmine had no statistically-significant effect (the 95% confidence interval of the relative risk included 1).

Edrophonium: one trial in children showed no effect of edrophonium on early or late vomiting.

Adverse events: two trials reported clinically relevant (author-defined) muscle weakness in the immediate post-operative period in 3 of the 90 patients who received placebo but in none of the 90 patients who received edrophonium or neostigmine; however, the effect was not statistically significant.

Authors’ conclusions
Omitting neostigmine may have a clinically relevant anti-emetic effect when high doses are used. Omitting antagonism, however, introduces a non-negligent risk of residual paralysis even with short-acting neuromuscular blocking agents.

CRD commentary
This was a well-presented review with a clearly defined research question and a comprehensive literature search. Unpublished data were not sought and the handsearched journals were not specified. The inclusion criteria were clearly stated and the validity assessment was described. Details of the patients included in the studies, such as age and gender, were not reported. The presentation of the results was complete, although there was some confusion over prevention as opposed to non-incidence of outcomes. In the meta-analysis, the authors did not report any weighting of the studies. There was insufficient evidence to fully support the authors’ conclusions at this stage.

Implications of the review for practice and research
The authors state that large RCTs are needed to test the evidence that neostigmine has an impact on post-operative nausea and vomiting, and that this effect is dose-dependent. They suggest that until the effect of anticholinesterase drugs on these symptoms can be based on strong evidence, the drugs should be adequately controlled and reported in RCTs.

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