

Early postoperative vomiting and volatile anaesthetics or nitrous oxide

Editor—The article by Apfel and colleagues¹ on volatile anaesthetics being the main cause of early postoperative vomiting is interesting. They separate out the effect of nitrous oxide and consider volatile anaesthetics to be the emetogenic factor. Have they considered the combined synergistic effect of nitrous oxide and volatile anaesthetics as the cause of postoperative nausea and vomiting? Furthermore, propofol may attenuate the effect of the nitrous oxide if given before the inhalational aspects.

Buffington² has noted a 3.5-fold greater incidence of vomiting in patients given isoflurane with nitrous oxide than in patients given isoflurane only. Several other studies were to follow; Apfel and colleagues do not cite Tramer's³ meta-analysis, where omitting nitrous oxide significantly reduced postoperative vomiting compared with a nitrous oxide regimen.

The authors also used succinylcholine. What about the muscarinic effects of this drug, with respect to secretions and opening of sphincters, on nausea and vomiting in susceptible patients? Neither this study, nor any other study on the subject, mentions the blood pressure variations during induction and maintenance of anaesthesia, which do effect the incidence of nausea and vomiting. I have seen several North American colleagues giving ephedrine 50 mg i.m. or subcutaneously to avoid hypotension and subsequent nausea and vomiting in day-case patients.

If nitrous oxide is used mainly for economic reasons, let us, for the patients' sake, make the anaesthetic comfortable.⁴

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Editor—Thank you for the opportunity to reply to Dr Verheecke. In our study, all patients received nitrous oxide, irrespective of whether anaesthesia was maintained with volatile anaesthetics or propofol.¹ The dose–response relationship between volatile anaesthetics and postoperative nausea and vomiting (PONV) is indeed strongly suggestive that volatile anaesthetics are emetogenic. At the same time, the argument from Dr Verheecke that this could be attributable to a combined synergistic effect of volatile anaesthetics *in conjunction with* nitrous oxide is—at least theoretically—correct.

Divatia and colleagues⁵ demonstrated a relatively limited overall relative risk reduction (rRR) of 28% when air is used instead of nitrous oxide. In contrast to the paper from Tramer and colleagues³ the meta-analysis from Divatia and colleagues also provided some interesting subgroup analyses on the effect in females of certain surgical procedures etc. (see Table 2 of reference 5). Moreover, one subgroup analysis demonstrated that the rRR was 26% when isoflurane or enflurane was used, which is very similar to the average result. It is therefore unlikely that it is the combination of volatile anaesthetics *and* nitrous oxide which causes PONV.

The odds ratio of 3.5 reported by Buffington and colleagues² is not supported by the point estimates from both the meta-analyses; the relative risk for PONV when nitrous oxide is used is more likely to be in the range of 1.4 ($1/(1-0.28)=1.39$). The adjusted odds ratio for volatile anaesthetics in our study was in the range of 3, and thus considerably higher. More importantly, the analysis of the data revealed that the difference was mainly attributable to the difference in the first 2 h after operation, with an odds ratio of more than 10. After this time, volatile anaesthetics had no impact on PONV. As described in the paper, one reason for such a strong effect of volatile anaesthetics may be that very small doses of opioids were given and higher doses of inhalation anaesthetics were needed. Thus, these results need further investigation in other centres.

We agree that the muscarinic effects of succinylcholine could—at least theoretically—affect the incidence of PONV in susceptible patients. However, succinylcholine was only given to facilitate intubation. During anaesthesia, vomiting reflexes are suppressed,⁶ and it seems unlikely that the proemetogenic effect of succinylcholine outlasts the duration of anaesthesia. Furthermore, we are not aware of any studies in support of this hypothesis.

In contrast, there is one study which found that patients with PONV had significantly more frequent decreases of >35% in systolic arterial pressure during induction.⁷ However, the degree of blood pressure change did not differ significantly and, in a multivariable analysis of these data, the systolic blood pressure decrease during induction was not an independent predictor of PONV (unpublished analysis based on data from Pusch and colleagues⁷).

To put an end to the discussion of nitrous oxide *vs* air; volatile anaesthetics *vs* propofol; remifentanyl *vs* fentanyl; ondansetron *vs* control; dexamethasone *vs* control; and droperidol *vs* control, as antiemetic strategies, we have now included over 5000 patients in 'An International Multicenter Protocol to Assess the single and combined benefits of antiemetic strategies in a controlled Clinical Trial of factorial design' (IMPACT). The impact of nitrous oxide—and whether this depends on which other aspects are also used, such as propofol, volatile anaesthetics, or antiemetics—will also be considered in the analysis.

Perhaps we should avoid both volatile anaesthetics *and* nitrous oxide (lowering the baseline risk) in the first place? Perhaps this may only be justified in patients at increased risk that can now be identified easily using simplified risk scores?^{8,9} However, in patients at very high risk, lowering the baseline risk may not be sufficient, and we may still need to add one or two antiemetics.

For the sake of our patients, we hope that IMPACT will tell us the answers.

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