



Nitrous oxide and PONV: Small or big problem, or maybe it is dose/response related?

Last post 07 May 2010, 1:03 PM by [Jaime Fernández-Guisasola](#). 1 replies.

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Boris Mraovic

Joined on 27 Apr 2010

[Submissions 1](#)

Nitrous oxide and PONV: Small or big problem, or maybe it is dose/response related?

We read with great interest the article by Fernandez-Guisasola et al in which the authors analysed the association between nitrous oxide and postoperative nausea and vomiting [1]. The study concluded that avoiding nitrous oxide has modest impact in reducing postoperative nausea and vomiting by 18%, although the recent and largest nitrous oxide trial (ENIGMA) found a reduction of 56% [2].

Moreover, the ENIGMA trial patients are not included in this study. Apparently, the ENIGMA trial did not meet the meta-analysis inclusion criteria in terms of the fact that the groups did not differ in the type of surgery, the antiemetic medication or the anaesthetic agents utilised. The authors may have included the patients from the ENIGMA trial after excluding the patients on propofol maintenance (267), and thus used the data from the remaining patients (1788); these patients differed only in the oxygen concentration used.

Furthermore, our study published in 2008 looking at dose/response of nitrous oxide on postoperative nausea and vomiting was not included [3]. Although we had three groups of patients, the group with 70% nitrous oxide and the group with no nitrous oxide may have been included. Our study had more patients in each group, than most of the studies included in the meta-analysis.

Adding the two groups from our study (91 patients) and the patients from the ENIGMA trial (after excluding the patients on propofol maintenance), would give a total number of 1879 patients, which is close to the number of patients (2397) used in the meta-analysis of the articles published from 1994 [1]. Since these two studies found a significantly larger difference than the meta-analysis, adding them together would almost double the number of patients, and possibly decrease the relative risk ratio, the odds ratio, and the number needed to treat found in the meta-analysis. Hence, the conclusion of the meta-analysis may have shown a stronger influence of nitrous oxide on postoperative nausea and vomiting.

Finally, the authors could have explored the influence of different nitrous oxide concentrations on postoperative nausea and vomiting. All volunteers with a MAC of one for nitrous oxide (hyperbaric chamber) had nausea or vomiting [4], and the inspiratory concentrations that are usually used clinically (50 to 70 %) may have had a dose/response effect, as the data from our pilot study suggested [3].

The conclusion of the meta-analysis was that future studies should try and determine those groups of patients in whom the omission of nitrous oxide may be most beneficial. We think that the future studies and/or meta-analyses should answer if nitrous oxide causes an increase in postoperative nausea and vomiting in a dose/response fashion, and in clinically used concentrations.

B Mraovic, T Šimurina

Department of Anesthesiology

Jefferson Medical College
Thomas Jefferson University
111 South 11th Street Suite G8280
Philadelphia, PA 19107

Boris.Mraovic@jefferson.edu

1. Fernández-Guisasola J, Gómez-Arnau JI, Cabrera Y, et al. Association between nitrous oxide and the incidence of postoperative nausea and vomiting in adults: a systematic review and meta-analysis. *Anaesthesia* 2010; **65**: 379-87.
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3. Mraovic B, Simurina T, Sonicki Z, et al. The Dose–Response of Nitrous Oxide in Postoperative Nausea in Patients Undergoing Gynecologic Laparoscopic Surgery: A Preliminary Study. *Anesthesia Analgesia* 2008; **107**: 818-23.
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498 in reply to **493**

Jaime Fernández-Guisasola

Joined on 07 May 2010

[Submissions 2](#)

Re: Nitrous oxide and PONV: Small or big problem, or maybe it is dose/response related?

We appreciate the competent comments of Dr Mraovic and Dr Simurina about our study [1]. The question of whether nitrous oxide should be used or omitted clearly depends upon several factors, which in general revolve around the benefits of the drug versus its detrimental effects (which we have shown with a quantitative systematic review that includes postoperative nausea and vomiting, especially in women). The validity of a meta-analysis depends on the quality of the selected trials. In our meta-analysis, we included prospective clinical trials that investigated nausea and vomiting in groups that were randomised to nitrous oxide. We stipulated that the two groups did not differ in terms of the type of surgery, the antiemetic medication or the anaesthetic agents utilised. This is the reason for not including in our review the ENIGMA trial [2]: in this study all anaesthetic interventions, apart from nitrous oxide and oxygen administration, were made at the discretion of the anaesthetist (anaesthetic maintenance, opioid dose, antiemetic use and monitoring) and were not randomized; moreover, there were significant differences in some types of surgery between the nitrous oxide based and the nitrous oxide free anaesthesia.

We could have included Dr Mraovic et al's study [3] in our meta-analysis. In any case, the inclusion in the analysis of the group with 70% nitrous oxide and the group with no nitrous oxide data does not change the global results: pooled relative risk 0.79, 95% confidence interval, CI, 0.70–0.89, $p = 0.0001$.

It is not entirely clear, as Dr Mraovic and Dr Simurina postulate, if limiting nitrous oxide to a lower clinical concentration decreases the risk of postoperative nausea and vomiting (many confounding factors may be

involved: for example, different oxygen concentrations) [4]. In fact, in their study [3] there were no significant differences between 50% nitrous oxide and oxygen/air groups or between 50% versus 70% groups in female sex patients, in whom nitrous oxide would have had maximum emetic effect. Nonetheless, we did not explore the influence of different nitrous oxide concentrations because it was not the purpose of our study.

J Fernández-Guisasola

Anaesthesia Department, Hospital Rúber, Madrid, Spain

jfguisasola@telefonica.net

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