



Nitrous oxide and length of stay in the postanesthesia care unit

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To the Editor,

We read with great interest the article by Obeidat *et al.*,¹ who retrospectively analyzed 148,284 patients and found that use of nitrous oxide (N₂O) at any time during anesthesia was dose-dependently associated with a shorter postanesthesia care unit (PACU) length-of-stay (LOS). High-dose N₂O significantly decreased patients' PACU LOS by 9.1 min (95% confidence interval, -10.5 to -7.7), and the effect was most pronounced (38.9 min) after complex surgery with intraoperative antiemetic therapy.¹ We think this is an important finding—that simple use of N₂O could make a significant clinical difference.

Groups were created by dividing N₂O concentration with total duration of anesthesia. The high-dose N₂O concentration in this study was 39% [interquartile range (IQR), 30–47] and the low-dose concentration was 2.8% [IQR, 0.4–6.0].¹ These numbers, especially the low-dose concentrations of N₂O, do not make much sense to anesthesia providers who usually utilize 50–70% N₂O

and rarely 25–30%. Indeed, in our study,² which was the first to specifically show the dose-response of N₂O on postoperative nausea and vomiting (PONV) after inhalational anesthesia, we used 50% and 70% of inhaled N₂O but not lower doses, since they are rarely used in operating rooms.

The duration of N₂O administration was not provided by Obeidat *et al.*¹ who suggested that administration of high-dose N₂O for only a brief period at the end of surgery resulted in an overall lower median dose. Therefore, the authors¹ could not recommend how to administer N₂O. But timing, duration, and concentration of N₂O administration is of crucial importance. When N₂O is administered throughout the anesthetic, it increases PONV in a dose-dependent fashion,² but if 70% N₂O is administered for only 30 min, it does not increase the risk of PONV even without PONV prophylaxis, as we found in the *ISONATE* study³ when 70% N₂O was administered at a mean (standard deviation [SD]) of 27.1 (10.1) min at the end of isoflurane anesthesia.

The analgesic effects of N₂O could help reduce pain in the PACU. Unfortunately, tolerance of N₂O analgesia develops quickly. Ruprecht *et al.*⁴ showed in volunteers that received three hours of 60–80% N₂O that significant antinociception developed within two minutes of exposure to N₂O. The maximal analgesic effect was observed between 20 and 30 min of exposure but the analgesic effect gradually decreased and was absent in all volunteers within 150 min.⁴ This effect was clearly shown in our two studies with N₂O.^{2,3} When we used 0%, 50%, and 70% N₂O during anesthesia with a duration > 70 min, there was no difference in mean (SD) 100-mm visual analogue scale (VAS) pain scores in first two hours postoperatively (21.6 [13.0] vs 25.4 [12.9] vs 23.9 [15.1] mm; *P* = 0.30) nor in

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postoperative meperidine consumption (6.5 [22.0] vs 7.1 [16.4] vs 10.1 [19.6] mg; $P = 0.27$).² In contrast, when 70% N₂O was used for about 30 min at the end of two hours of anesthesia, VAS pain scores were significantly lower in patients who received N₂O (38.2 [14.6] vs 47.4 [15.2] mm; $P = 0.008$).³ Moreover, 18% of N₂O patients ($n = 7/40$) were never administered any postoperative opioids but all patients without N₂O ($n = 42$) received opioids postoperatively ($P = 0.005$).³ This suggests that N₂O's analgesic effects might not be dose-dependent and could last even after N₂O administration is stopped.

Using 70% N₂O for 30 min at the end of surgery maximizes benefit of the analgesic effect of perioperative N₂O while eliminating its PONV side effects even without PONV prophylaxis. Combination of these two beneficial effects of the *ISONATE* technique³ should help reduce LOS in the PACU. A prospective randomized controlled study looking specifically at PACU LOS in longer and more complex surgeries would give the definitive answer.

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