

# Anesthesia for Laparoscopic Cholecystectomy

## Is Nitrous Oxide Contraindicated?

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Since it has been suggested that the use of nitrous oxide ( $N_2O$ ) may contribute to bowel distention, we evaluated the effects of  $N_2O$  on operating conditions during laparoscopic cholecystectomy in 50 healthy patients using a double-blind protocol design. All patients received the same preanesthetic medication (midazolam, 2 mg intravenously) and induction of anesthesia consisted of intravenously administered fentanyl  $1.5 \mu g \cdot kg^{-1}$ , thiopental 4–6 mg  $\cdot kg^{-1}$ , and a nondepolarizing muscle relaxant. For maintenance of anesthesia, patients were randomly assigned to one of two treatment groups: group 1 ( $n = 26$ ) received isoflurane with 70%  $N_2O$  in oxygen ( $O_2$ ), whereas group 2 ( $n = 24$ ) received isoflurane in an air/ $O_2$  mixture. The surgeon (blinded to the anesthetic technique) estimated the degree of technical difficulty before beginning the operation using a five-point scale. At 15-min intervals throughout the operation, the surgeon was asked to evaluate both "overall operating conditions" and degree of "bowel distension" using independent five-point scales. At the end of the operation, the surgeon was asked whether or not  $N_2O$  had been used as part of the anesthetic technique. There were no significant intraoperative differences between the two groups with respect to operating conditions or bowel distension. More importantly, there was no time-related change in either variable during the course of the operation. Finally, the incidence of postoperative nausea and vomiting was similar in both treatment groups. The surgeon was able to correctly determine that  $N_2O$  had been administered only 44% of the time. Thus,  $N_2O$  had no clinically apparent deleterious effects during laparoscopic cholecystectomy. (Key words: Anesthesia; laparoscopic cholecystectomy. Anesthetics, volatile: nitrous oxide. Postoperative complications: nausea; vomiting.)

CONCERNS regarding the ability of nitrous oxide ( $N_2O$ ) to expand bowel gas during laparoscopic cholecystectomy have led to the use of anesthetic techniques that avoid this popular anesthetic adjuvant.<sup>1</sup> Although laparoscopic cholecystectomy has recently become a widely used surgical technique, the question of whether or not  $N_2O$  adversely affects the operating conditions or the incidence of postoperative side effects remains unanswered.

$N_2O$  is a commonly used adjuvant during general anes-

thesia because its physical properties allow for a rapid uptake and elimination.  $N_2O$  is less soluble than the other currently available volatile anesthetics, but it is about 30 times more soluble than nitrogen. Thus, a closed air-containing space can accumulate  $N_2O$  more rapidly than nitrogen can be eliminated, resulting in expansion of the space. When air was introduced into the bowel, Eger and Saidman<sup>2</sup> demonstrated that breathing  $N_2O$  for 4 h resulted in an increase as great as 200% in the intestinal lumen. Lindgren and Scheinin<sup>3</sup> also reported that the surgeon's evaluation of bowel distension was significantly different when  $N_2O$  (*vs.* air) was used during colonic surgery. These investigators suggested that  $N_2O$ -induced bowel distension impaired operating conditions and contributed to prolonging the period of postoperative hospitalization.

Therefore, we designed a randomized, double-blind study to evaluate the effect of  $N_2O$  on operating conditions and emetic sequelae following elective laparoscopic cholecystectomy.

### Materials and Methods

Fifty consenting, ASA physical status 1 or 2 patients undergoing elective laparoscopic cholecystectomy were enrolled in a study approved by the Human Studies Committee at Washington University. Morbidly obese patients, as well as those with clinically significant major organ system dysfunction, were excluded.

All patients received midazolam 2 mg intravenously (iv) for preanesthetic medication in the preoperative holding area, and anesthesia was induced intravenously with fentanyl  $1.5 \mu g \cdot kg^{-1}$ , thiopental 4–6 mg  $\cdot kg^{-1}$ , and a nondepolarizing muscle relaxant (*e.g.*, vecuronium, 0.1 mg  $\cdot kg^{-1}$ ). The patients were randomly assigned to one of two treatment groups for maintenance of anesthesia: group 1 received isoflurane with 70%  $N_2O$  in  $O_2$ , and group 2 received isoflurane in an air/ $O_2$  mixture. Although the initial isoflurane concentration (1%) was identical in both groups, the inspired concentration was varied subsequently as necessary to maintain hemodynamic stability during the operation. Small incremental bolus doses of the nondepolarizing relaxant (*e.g.*, vecuronium 0.5–1.0 mg iv) were administered as needed to maintain adequate muscle relaxation. Abdominal insufflation for the

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laparoscopic procedure was accomplished with carbon dioxide. At the end of surgery, the inhaled anesthetic agents were discontinued and neostigmine 40–70  $\mu\text{g} \cdot \text{kg}^{-1}$  iv and glycopyrrolate 8–14  $\mu\text{g} \cdot \text{kg}^{-1}$  iv were administered to reverse residual neuromuscular blockade.

Prior to the start of the operation, the surgeon (NS), who was blinded to the anesthetic technique (the flow meters on the anesthesia machine were covered), was asked to estimate the degree of difficulty he anticipated in performing the procedure using a five-point scale: 1 = extremely difficult, 2 = difficult, 3 = average, 4 = easy, and 5 = extremely easy. During the operation, the surgeon also was asked to evaluate both "overall operating conditions" (where 1 = extremely poor conditions, 2 = poor conditions, 3 = average conditions, 4 = good conditions and 5 = very good conditions) and the degree of "bowel distension" (where 1 = marked distension, 2 = distended, 3 = average, 4 = less than average, and 5 = minimal distension) at 15-min intervals. Any technical difficulties that the operating surgeon attributed to bowel distension were noted. The surgeon was given the option of asking for  $\text{N}_2\text{O}$  to be discontinued at any time if he thought that it was adversely affecting the operating conditions. At the conclusion of the operation, the surgeon was asked to indicate whether or not he believed that  $\text{N}_2\text{O}$  had been administered.

Patients completed visual analogue scales for nausea (0 = none to 100 = severe) prior to the operation and again at the time of discharge from the postanesthesia care unit (PACU). Complaints of nausea and episodes of vomiting (or retching) were recorded by the PACU nurse, who was blinded as to the anesthetic treatment group. Standard PACU discharge criteria required that patients be awake and alert, have stable vital signs for a minimum of 60 min (with a room-air hemoglobin  $\text{O}_2$  saturation value > 90%), and be in no acute distress (secondary to pain or nausea/vomiting).

Data were analyzed using: 1) Wilcoxon's rank sum test (Mann-Whitney U test), a nonparametric test to compare median values of the surgeon's evaluation of operating conditions and bowel distention; 2) Student's *t* test; or 3) the chi-square test whenever appropriate, with *P* values

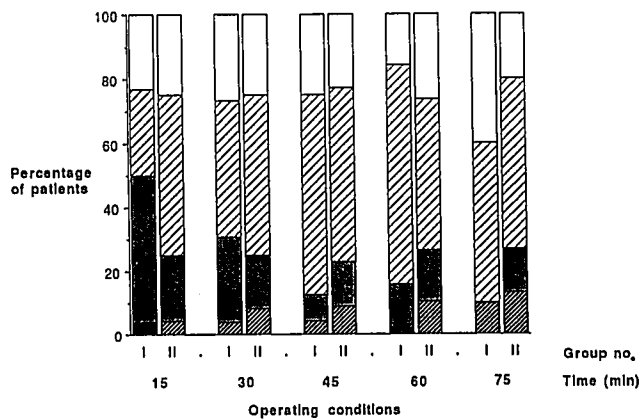


FIG. 1. Operating conditions at 15-min intervals, shown as percentages of the total number of evaluations at each time. Group 1 (I) is the nitrous oxide group; group 2 (II) did not receive nitrous oxide. Solid black bar = very poor conditions; dark hatched bar = poor conditions; dotted bar = average; light hatched bar = good operating conditions; open bar = very good conditions.

< 0.05 considered to be statistically significant. A statistical power analysis was performed to determine the probability of a type II (or  $\beta$ ) error. The power analysis suggested that the number of subjects was adequate to determine with a 95% certainty if a difference in the operating conditions or degree of bowel distention existed between the  $\text{N}_2\text{O}$  (group 1) and air (group 2) treatment groups.

## Results

The two treatment groups were comparable with respect to age, weight, sex distribution, surgeon's preoperative estimate of difficulty, and patients' preoperative visual analogue scale nausea scores (table 1). The duration of surgery (mean value  $\pm$  SD) was also similar in groups 1 and 2 ( $72 \pm 23$  and  $82 \pm 39$  min, respectively). The total vecuronium dose requirements were  $11.5 \pm 3.2$  mg in group 1 and  $12.9 \pm 4.4$  mg in group 2 ( $P = 0.08$ ). The overall surgical conditions and degree of bowel distention were also comparable in the two groups at each time interval during the operation (figs. 1 and 2). Furthermore, there were no significant changes in either of these parameters during the course of the study period. The length of stay in the PACU ( $72 \pm 27$  and  $73 \pm 19$  min), requirement for postoperative antiemetic therapy (35 and 53%), as well as nausea scores at the time of discharge from the PACU ( $25 \pm 27$  and  $17 \pm 22$  mm) were similar in groups 1 and 2, respectively.

Only 44% of the time were the surgeons able to determine correctly whether or not  $\text{N}_2\text{O}$  had been administered. In group 1, 7 of 26 patients were believed to have received  $\text{N}_2\text{O}$ , compared to 9 of 24 patients in group 2. On two occasions, the surgeon requested that the  $\text{N}_2\text{O}$

TABLE 1. Patients' Demographic Characteristics and Preoperative Assessment in the Two Treatment Groups

	Group 1	Group 2
Number	26	24
Age (yr)	$50 \pm 16$	$48 \pm 15$
Weight (kg)	$78 \pm 19$	$76 \pm 17$
Sex (M/F)	6/19	5/20
Median estimate of difficulty (range)	3 (2–4)	3 (2–4)
Nausea score (mm)	$8 \pm 16$	$4 \pm 7$

Numbers or mean values  $\pm$  SD.

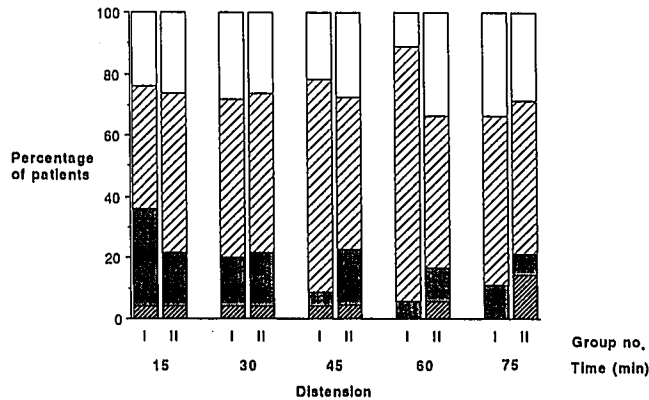


FIG. 2. Bowel distension at 15-min intervals, shown as percentages of the total number of evaluations at each time. Group 1 (I) received nitrous oxide; group 2 (II) did not. Solid black bar = represents marked distension; dark hatched bar = distended; dotted bar = average distension; light hatched bar = less distension than average; and open bar = minimal distension.

be discontinued because of difficulties visualizing the operative field; however, only one of these patients was actually receiving N<sub>2</sub>O. The latter patient was excluded from the subsequent analysis of postoperative symptoms. There was one patient in each group who required an open cholecystectomy because of technical difficulties, and these two patients also were excluded from our analysis.

### Discussion

Although N<sub>2</sub>O possesses many useful pharmacokinetic and pharmacodynamic properties, it remains under scrutiny because of concerns regarding its ability to produce bowel distention during surgery and to increase postoperative emetic sequelae.<sup>4-6</sup> Our data suggest that the surgeon was unable to detect any deterioration in surgical conditions as a result of the adjunctive use of N<sub>2</sub>O. Similarly, the surgeon could not determine whether or not N<sub>2</sub>O had been administered during laparoscopic cholecystectomy procedures. Finally, there was no evidence that N<sub>2</sub>O increased the incidence of postoperative emetic sequelae in this surgical population.

These findings differ from those of Lindgren and Scheinin<sup>3</sup> when they used a similar methodology to evaluate bowel distension during "open" intraabdominal surgery. The most likely explanations for this difference relate to either or both of the following. 1) Lindgren and Scheinin injected 200 ml air through a nasogastric tube at the start of the operation as a "seed volume." The injected air would have been further expanded by the less soluble N<sub>2</sub>O as it diffused into the closed bowel space. 2) N<sub>2</sub>O-induced changes in intestinal volume occur more slowly than changes in other closed spaces. The duration of exposure to N<sub>2</sub>O in our study may not have been long

enough (72 ± 23 min) to allow for significant alterations in bowel gas.

Using data published by Eger and Saidman,<sup>2</sup> we estimate that during the course of a 70-75 min operation, approximately 40% equilibration would occur between end-tidal and bowel N<sub>2</sub>O concentrations. Because our patients were administered 70% N<sub>2</sub>O in O<sub>2</sub>, a N<sub>2</sub>O concentration of ≤ 30% in the bowel would result. This theoretical calculation suggests that the use of 70% N<sub>2</sub>O during a laparoscopic cholecystectomy procedure lasting approximately 75 min would result in only a 40% increase in the volume of bowel gas. Obviously, longer surgical procedures would result in greater equilibration between bowel gas and end-tidal N<sub>2</sub>O, producing a greater increase in bowel volume.

The average intestinal gas content is approximately 100 ml,<sup>7</sup> which, even if it tripled during the laparoscopic cholecystectomy procedure, would probably have little effect on total intestinal volume. However, if large volumes of air are present in the bowel because of air-swallowing or mask-assisted ventilation, or if the operation required a significantly longer period of time, N<sub>2</sub>O might impair operating conditions during laparoscopic surgery. Although the amount of intraoperative muscle relaxant could have influenced the surgical conditions, there was no significant difference between the two treatment groups.

In conclusion, we demonstrated that the use of N<sub>2</sub>O has no clinically significant effect on surgical conditions during laparoscopic cholecystectomy and did not increase the incidence of postoperative emesis.

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