



A LOOK BACK IN TIME

HISTORY

Nitrous oxide was first produced by the English chemist and Presbyterian minister, Joseph Priestley, in 1772 and further investigated by Humphrey Davy in 1800 at the Pneumatic Medical Institution in Bristol. In his book on nitrous oxide, Davy recorded that breathing the gas helped to relieve toothache - from which he was suffering at the time - and suggested: 'it may probably be used with advantage in surgical operations'. But the pain-relieving properties of nitrous oxide were not explored any further until nearly fifty years later. Initially, society was more interested in nitrous oxide as a source of amusement and entertainment. It is for this reason, no doubt, that nitrous oxide was commonly called 'Laughing Gas'. (This term has always seemed rather odd to me, because in my experience, laughter is rarely observed!)

Setting the record straight

Not a Laughing Matter

This article is in response to a challenge put before me to find articles that would reinforce my stance on eliminating nitrous oxide from my general anesthetic practice. I would like to set the record straight from the onset: I am not against the use of nitrous oxide but I feel it should be restricted under certain situations.

I reviewed articles going back to 1987 and found the results equivocal which should not be a surprise to most anesthesia clinicians. In five studies involving over a thousand patients, the various authors (1,2,3,4,5) found no correlation between the use of nitrous oxide and post nausea and vomiting. They did, however, find that the female gender, recent menstruation, younger age patients, history of postoperative nausea, and a history of motion sickness were independent factors that correlated significantly. I found it odd, however, that none of these authors found it unusual that between 30 to 54% of their study populations experienced nausea. It is my opinion that their methodology is questionable. For example had Muir et al(1) not given all their patients a morphine premed would difference in nausea and vomiting in their pediatric group, I personally think that an incidence of 50% is just too high.

I think these authors would be hard pressed validating their results against Hartung's meta-analysis (7). He examined 27 studies published over 25 years which involved a wide variety of patients. In all the studies, nitrous oxide was compared with other agents and the incidence of nausea and vomiting was

determined. I know there are inherent statistical problems with meta-analyses but with his statistical probability set at less than 0.00005 he found that in 24 of 27 studies the incidence of nausea and vomiting associated with nitrous oxide is much higher than would be expected by chance alone. A much stronger meta-analysis came from Divatia and colleagues who examined 37 randomized controlled studies published between 1966 and 1994. Their analysis was set up to determine whether omission of nitrous oxide significantly reduced the odds of postoperative nausea and vomiting (PONV). They found that omission of nitrous oxide reduced the risk for PONV by 28% and not surprisingly the omission of nitrous oxide reduced PONV to the greatest extent in women.

Propofol and Postoperative Nausea

Let me deviate for a moment and discuss, albeit in somewhat a perfunctory manor, the issue of propofol and its effects on the incidence of PONV.

Many clinicians feel that the inclusion of propofol into our anesthesia armamentarium was a great boom to reducing the incidence of PONV, but let me submit for your consideration the findings of Harper et al (9). They conducted a prospective, double-blind, randomized trial involving 77 unpremedicated, ASA grade 1 or 2, nonobese women undergoing gynecologic laparoscopy under general anesthesia with thiopentone, isoflurane, nitrous oxide, fentanyl, and vecuronium.

Forty eight(48) women complained of postoperative nausea in the postanesthesia care unit and were randomized to receive placebo (Intralipid) or IV propofol in a dose of 3, 9, or 27 mg. Posttreatment scores for nausea (0 to 3, none to severe), vomiting, and sedation were recorded by a blinded observer for 90 minutes after treatment. The overall incidence of emesis was similar between the groups (25% to 41%) and the incidence of requests for rescue antiemetics was similar in all groups (25% to 58%). I know I like to believe that propofol as an induction agent helps reduce the incidence of PONV but I think it is the avoidance of pentathal that is the primary reason for the reduction in PONV. The study by Visser et al (10) confirms this and takes it one step further. The purpose of their study was to compare the incidence of nausea and the overall costs of total intravenous (IV) anesthesia with propofol versus isoflurane-nitrous oxide. In their prospective double blind study, they randomized, 2,010 adults undergoing elective surgery under general anesthesia, (1,447 inpatients, 563 outpatients) to receive either total IV anesthesia with propofol and air-oxygen, or isoflurane and 60% nitrous oxide following induction of anesthesia with either propofol or thiopental. Perioperative complications were assessed by a blinded nurse at 24 hours and 72 hrs. Patient demographics were similar in both groups, with a younger mean age in outpatients (38 years versus 45 years). Mean duration of anesthesia was similar in both groups (~120 minutes for inpatients and ~60 minutes for outpatients). All patients received intraoperative opioids. Not surprisingly, the overall incidence of nausea was significantly lower in the propofol group than the isoflurane group for both inpatients (46% versus 61%) and outpatients (29% versus 47%). But here's the kicker: Although antiemetics were required more often with isoflurane/ nitrous oxide than with propofol

(inpatients 36% versus 18%, outpatients 20% versus 18%) and the mean postanesthesia care unit (PACU) stay was longer for both the inpatient and outpatient isoflurane group than in the inpatient and outpatient propofol group (135 minutes versus 115 minutes for inpatients)(160 minutes versus 150 minutes for outpatients,), the mean overall costs were significantly higher in the propofol group. The additional cost per surgical session for propofol compared to isoflurane was \$28.98 for inpatients and \$14.87 for outpatients). So what I carry away from this study is that total IV anesthesia with propofol compared to isoflurane-nitrous oxide results in a reduction in perioperative nausea, but only a slight decrease in recovery times and it does this at an increase in costs. Would the incidence of PONV and the costs associated with its treatment been further reduced, had the researchers avoided nitrous oxide? Another earlier study seems to address this question. To determine whether the use of propofol as an anesthetic for breast surgery may decrease levels of postoperative nausea and vomiting below those found after inhalational anesthesia, a group of researchers from Sweden, randomly assigned ninety otherwise healthy female patients who were undergo breast surgery to one of three anesthetic regimes: general anesthesia with propofol alone, propofol for induction with isoflurane maintenance, or thiopental for induction with isoflurane for maintenance. No nitrous oxide was used. Blinded nurse observers recorded complaints of nausea and vomiting for 24 hours postoperatively. The patients in the propofol-only group received a mean total fentanyl dose of 4 ug/kg intraoperatively for inadequate anesthesia, which was statistically higher than the mean dose of 3 ug/kg needed by the other two groups. There were no differences between the groups in postoperative analgesic requirements nor were there any differences in the incidence of postoperative nausea and

vomiting were observed between the groups, either in the postoperative unit or after discharge to the surgical ward. Approximately 20% of patients in each group had nausea or vomited in the postoperative unit, and approximately 35% experienced nausea or vomiting on the surgical ward. It seems to me that the use of propofol for induction or maintenance of general anesthesia during breast surgery does not significantly affect the incidence or severity of postoperative nausea and vomiting and that the avoidance of nitrous oxide makes for an even playing field. And, in fact, the use of sevoflurane and ondansetron along with avoidance of nitrous oxide is more effective in reducing the incidence of PONV than propofol alone. In a randomized, controlled study(12), 180 female patients undergoing breast surgery assigned to 1 of 3 anesthetic groups: sevoflurane alone (group S), sevoflurane plus ondansetron (group SO), or propofol alone (group P). Anesthesia was maintained with a continuous infusion of propofol in group P and with sevoflurane in groups S and SO. Again, no nitrous oxide was used. In group SO, 8 mg of ondansetron was administered at the end of surgery. All groups received intermittent doses of 1 to 2 mcg/kg of fentanyl as needed. For pain relief, oxycodone was given in the postanesthesia care unit (PACU) and paracetamol on the ward. The incidence of PONV was monitored for the first 2 hours in the PACU and from 2 to 24 hours on the ward. During the 2-hour period in the PACU, the incidence of emesis was very low (0%) in groups S and SO and only 2% in group P. On the other hand, the incidence of nausea was greater in the sevoflurane(S) group(32%) as compared to the SO group(7%) and P group(8%). The playing field was again equalized 2 to 24 hours postoperatively, when the incidence of PONV associated with the P group (33%) approached that of the S group(35%). On the other hand PONV remained significantly lower in the SO group(10%). Thus, for 2 hours in

the PACU, emetic episodes were minimal in all groups, whereas nausea was a significant problem but only in group S which was effectively reduced when ondansetron was given prior to emergence from anesthesia. On the other, propofol's antiemetic effects seemed to disappear after 2 hours, with only ondansetron providing significant prophylaxis against emesis for the entire 24-hour study period.

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