ORIGINAL ARTICLE

The Effect of 50% Nitrous Oxide on Postoperative Nausea-Vomiting in Patients Undergoing Laparoscopic Cholecystectomy

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ABSTRACT

Background: Postoperative nausea and vomiting (PONV) is a common problem and its cause is multifactorial. The relationship between PONV and nitrous oxide is under debate.
Aim: To evaluate the relationship between nitrous oxide and PONV in patients undergoing laparoscopic cholecystectomy.
Methods: We randomly divided 60 female patients, ASA I or II, age 18-60 years and weighing between 50-100 kg, scheduled for elective laparoscopic cholecystectomy into two groups. Anaesthesia was induced in all patients with propofol, nalbuphine and atracurium. Anaesthesia was maintained with sevoflurane, nitrous oxide in oxygen in group I and sevoflurane in oxygen in group II. Perioperatively paracetamol was infused in all patients. The patient's PONV and pain scores were assessed 24 hours postoperatively.
Results: In group I, PONV scores were significantly higher at 1st and 6th hour postoperatively; however, there was no significant difference in group II. However there was no significant difference in PONV and pain scores and the percentage of patients needing antiemetics between two groups. We could not find any correlation between PONV and use of 50% Nitrous oxide.
Conclusion: Our data concludes that 50% nitrous oxide does not increase the incidence or severity of PONV in patients undergoing laparoscopic cholecystectomy.
Keywords: Nitrous oxide, nausea, vomiting, laparoscopic cholecystectomy

INTRODUCTION

Postoperative nausea and vomiting (PONV) has been challenging in laparoscopic cholecystectomy and therapeutic challenge for anesthesiologist, as well as big problem of ambulatory surgery[1,2].

There are many factors enlisted causing PONV. Few factors are well established, while others remain poorly understood. Lot of Studies have conducted to explore factors associated with PONV and to predict which population is at the highest risk for this complication[3,4]. These factors may be related to the patient, the surgical procedure, or the choice of anesthesia[5]. However, one important factor contributing to PONV is the use of nitrous oxide during Generalanesthesia[6]. Several studies investigating relationship between PONV and nitrous oxide in adults have produced conflicting results, some claiming that nitrous oxide increases PONV[7,8] while others were opponent to confirm these findings[6,9]. We conducted prospective, randomized, double-blind study, to evaluate the role of nitrous oxide in incidence PONV was studied in laparoscopic cholecystectomy.

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METHODS

After approval from ethical Committee and patients' written consent, 60 female patients, ASA physical status I or II, aged 18-60 years and weighing between 50-100 kg, undergoing elective laparoscopic cholecystectomy were recruited in study. Patients were allocated randomly into two study groups of 30 patients each. Exclusion criteria was patients with significant cardiac, respiratory, hepatic, renal or hematologic disorders, contraindications or allergic to administration of the study drugs and motion sickness or previous PONV. After preoxygenation, Induction of anaesthesia was done in all patients with Propofol 2 mg/kg IV. Atracurium 0.5mg/kg IV was administered to achieve muscle relaxation prior to tracheal intubation. Anaesthesia was maintained with 2% sevoflurane, 50% nitrous oxide in oxygen in group I and 2% sevoflurane in oxygen in group II. Perioperatively nalbuphine 0.1mg/kg and paracetamol infusion @ 15mg/kg was given in all patients. The sevoflurane concentration was titrated to maintain mean arterial pressure and heart rate within 20% of baseline values. Mechanical ventilation was maintained. Heart rate, non-invasive arterial blood pressure, oxygen saturation and ECG were measured and recorded every five minute during surgery. In both groups, toradol 30 mg IV

was administered 10 minutes before the end of surgery.

The patients were then extubated and transported to the postanaesthetic care unit (PACU). Routine PACU management included recording of vital signs. Oxygen (6 lt/min) was administered on admission and discontinued before discharge to the ward. After the patient arrived in the PACU, a blind investigator observed the patient postoperatively. The patient's PONV and pain scores were assessed at 30 minute, 1^{st} ,2^{nd} ,4^{th} , 6^{th} ,12^{th} , 24^{th}hour postoperatively. PONV scores ranged from 0 to 3 (0: no nausea and vomiting, 1: mild nausea not vomiting and not requiring treatment, 2: moderate nausea, mild vomiting and requiring treatment, 3: severe vomiting). Ondansetron 4 mg IV was administered when the PONV score was greater than 1. The incidence of nausea and vomiting separately during early (0-6 h) and delayed (6-24 h) period and the percentage of patients requiring antiemetic therapy were also recorded. Pain intensity was assessed with 5 point verbal pain scale (0; no pain, 1: mild pain, 2: moderate pain, 3: severe pain, 4: excruciating pain). Nalbuphine 0.05mg/kg IV was administered when the pain score was greater than 1 (until a subsequent pain score was <2).

The χ^2 test with Fisher correction was utilized to analyze differences between groups in demographics and the incidence of PONV. Pain and PONV scores were compared by using repeated measures of ANOVA and student's t-test. $P<0.05$ was considered as significant. All data were recorded as mean ± SD.

RESULTS

There was no significant difference in the demographic characteristics of patients and duration of operation between groups. There was no significant difference in the incidence of nausea or vomiting between groups during the 24 h postoperative period (Table **II**). The incidence of nausea during early period (0-6 h) was 20% in group I and 15% in group II while it was 20% in group I and 10% in group II during delayed period (6-24 h) ($p>0.05$). The incidence of vomiting during early period was 40% in group I and 25% in group II while it was 5% in group I and group II during delayed period ($p>0.05$). 40% of patients in group I and 55% of group II did not experience PONV symptoms during 24 h postoperatively. In group I, PONV scores were significantly increased at 1^{st} and 4^{th} h ($p<0.05$) but there was no significant change in group II (Figure **I**). However no difference was found in PONV scores of patients between groups. Eight patients (40 %) in group I and 5 patients (25%) in group II required antiemetic therapy once or more time during 24 h postoperatively (Table **II**). There was no significant difference in the percentage of patients requiring antiemetic therapy between groups (Table **II**).

0-6 hours PONV * Anesthesia type Crosstabulation

0-6 hours PONV	**2% sevoflurane, 50% nitrous oxide in oxygen**	**2% sevoflurane in oxygen**	**Total**
No nausea or vomiting	15	13	28
Mild nausea, no vomiting, no treatment	7	13	20
Moderate nausea, mild vomiting requiring treatment	6	4	10

6-24 hours PONV * Anesthesia type Crosstabulation

0-6 hours PONV	**2% sevoflurane, 50% nitrous oxide in oxygen**	**2% sevoflurane in oxygen**	**Total**
No nausea or vomiting	15	13	28
Mild nausea, no vomiting, no treatment	7	13	20
Moderate nausea, mild vomiting requiring treatment	6	4	10

ASA Physical Status Anesthesia type 6-24 hour PONV Crosstabulation

6-24 hours PONV			**2% sevoflurane, 50% nitrous oxide in oxygen**	**2% sevoflurane in oxygen**	**Total**
No nausea or vomiting	ASA physical status	!	16	23	39
		II	11	6	17
	Total		27	29	56
Mild nausea, no vomiting, no Treatment	ASA Physical Status	I	1	1	2
	Total		1	1	2
Total	ASA Physical Status	I	17	24	41
		II	11	6	17
	Total		28	30	58

ASA Physical Status * Anesthesia type * 0-6 hours PONV Crosstabulation

6-24 hours PONV			2% sevoflurane, 50% nitrous oxide in oxygen	2% sevoflurane in oxygen	Total
No nausea or vomiting	ASA Physical Status	!	12	13	25
		II	3	0	3
	Total		15	13	28
Mild nausea, no vomiting, no treatment	ASA Physical Status	I	4	8	12
		II	3	5	8
	Total		7	13	20
Moderate nausea, no vomiting, no treatment	ASA Physical Status	I	1	3	4
		II	5	1	6
	Total		6	4	10
Total	ASA physical status	I	17	24	41
		II	11	6	17
	Total		28	30	58

Statistics

		Weight of Pts	Age of Pts
N	Valid	058	58
	Missing	0	0
Mean		66.02	39.07
Std. Deviation		8.795	11.576
Minimum		52	20
Maximum		90	70

DISCUSSION

Postoperative nausea and vomiting remained unpleasant complication for many years with the use of general anesthetics for surgical procedures [5,10] Postoperative nausea and vomiting is a sole strong predictor for delay in discharge from hospital, increasing hospital stay and cost. The incidence of PONV is very high, approximately 9% to 10% in PACU(post anesthesia care unit) and increases to 30% during the first 24 hours postoperatively[11]. Many researchers tried to investigate the causes of PONV and trials are continued to establish its causes. However there is lot to debate [12]. Attempts were made to identify patient related and non-related risk factors for PONV. Sinclair et al [13] in their prospective study with 17638 outpatients concluded that age, sex, smoking status, previous history of PONV, type and duration of anaesthesia and type of surgery are independent risk factors of PONV. Also Apfel et al[14] found that the four main risk factors for PONV were female gender, prior history of PONV and motion sickness, nonsmoking and the use of opioids. Among all these risk factors, lot of work has been done to evaluate the effect of general anesthetics, in particular nitrous oxide. However the results are not clear and today there is still no consensus for omitting nitrous oxide during general anaesthesia. Divatia et al [15] performed a meta-analysis of published randomized controlled trials studying the effect of nitrous oxide on PONV. They recruited twenty four studies, found to be eligible for meta-analysis. There came across only 5 statistically significant “positive” trials showing that omission of nitrous oxide decreased PONV. On the other hand there were 15 “negative” trials and no effect in 4 trials. However they concluded that omission of nitrous oxide can reduce the risk for PONV by nearly 30% stressing the need for further studies and randomized controlled trials. The main reason for the controversial results is the methodological problems in the studies looking at PONV. Kortilla [4] and Watcha [5] stated that it is important to have an appropriate study design whereby all confounding factors are evenly distributed between the study groups and this is achieved by limiting the study to a standardized surgical procedure during a standardized anaesthetic and assigning patients to receive an intervention according to a predetermined randomized double blind method. Also populations included in PONV trials should represent a reasonable clinically relevant baseline risk [16]. In our study; we studied a population having relevant risk factors: those who were female, non-smoker,undergoing laparoscopic cholecystectomy and those who were administered opioids in peri and postoperative period.

We also standardized the surgical procedure and anaesthetics as all patients received the same anaesthetics (propofol, nalbuphine and sevoflurane) with nitrous oxide being the sole variable.

Watcha[5] and Tramer[12] in their reviews of PONV suggested that nausea and vomiting must be considered separate endpoints for more precise results. Also Kortilla [4] stated that the outcome should

be included in studies on PONV as the need to give antiemetic and the number of patients needing antiemetics are good endpoints for statistical analyses. In our study; we considered nausea and vomiting and the number of patients needing antiemetics as separate endpoints and found no significant difference in the incidence of nausea or vomiting and the percentage of patients needing antiemetics when nitrous oxide was omitted. According to Watcha [5,] separate time based analyses should be performed for the early (0-6 h) or delayed (6-24 h) postoperative period in the studies. Short term efficacy has an economic impact mainly in day surgery where patients are meant to be discharged within hours after surgery while long term efficacy is a better indicator of antiemetic efficacy and patient comfort[16]. We also studied early and delayed effects of nitrous oxide on PONV and could not find a significant difference.

In the reviews about PONV, it was emphasized that the effect of omitting nitrous oxide was most pronounced for postoperative emesis in adults undergoing procedures known to be associated with a high risk for PONV and have little influence on nausea itself[5,12,15]. In our study although the patients were female, nonsmoker, administered opiods and underwent laparoscopic surgery, the omission of nitrous oxide did not have a significant influence on either nausea or vomiting. The decrease in PONV when nitrous oxide is avoided may reflect the use of higher inspired oxygen concentration rather than a direct effect of nitrous oxide[17].

Postoperative pain is another important predicting factor for PONV [18,19]. Pain significantly prolongs recovery time and increases hospital stay and contributes to postoperative nausea and vomiting. Cholecystectomy can cause inflammation or local irritation around the gall bladder bed,liver, diaphragm and/or peritoneum exacerbating pain [20]. The intensity of pain is most severe during the first 2-3 h after the laparoscopic cholecystectomy [21]. Postoperative pain control for laparoscopic cholecystectomy is attainable using a multimodal pain management approach. Michaloliakua[20] stated that the concomitant use of local anaesthetics, nonsteroidalantiinflammatory drugs and opioids proved to be highly effective in pain relief after laparoscopic cholecystectomy. However in our study we could not establish any correlation between PONV and pain.

It is commonly observed that the use of opioids during surgery increases the incidence of PONV[3,12,14]. Whether there is a synergistic effect between opioids and nitrous oxide in increasing emetic symptoms in the postoperative period is still a matter of debate [7]. Our results do not support the idea that there is correlation between intraoperative and postoperative opioids (Nalbuphine) and nitrous oxide for higher incidence of nausea or vomiting in nitrous oxide group as in the study by Pandit et al [6].

CONCLUSION

We concluded that 50% nitrous oxide did not increase the incidence of early or delayed nausea and vomiting postoperatively. Furthermore nitrous oxide did not increase the percentage of patients needing antiemetic therapy in female patients undergoing laparoscopic cholecystectomy.

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