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Propofol alone and combined with dexamethasone for the prevention of postoperative nausea and vomiting in adult patients undergoing laparoscopic cholecystectomy

Sourabh Roy | M.D., Associate professor, Department of Anesthesiology, KPC Medical College, Kolkata, India

Krishna Gupta | MD, Professor & HOD, Department of Anesthesiology, KPC Medical College, Kolkata, India

ABSTRACT

We did a prospective, randomized, double-blind study to evaluate the efficacy and safety of a small dose of propofol when combined with dexamethasone, for the prevention of postoperative nausea and vomiting in adult patients listed for laparoscopic cholecystectomy. Sixty patients, 25 men and 35 women aged 17–48 years, were given dexamethasone 8mg at the start of operation. In addition only the study group received propofol 0.5 mg/kg intravenously at the end of the operation. A standard general anaesthestic was used, including isoflurane and nitrous oxide in oxygen. Patients' characteristics were comparable in all two groups. The antiemetic efficacy of propofol combined with dexamethasone was superior to that of dexamethasone alone ($p < 0.05$). There were no clinically important adverse events. We conclude that a small dose (0.5 mg/kg) of propofol combined with dexamethasone 8 mg was more effective than dexamethasone alone for the prevention of postoperative nausea and vomiting in adult patients having general anaesthesia for laparoscopic cholecystectomy.

KEYWORDS | Complications; Vomiting; Antiemetics; Propofol; Dexamethasone

INTRODUCTION

Postoperative nausea and vomiting after (PONV) surgery are distressing and there are frequent adverse events after receiving general anesthesia during surgery [1], with a high incidence in patients undergoing laparoscopic cholecystectomy [2, 3]. The corticosteroid dexamethasone when given i.v. has been used effectively as an antiemetic in patients undergoing laparoscopic cholecystectomy [4,5]. But use of dexamethasone alone have resulted in only a partial reduction in emesis the incidences ranging from 20% to 23% in various studies [6,7]. It has been observed that propofol given at a small dose possesses direct antiemetic properties in various situations [8]. Thus combining propofol with dexamethasone may augment its antiemetic efficacy further [9,10]. For this purpose we did a prospective, randomized, double-blind study to evaluate the efficacy and safety of a small dose of propofol combined with dexamethasone compared to dexamethasone alone for the prevention of postoperative nausea and vomiting in adult patients listed for laparoscopic cholecystectomy

METHODS

Approval of our institutional review board and written informed consent from patients were obtained. Sixty patients (35 females, 25 males) with American Society of Anesthesiologists physical status 1 & 2, aged 17 to 48 years, and scheduled for laparoscopic cholecystectomy were enrolled in the study. Patients who had gastrointestinal tract diseases, history of motion sickness, those who were pregnant, menstruating or menopausal, and those who had taken antiemetics within 48 hours before surgery were excluded from the study. All operations were performed between 8.00 hours & 14.00 hours.

In the preoperative holding area the patients were randomly allocated into two groups on the basis of a computer generated random number table. Premedication consisted of orally administered diazepam, 5 mg. one minute before induction all the patients received 8 mg dexamethasone i.v. Anesthesia was induced with intravenous (IV) administration of a combination of thiopental sodium, 5 mg/kg, and fentanyl citrate, 2 µg/kg, and vecuronium bromide, 0.1 mg/kg, was used to facilitate tracheal intubation. After tracheal intubation, anesthesia was maintained with 0.4% to 1.0% (inspired concentration) of isoflurane and 66% of nitrous oxide in oxygen. Additional analgesia during surgical procedure was achieved with fentanyl citrate, 50 µg IV. Ventilation was mechanically controlled and was adjusted to keep an end-tidal PCO2 at 35 to 40 mm Hg throughout the surgical procedure as measured by an anesthetic–respiratory gas analyzer. Muscle relaxation was maintained with top-up doses of vecuronium as required. At the end of surgery, patients received placebo in the form of 10% intralipid (group D) or propofol 0.5 mg/kg (group P) intravenously. Intralipid 10 % was chosen as placebo since it is an excipient of propofol and devoid of antiemetic & emetogenic side effects[11]. For reversal of muscle relaxation, a combination of atropine sulfate, 0.02 mg/kg, and neostigmine methylsulfate, 0.04 mg/kg, was administered IV, and then the trachea was extubated when the patient was awake. No patient had a nasogastric or an orogastric tube placed during surgery. Postoperatively, patients received rectally diclofenac sodium 100 mg when they reported pain. The use of oral narcotic analgesics was not permitted in any of the 2 groups.

All episodes of PONV (nausea, retching, or vomiting) were recorded by the nursing staff without knowledge of which antiemetic the patients had received during the 2 periods within the first 24 hours after receiving anesthesia i.e. 0 to 3 hours in the postanaesthetic care unit and 3 to 24 hours in the postoperative ward. Nausea was defined as the subjectively unpleasant sensation associated with awareness of the urge to vomit; retching was defined as the labored, spasmodic, rhythmic contraction of the respiratory muscles without the expulsion of gastric contents; and vomiting was defined as the forceful expulsion of gastric contents from the mouth.[1] These nurses asked the patients if retching or vomiting had occurred and if they felt nauseous, with only 2 possible answers (yes/no). If 2 or more episodes of PONV occurred during the first 24 hours after receiving anesthesia, another rescue antiemetic (ondansetron 4 mg) was given intravenously. The details of any adverse effects throughout the study were recorded.

Al parametric data were analyzed by students' t test. The number of patients experiencing emetic episodes and requiring rescue medication, and the incidence of adverse events were compared with Fisher exact probability test. $P < .05$ was considered statistically significant. All values were expressed as mean ± SD or number (percentage). Sample size was predetermined it was calculated that 30 patients per group would be required to demonstrate a 30% difference in values for PONV (which was regarded as the primary end point) at $\alpha = 0.05$ with a power $(1 - \beta) = 0.8$.

RESULTS

variables	group D (n=30)	group P(n=30)
age (years)	35 ± 8	35 ± 9
sex (female/male) no.	17 /13	18 /12

height (cms)	135 ± 12	135 ± 14
weight (kg)	45 ± 11	44 ± 10
last menstrual cycle(days)	16± 3	16 ± 3
duration of operation (min)	65 ± 14	63 ± 13
duration of anaesthesia)	72 ± 16	73 ± 15
values are expressed as mean ± SD		

Table 1. demographic and surgical profile of Patients in Each Group

Patient profile and information on surgery and anesthesia are summarized in Table 1. The treatment groups were comparable for demographics of patients as well as the duration of operation and anaesthesia.

There were no differences among the groups for the number of patients who experienced only nausea, retching, or vomiting, or who required rescue medication. The only difference was found in the incidence of emesis-free patients during the 0- to 3-hour and the 3-24 hour postoperative period after receiving anesthesia. The numbers of patients who developed postoperative nausea and vomiting during the 0 -3 hour after anaesthesia were 7 with dexamethasone alone and 2 with propofol plus dexamethasone. The corresponding incidence during the 3- to 24-hour period after anesthesia was 11 and 4 respectively (Table 2). Thus, the efficacy of propofol combined with dexamethasone therapy is superior to the steroid alone for increasing an emesis-free episode during the 2 test periods for patients undergoing laparoscopic cholecystectomy ($p<0.05$).

Table 2. Number of Patients in Each Group Having Each Emetic Symptom During Both Study Periods

symptoms	group D (n=30)	group P (n=30)
0-3 hours postoperative period		
emesis free.	23 (77)	28(93)*
nausea	5(17)	2(7)
retching	0(0)	0(0)
vomiting	3(10)	1(3)
rescue antiemetic	3(10)	1(3)
3-24 hours postoperative period		
emesis free	19(63)	26(87)*
nausea	6(20)	2(7)
retching	1(3)	0(0)
vomiting	6(20)	2(7)
rescue antiemetic	3(10)	1(3)
values are expressed as number (percentage)of patients p value < 0.05		

The most common untoward adverse events were headache and dizziness, which were not serious. No difference in the incidence of adverse effects was observed among the groups (Table 3).

Table 3. Number of Patients in Each Group Having adverse effects during Both Study Periods

events	group D (n=30)	group P (n=30)
headache	3	2
dizziness	2	1
others	2	2
values are expressed as number of patients		

DISCUSSION

Laparoscopic cholecystectomy has become the gold standard for patients suffering from symptomatic cholecystitis. However the reported incidence of PONV after laparoscopic cholecystectomy is 53% to 72% when no prophylactic antiemetic is given2, 3. Our results demonstrated that the incidence of patients experiencing an emesis-free episode during the 2 study periods—0 to 3 hours and 3 to 24 hours after receiving anesthesia—was less in patients who had received propofol therapy in addition to preoperative dexamethasone than in those who had received only dexamethasone ($p<0.05$).

The cause of PONV is multifactorial1.A number of factors, including age, female sex, obesity, long period of carbon dioxide insufflation, operative procedure, anesthetic technique like use of glycopyrrolate, isoflurane & fentanyl, and postoperative pain, is considered to affect the incidence of PONV[1]. In this study, however, all these factors were well balanced among the groups. Moreover all the surgeries were performed by the same surgical & anaesthestic group. Therefore, the difference in the incidence of PONV among the groups can be attributed to the drugs studied.

Dexamethasone has reduced the incidence of nausea & vomiting since its first use in 1981 [4,5]. However approximately 20 % of patients receiving the steroid still complain of emetic episodes [6,7]. Propofol possesses direct antiemetic properties[8], and this effect is not due to the lipid emulsion (Intralipid) in the formulation of propofol [11].The exact mechanism by which propofol acts as an antiemetic is unknown, but propofol is not considered to have vagolytic properties[8] . Hammas et al have recently evaluated the effects of propofol on nausea and vomiting induced by ipecacuanha which is known to release serotonin and have demonstrated that propofol reduces the intensity of retching after ipecacuanha administration[12]. These findings suggest that propofol may have a weak serotonin3-antagonistic effect. Propofol at small doses, less than 1.0 mg·kg–1, lacks sedative, dysphoric, and extrapyramidal signs [13,14].

The major deficiency in our study was the failure to include a control group receiving only placebo. However, we have already shown a high incidence of PONV after laparoscopic surgery in patients who had received placebo. Moreover, Aspinall and Goodman have shown that there is a lack of reliable clinical information concerning placebo-controlled trials of the serotonin3-receptor antagonist ondansetron for the prevention of PONV. Therefore, the control group receiving placebo was excluded from this clinical trial [15].

Adverse events observed in this study were not serious, and there were no differences in the incidence of headache and dizziness among the groups. No patient had a sedation score over 3 in the postoperative period (the patients remained awake and/or responded to verbal contact) as was the case in the study by H. Unlugenc et al [16]. None of the patients of either group complained of pain at the site of administration of propofol or placebo.

In conclusion, we have shown that a small dose (0.5 mg/kg) of propofol administered IV at the completion of surgery in addition to preoperative dexamethasone is a better antiemetic than dexamethasone alone for preventing PONV in patients undergoing laparoscopic cholecystectomy.

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