

Original Article

Prophylactic Use of Ondansetron for Prevention of Postoperative Nausea and Vomiting in Laparoscopic Cholecystectomy

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ABSTRACT:

The prophylactic antiemetic efficacy of intravenous ondansetron was evaluated in a prospective randomized, double blind comparison with the placebo in 80 patients undergoing laparoscopic cholecystectomy under general anaesthesia. Patients were randomly allocated to receive ondansetron 8mg (4 ml) or placebo (Normal saline, 4ml) before induction of a standardised general anaesthesia. The incidence of nausea was 60% in placebo and 35% in the ondansetron group ($p < 0.01$). Similarly the incidence of vomiting was 22.5% in the placebo group and 5% in the ondansetron group ($p < 0.01$). Finally, only 32.5% of the ondansetron treated patients required a rescue antiemetic compared with 57.5% in the placebo group. Thus, in patients undergoing laparoscopic cholecystectomy ondansetron (8mg) before induction of anaesthesia appears to be a promising antiemetic for the prevention of PONV.

Key words: PONV - postoperative nausea and vomiting, 5-HT - 5-hydroxy tryptamine, P - probability.

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INTRODUCTION

With advancement of technology and minimally invasive surgery, laparoscopic cholecystectomy has become a standard of care in patients with symptomatic gallstones. Chief among its benefits are decreased postoperative pain, earlier return to full activity and reduced hospital stay. But this realisation of laparoscopic cholecystectomy has been frustrated by the commonly encountered complication of postoperative nausea and vomiting (PONV). This has driven the investigation to improve strategies for prevention.

Despite the many advances in surgery and general anaesthesia, PONV remains a frequent and distressing source of discomfort during the postoperative recovery period. This has been especially significant after laparoscopic procedures. The frequency of nausea is as high as 75% and 56% with placebo and ondansetron and the corresponding frequency of vomiting is 60% and 37%.¹ Ondansetron a 5-hydroxytryptamine subtype 3 (5-HT₃) receptor antagonist, has been documented as an effective antiemetic in the prevention and treatment of PONV. Its lack of sedative and extrapyramidal side effects often observed with more conventional antiemetic agents, has made it particularly attractive in the present scenario. The objective of this study was to evaluate the

efficacy of intravenously administered ondansetron at induction of anaesthesia on PONV.

MATERIALS AND METHODS

The patients were taken for study in the department of General Surgery at Government Medical College, Patiala. Only the patients undergoing elective cholecystectomy aged between 25-65 years were taken for study. Any patient of acute cholecystitis, undergoing emergent laparoscopic cholecystectomy, younger than 25 years and older than 65 years of age, already taking drugs with known antiemetic properties, suffering from motion sickness, pregnant, previous allergic reaction to any drug were excluded. The study was approved by hospital ethics committee. Written informed consent was obtained from all the patients.

Study was prospective and double blinded and patients were randomly allocated to receive either placebo (4ml, normal saline) or intravenous ondansetron (8mg) 10 minutes before induction of anaesthesia. The patient and all members of the operative team were blinded to the randomization results.

Standard balanced general anaesthesia was given to all patients. Premedication was given with midazolam and atropine. Induction of anaesthesia was done with propofol

1.5-2 mg/kg, fentanyl 2-4 µg/kg, midazolam 1-2mg, O₂ and N₂O (50:50) and halothane 2%. After induction was confirmed with loss of eyelash reflex, succinyl choline was given to facilitate intubation. Maintenance of anaesthesia was achieved with O₂ and N₂O (50:50), halothane 1-2% and pancuronium bromide. Reversal of neuromuscular blockade was achieved with neostigmine 0.05 mg/kg and atropine 0.01 mg/kg.

Laparoscopic cholecystectomy was performed with four port technique and all the skin wounds closed with suture or staples. Patients were asked to assess their nausea at 0,½,1,2,3,4,6 and 24 hours postoperatively. Data was collected by the resident in the surgery unit without knowledge of medication given at induction. The score at each point time was based on a 5-point whole number linear scale with 1=no nausea, 2=mild nausea, 3= moderate nausea, 4= severe nausea and 5 emesis. The nausea scores, emetic episodes, pain and vital signs were assessed in the postoperative period. Ondansetron 8mg i.v. was given as rescue dose in both the groups for

PONV and patients were discharged when standard discharge criteria were met. Length of stay was defined as the time between the operative incision and the patients discharge from the hospital. All the patients were seen postoperatively in 10-14 days for a follow up examination. Results of the two treatment groups were compared using a paired students t test with p <0.01 being accepted as significant.

RESULTS

Eighty patients were enrolled in the study. 40 received placebo and 40 ondansetron. Demographically there was no significant difference between treatment groups with respect to age, gender or significant medical history. Variables assessed in this study such as anaesthesia time, use of preoperative antibiotic, gallbladder tear, adhesion, unclear anatomy, bleeding and performance of intraoperative cholangiogram were also similar between the two treatment groups (Table I).

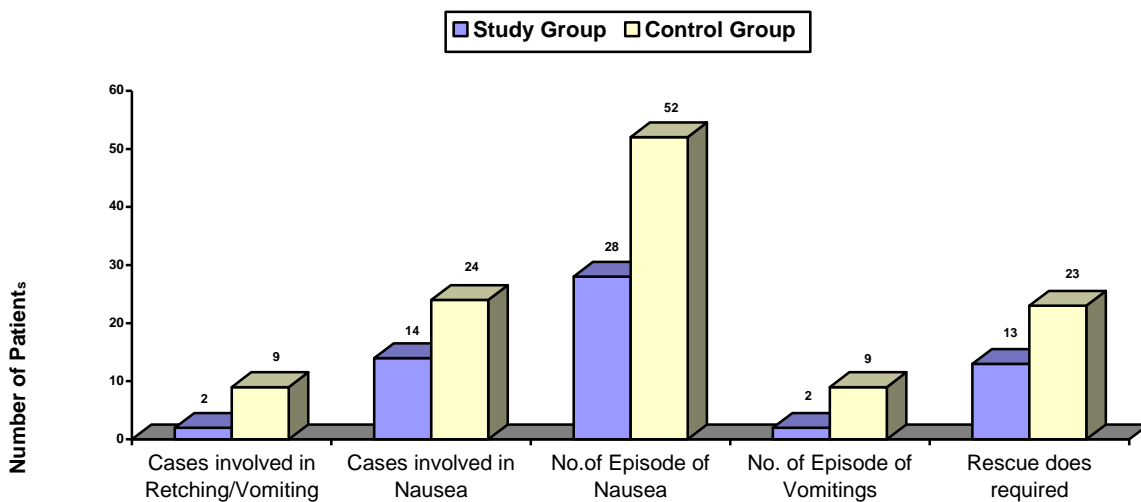
Table I: Demographic Characteristics of Groups

	Placebo	Ondansetron
Number of patients	40	40
Age (years)	42.9	41.8
Female:male	87.5:12.5	87.5:12.5
Significant medical history	0	0
Duration of anaesthesia (mins)	57.9	63.9
Preoperative antibiotics	40	40
Intraoperative gallbladder tear	6	8
Unclear anatomy	3	4
Adhesions	13	15
Bleeding	5	7

Table II: Comparative incidence of Nausea and Vomiting

Study	Nausea		Vomiting	
	Placebo	Ondansetron	Placebo	Ondansetron
Kenny et al 1992	75	56	60	37
Suen et al, 1994	58	43	56	25
Helmy, 1999	42.5	7.5	47.5	7.5
Wilson et al,2001	-	-	22.0	4.0
Present study	60	35	22.5	5.0

Figure 1: Bar Diagram showing Distribution of Case Involved, No. of Episode of Nausea and Vomiting & Rescue Doses required in Study and Control Groups



The patients receiving placebo had significantly more episodes of nausea (52 vs 28; $p < 0.01$), emesis (9 vs 2; $p < 0.01$) and need for additional postoperative antiemetics (23 vs 13; $p < 0.05$) than those receiving ondansetron. The number of patients experiencing nausea (24 vs 14; $p < 0.01$) or emesis (9 vs 2; $p < 0.01$) and the overall total mean nausea and vomiting score (7.64 vs 5.72) was greater in the placebo group (fig 1). There was no significant differences in overall length of stay. (3.4 vs 3.3 days ; $p > 0.05$), postoperative pain ($p > 0.05$) between the placebo and ondansetron groups.

DISCUSSION

PONV are troublesome complications of anaesthesia. Despite the dramatic advances in surgery and anaesthesia, PONV is distressing and uncomfortable for patients and can lead to delays in recovery resulting in significant additional costs.² Serious complications are relatively rare and include aspiration of vomit, dehydration, alkalaemia, rupture of the oesophagus and Mallory Weiss syndrome. PONV is multifactorial in etiology encompassing those factors determined by the patient, the anaesthesia and the postoperative care.³ Although the specific causes of PONV are unclear, patient characteristics that increase the incidence of PONV include female gender, obesity, extremes of age and history of motion sickness. The length of operation as well as type of operation are also significant, with an incidence of PONV as high as 70% in patients undergoing operations on the gallbladder, stomach or duodenum.⁴ Postoperative pain and the subsequent need for opioid also result in higher rates of PONV. As most of these factors are predetermined and cannot be modified, there has been great interest in finding an effective antiemetic.

Various antiemetic which have been in use produce undesirable side effects and prolong anaesthesia. Phenothiazines and antihistaminics can produce sedation and lethargy. Butyrophenones such as droperidol can also be associated with significant drowsiness that can delay discharge as well as the potential for extrapyramidal side effect.⁵

The above mentioned side effects profile of antiemetic have driven research in the development of new agents. Ondansetron a 5-HT subtype 3 receptor antagonist, has been documented as an effective antiemetic in the prevention of nausea and emesis associated with cancer patients receiving chemotherapy and radiotherapy.⁶ Several studies for eg. Kenny et al (1992), Suen et al (1993), Wilson et al (2001) and Scuderi et al (1993) found ondansetron to be highly effective in reducing PONV in different surgical procedures.^{1,7,8,9} The comparative incidence of nausea and vomiting is shown in Table II.

In conclusion ondansetron at induction was highly effective in decreasing PONV as it is devoid of distressing side effects, haemodynamically stable, does not prolong sedation caused by general anaesthetics and should become the standard.

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