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Role of Ondansetron with Dexamethasone and Palonosetron with Dexamethasone as Antiemetic in Laproscopic Surgery under General Anaesthesia: A Comparative Study

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Abstract
Background and Aim: *Postoperative nausea and vomiting (PONV) is commonly seen after laparoscopic surgery. In this randomized double blind prospective clinical study, we investigated and compared the efficacy of palonosetron with dexamethasone and ondensetron with dexamethasone to prevent postoperative nausea and vomiting after laparoscopic cholecystectomy.*
Materials and Method: *Sixty patients (18-60 yrs of age) undergoing elective laparoscopic cholecystectomy were randomly allocated one of the two groups containing 30 patients each. Group 1 received ondensetron 4 mg and dexamethasone 8 mg intravenously as a bolus before induction of anaesthesia. Group 2 received palonosetron 0.075 mg and dexamethasone 8 mg intravenously as a bolus before induction.*
Result: *The incidence of a complete response (no PONV, no rescue medication) during post operative period is 86.6%,86.6%,93.4% and 93.4% in palonosetron group in 0-4,4-12,12-24 and 24-48 hrs respectively in comparison to ondensetron group in which 50%,63.34%,90% and 93.3%.*
Conclusion: *Prophylactic therapy with palonosetron is more effective than ondensetron for prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy.*
Keywords: *Palonosetron, Ondensetron, Postoperative Nausea and Vomiting (PONV), Laparoscopic surgery.*

Introduction

Postoperative nausea and vomiting (PONV) is the most common distressing symptom occuring after surgery. Despite the advances in anaesthetic and surgical techniques, PONV is still persistent. Various factors contributing to PONV include patient characteristics, anaesthetic technique, type of surgery, and postoperative care. Patients undergoing laparoscopic surgeries are particularly at risk.

Postoperative emesis predispose the patients to aspiration of gastric contents, electrolyte imbalance, tension on suture line, venous hypertension, wound dehiscence, and it frequently delays discharge from post anaesthesia care unit (PACU) and is the leading cause of unexpected

hospital admissions after planned ambulatory surgery.

Patients undergoing laparoscopic cholecystectomy are particularly at high risk for developing postoperative nausea and vomiting. Patient's overall incidence can be raised up to 80%. [1]

Non-pharmacologic methods have been studied for their efficacy in PONV prevention. These include acupuncture, electroacupuncture, transcutaneous electrical nerve stimulation, acupoint stimulation, and acupressure. These methods have not been shown to have consistent antiemetic property [2,3].

Traditional antiemetic drugs used for PONV include anticholinergics (e.g. scopolamine) phenothiazines (e.g.prochlorperazine) antihista-mines (e.g.promethazine), butyrophenones (e.g.droperidol), and benzamide (e.g. metoclopramide).

Promethazine and prochlorperazine belong to a group of drugs known as phenothiazines, which act primarily via a central antidopaminergic mechanism in the chemotactic zone but it is associated with drowsiness [4].

Metoclopramide is an antiemetic used widely in clinical practice. It is an effective antiemetic when administered at dose of 0.2mg/kg but higher doses (> 0.2 mg/kg) of metoclopramide are associated with extrapyramidal reactions, such as akathisia and motor restlessness[5,6].

Dexamethasone is an inexpensive and effective antiemetic drug, with minimal adverse effects after a single-dose administration. The exact mechanism of antiemetic action of dexamethasone is not fully understood [7].

5-hydroxytryptamine subtype 3 (5HT-3) receptor antagonist produce pure antagonism of the 5-HT3 receptor. The introduction of this class of drugs in the 90s represents a major improvement in the pharmacotherapy of chemotherapy and radiation therapy-induced nausea and vomiting. They have since proven to be highly effective in the prevention and treatment of postoperative nausea and vomiting. They are not effective in the treatment of motion induced nausea and vomiting. Their actions involve both central and peripheral mechanism[8].

Ondansetron, the first 5-HT3 receptor antagonist to be introduced, is the most commonly used drug of this class. Other includes granisetron, tropisetron, dolosetron, palonosetron and ramosetron. Several other studies [9] have shown ondansetron to be superior antiemetic than dexamethasone.

Palonosetron is a second generation 5HT3 receptor antagonist and having long elimination half life. Several studies[10] have concluded that palonosetron is a better antiemetic than ondansetron in prevention of PONV.

When used in combination with Ondansetron and Palonosetron, Dexamethasone[11,12] was reported to be effective in reducing PONV. There is no evidence that any dose of a single antiemetic can achieve more than 60–70% prevention of nausea and vomiting.

Our study sought to compare the effectiveness of 0.075mg Palonosetron plus 8mg Dexamethasone with that of 4mg Ondansetron plus 8mg Dexamethasone for PONV in patients undergoing laparoscopic surgery. We also studied the incidence of early or delayed vomiting, and the requirement of rescue antiemetics, and any side effects.

Materials and Method

Sixty patients age between 18 to 60 years belonging to American Society of Anaesthesia grade 1and 2 randomly divided into 2 groups,each consist of 30 patients.

Group A: Palanosetron 0.075mg and Dexamethasone 8 mg

Group B: Ondansetron 4mg and Dexamethasone 8 mg

On day of surgery Anaesthesia machine, circuit, resuscitation equipments were kept ready. After confirmation of Nil Per Oral status patient was shifted to the operating room and connected to multi parameter monitor. Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Meanarterial pressure(MAP), Pulse rate and

saturation of Oxygen (SpO2) were recorded. Patient was premedicated with glycopyrrolate 0.2mg intravenous (iv) injection and fentanyl 2µg/kg injection. Group A received intravenous injection of 4mg ondansetron and 8mg Dexamethasone and group B received intravenous injection of 0.075mg Palanosetron along with 8mg Dexamethasone before induction. All patient were preoxygenated for three minutes and induced with propofol (1%) 1.5-2mg/kg and succinylcholine 1.5-2mg/kg to facilitate laryngoscopy and intubation. Oxygenation was continued by positive pressure mask ventilation using the Bains circuit. At the onset of apnea, using a laryngoscope with a Macintosh blade, intubation was performed with well lubricated, appropriate size cuffed oral endotracheal tube. After confirmation of the tube position, the cuff was inflated, and the tube was fixed.

Anaesthesia was maintained with oxygen (O_2), halothane and vecuronium 0.1mg/kg. Ventilation was controlled and adjusted to maintain the end tidal partial pressure of CO_2 between 4.7 and 5.3 kPa (35-40 mmHg).

Laparoscopic surgery was performed under video guidance and involved four punctures of the abdomen. During surgery, patient was placed in the reverse trendelenburg position with the right side of the bed elevated and abdomen insufflated with CO_2 through a veress needle to a pressure maximum of 12-14mmHg. At cessation of surgery, residual neuromuscular block was reversed using intravenous Glycopyrrolate 0.005mg/kg and Neostigmine 0.05mg/kg. After regaining muscle power to maintain spontaneous respiration and adequate tidal volume, patient was extubated. After extubation patient was oxygenated for 5 minutes. After discontinuation of oxygen via mask, patient was observed for oxygen saturation if it remains above 97%, patient was shifted to recovery room and/or postoperative ward.

The duty doctor was asked to administer intravenous inj.metoclopromide 10 mg as rescue antiemetic on every episode of vomiting in the 24 hours study duration and to document it.

Blood pressure, Heart rate, Respiratory rate was monitored and incidence of nausea, retching, and vomiting was recorded at 1hr, 4 hrs, 12 hrs, 24 hrs and 48 hrs postoperatively

The data was then collected and analysed.

Statistics: Dependence of one qualitative character on groups was tested using chi square test. The analysis was performed using IBM SPSS version 2016, $p<0.05$ was considered as statistically significant.

Observations & Results

In total, 60 patients were recruited, all of them completed the study. Baseline demographic profile and clinical characteristics were comparable between both the groups with no statistically significant difference between them (p-value>0.05).

Table 1 Baseline demographic profile and clinical characteristics

	ONDANSETRON GROUP	PALONOSETRON GROUP	p-VALUE
Male/Female	2/28	1/29	0.55
AGE in years (mean±SD)	39.86 ±9.353	43.22 ±8.541	0.0786
WEIGHT in kg (mean±SD)	54.62 ±6.779	55.46 ±5.383	0.5168
HEART RATE per min (mean±SD)	81.28 ±8.676	81.31 ±8.782	0.7325
ARTERIAL PRESSURE in mmhg (sys±SD)	122.67 ±6.997	124.56 ±6.240	0.5438
ARTERIAL PRESSURE in mmhg (dys±SD)	81.43 ±5.37	80.73 ±5.54	0.585

The incidence of nausea was significantly lower in the palonosetron group than in the ondansetron group during the first 12h ($p<0.05$, Table2). But as a long term (12-48 hrs) effect incidence of postoperative nausea and vomiting is less in Palonosetron Group but not statistically significant ($p>0.05$)

Table 2 Comparison of frequency of PONV in positive period

Post-operative period		ONDANSETRON (n=30)	PALONOSETRON (n=30)	p- VALUE
0-4 hours	NAUSEA	15 (50%)	4 (13.33%)	0.005
	VOMITING	8(26.66%)	2 (10%)	0.079
4-12 hours	NAUSEA	11 (36.66%)	4 (13.33%)	0.073
	VOMITING	4 (13.33%)	2 (6.66%)	0.667
12-24 hours	NAUSEA	3 (10%)	2 (6.66%)	0.640
	VOMITING	2(6.66%)	1(3.33%)	0.553
24-48 hours	NAUSEA	3 (10%)	2(6.66%)	0.640
	VOMITING	1 (3.33%)	0 (0%)	0.0079

Complete response (no PONV and no rescue antiemetic) was more in the palonosetron group compared with the ondansetron group and the need for rescue antiemetics was less during 0 - 48 h time interval (p>0.05) (Table3). Incidence of adverse effects (Fig. 3) were comparable between the two groups.

Table 3 Incidence of Complete Response and need for Rescue Anti-emetic

	ONDANSETRON (n=30)	PALONOSETRON (n=30)	p-VALUE
COMPLETE RESPONSE	22(74.11%)	27(89.44%)	0.182
RESCUE ANTIEMETICS	14(46.66%)	9(30%)	0.288

Fig 1 Incidence of Nausea in Different Groups Within Thke Defined Time Perio

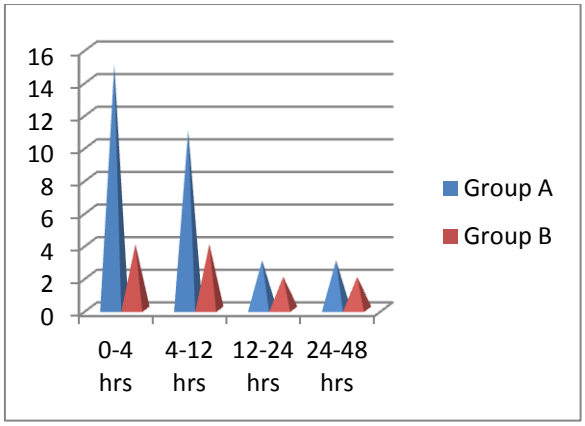


Fig 2 Incidence of Emesis in Different Groups Within the Defined Time Period

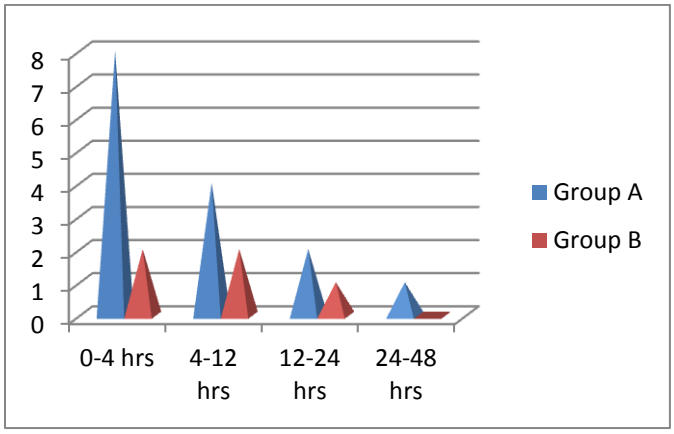
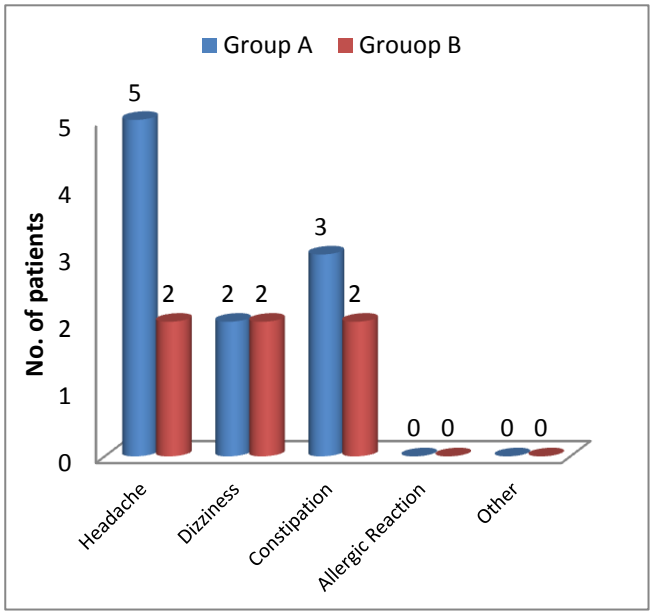


Fig 3 Comparison of the Incidence of Side Effects of in Different Groups



Discussion

A significant proportion of patients experience PONV despite the widespread use of prophylactic antiemetics, including 5-HT3 receptor antagonists.[13] 5HT3 receptor antagonist have an enviable safety profile, with minor side-effects and rare cardiac conduction abnormalities. Ondansetron was the first 5-HT3 receptor antagonist to be marketed and has frequently been used to controlPONV.[14] Palonosetron a second generation 5-HT3 antagonist has unique structural, pharmacological and clinical properties that distinguish it from other 5-HT3 antagonists.[15] It is the most

recently introduced member of this class of drugs in India. It has a greater binding affinity and longer half-life (40hrs) than older 5-HT3 antagonists. The present study was carried out mainly to see the see the comparative efficacy of the new and much promising long-acting 5-HT3 antagonist palonosetron against ondansetron in prevention of PONV in patients undergoing laparoscopic cholecystectomy.

In our study, the dose selection for palonosetron was based on the studies of Candiotti et al.[16], the minimum effective dose of palonosetron in the prophylaxis of PONV is 0.075 mg, and this has been approved by the food drug agency (FDA). US Food and Drug Administration (FDA) also approved a single dose of palonosetron 0.075 mg for preventing PONV for up to first 24 hours after the surgery.[8,17]

The incidence of PONV is associated with many factors like age and gender (female gender, younger age increase the risk of PONV),history of motion sickness or PONV, smoking status (smoking decreases the risk of PONV), postoperative opioid use, type and duration of surgery, anaesthesia and ambulation.[18,19] These factors were comparable between both groups in the present study.

In the present study, palonosteron 0.075 mg was more effective at reducing PONV than ondansetron 4mg. This could reflect the high receptor affinity of palonosetron for 5-HT3, with a low affinity demonstrated for other receptors and the longer duration of action.[20]

Conclusion

The current study concludes that efficacy of ondansetron4 mg plus dexamethasone 8 mg and palonosetron 0.075 mg plus Dexamethasone8 mg in post-operative nausea and vomiting was almost comparable. Since both drugs are serotonin antagonists with almost similar pharmacokinetic and dynamic behaviour profile was also similar in both treatment groups.. The overall patient satisfaction and adverse effect profile were comparable between both the groups.

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