Research Paper

Volume : 2 | Issue : 10 | October 2013 • ISSN No 2277 - 8179

A Comparative Study Between Palonosetron and Ondansetron to Prevent Post Operative Nausea and Vomiting After Laparoscopic Cholecystectomy

Medical Science

KEYWORDS : Laparoscopic cholecystectomy ,Palonosetrone ,ondansetrone ,post operative nausea and vomiting

Dr. Gauri. M. Panjabi — Assistant professor of anaesthesiology, Department of anaesthesia, Smt N.H.L Municipal medical college, Ahmedabad

Dr. Mehul. V. Chauhan — 3rd year resident doctor, Smt N.H.L Municipal medical college, Ahmedabad

ABSTRACT

The present clinical comparative study was carried out in 60 patients of ASA GRADE I and II scheduled for laparoscopic cholecystectomy.The patients in group A received palonosetron 75µg IV and patients in group B received ondansetron 4 mg IV.

In our study we have found that when patients are given palonosetron the incidence of post operative nausea and vomiting was similar to ondansetron. There was no statistical difference in the visual analogue scale for nausea.

So we concluded that palonosetron is as effective as ondansetron in preventing PONV

Introduction :

Post operative nausea and vomiting (PONV) is a common and distressing complication of surgery under general anesthesia. The incidence of PONV remains unacceptably high (40-75% in the first 24 hrs) following laparoscopic cholecystectomy.[2,3]

The 5-hydroxytryptamine-3 (5-HT_3) receptor antagonists are popular drugs for PONV prophylaxis. Most clinical research with the 5-HT_3 receptor antagonists has used ondansetron & its antiemetic efficacy is well established in prevention of PONV. However several alternatives to ondansetron like palonosetron, granisetron, tropisetron, ramosetron are now available.

Palonosetron is the most recently introduced member of this class of drugs. Its interaction pattern with the 5-HT_3 receptor is different from earlier 5-antagonists, enabling a higher binding affinity and longer half life [4,5]. The elimination half life following single IV dose, is approximately 40 hrs compared to ondansetron which is 3.5 to 5.5 hrs , therefore duration of action exceeds 24 hrs and may extend up to 48 hrs.

The present study was designed to evaluate the efficacy of palonosetron compared with ondansetron for preventing PONV during the first 24 post operative hours in patients undergoing laparoscopic cholecystectomy.

Material and methods:

In this prospective study, 60 patients aged 18-60 yrs of ASA GRADE-I and II scheduled for laparoscopic cholecystectomy after taking informed written consent at a tertiary care hospital, were randomly divided into two groups of 30 each .Group-A was given palonosetron 75 µg and Group –B was given ondansetron 4 mg.

Exclusion criteria were pregnancy, use of corticosteroids or psychoactive drugs, H/o alcohol or substance abuse and known hypersensitivity to any of study drugs.

All patients were kept fasting for 6-8 hrs and received Inj. Midazolam 1mg, Inj.Fentanyl 2µg/kg and Inj.Glycopyrrolate 0.2 mg as premedication. On the operation table, routine monitoring (ECG, pulse oximetry, $ETCO_2$, NIBP) was done and baseline vitals were recorded. An intravenous line was secured.

The study drug was given 1 min before induction of anesthesia. Patients received randomly pre induction dose of either palonosetron 75 µg IV (group-A) or ondansetron 4 mg IV (group-B). Anesthesia was induced with Inj. Thiopentone 5-7 mg/kg IV. Tracheal intubation was facilitated by

Inj.succinyl choline 2mg/kg IV. Anesthesia was maintained on O_2, N_2O and sevoflurane. Muscle relaxation was maintained with intermittent dose of Inj.Atracurium. Ventilation was controlled and adjusted to maintain the $ETCO_2$ between 35-40 mm of Hg. A nasogastric tube was inserted to make the stomach empty of air and other contents. For laparoscopic cholecystectomy , surgical procedure was performed under video guidance. Patients were placed in reverse trendlenberg position with the right side of the table elevated and the abdomen insufflated with CO_2 through a verres needle to a maximum of 15 mm of Hg. At cessation of surgery residual neuromuscular block was reversed with IV glycopyrolate and neostigmine and patients were subsequently extubated. All patients were received inj.diclofenac sodium 75 mg IV for post operative analgesia.

For the purpose of study, an episode of PONV denoted either a distinct spell of nausea, retching or vomiting. Nausea was defined as unpleasant sensation associated with awareness of urge to vomit. Retching was defined as an involuntary attempt to vomit but not actually productive of stomach contents. Vomiting was defined as the forceful expulsion of actual gastric contents. Complete response (free from emesis) was defined as no PONV and no need of any rescue medicine. The primary effectiveness measure was total no. of PONV episodes in the 24 hrs period following conclusion of laparoscopic surgery. Visual analogue score (as assessed using a 10 cm Nausea severity scale) at 2, 6 and 24 hrs after completion of surgery was noted. Inj.metoclopramide 10 mg iv was given as a rescue antiemetic when episodes of PONV occurred or at VAS >5 or on demand.[6]

Safety of the study drugs was assessed by monitoring vital signs, O_2 saturation, ECG and examination and asking the patients for adverse events for 24 hrs following surgery. The results were expressed in mean±SD and number (%).

Observation and Results:

Table – 1

Profile of Baseline Characteristics

Parameter	Palonosetron (mean±SD)	Ondansetron (mean±SD)
Age (year)	42.6±13.6	43.2±12.9
Weight (kg)	54.5±8.9	56.4±7.8
Duration of surgery (min)	67.4±34.2	66.3±36.2
Duration of anesthesia (min)	80.2±26.1	79.9±27.3

SD=standard deviation P<0.05

The groups were comparable with respect to age, weight and duration of surgery (table 1). Similarly surgery and anesthesia related parameters were also comparable as shown in table 1.

Table – 2
Comparison of frequency of Nausea, Retching and Vomiting

Group	0-2 hr		2-6 hr		6-24 hr		Total 0-24 hr	
	Number (%)	Mean±SD	Number (%)	Mean±SD	Number (%)	Mean±SD	Number (%)	Mean±SD
NAUSEA								
Palonosetron	8(26.6%)	0.26±0.44	12(40%)	0.4±0.49	13(43.3%)	0.43±0.5	13(43.3%)	0.43±0.5
Ondansetron	8(26.6%)	0.26±0.44	10(33.3%)	0.3±0.47	14(46.6%)	0.46±0.5	15(50%)	0.5±0.5
RETCHING								
Palonosetron	5(16.6%)	0.16±0.37	6(20%)	0.2±0.4	7(23.3%)	0.23±0.43	8(26.6%)	0.26±0.44
Ondansetron	4(13.3%)	0.13±0.34	3(10%)	0.1±0.3	8(26.6%)	0.26±0.44	9(30%)	0.3±0.46
VOMITING								
Palonosetron	9(30%)	0.3±0.46	11(36.6%)	0.36±0.49	12(40%)	0.4±0.49	14(46.6%)	0.46±0.5
Ondansetron	12(40%)	0.4±0.49	14(46.6%)	0.46±0.5	15(50%)	0.5±0.5	16(53.3%)	0.53±0.5

SD=standard deviation, P<0.05

The primary efficacy variable for this study, namely the frequency of all PONV episodes in the 24 hrs post operative period, did not show any statistically significant difference between groups (table2).

VAS scoring of nausea severity was comparable between both groups at 2, 6 and also 24 hrs following surgery . In group- A 8 (26%) patients and in group-B 7 (23%) patients received at least one dose of rescue medicine.

The number of complete responders (no PONV episodes, no rescue medicine) was 16 (53%) in group-A and 14 (46%) in group-B which were statistically non significant.

Regarding safety assessment, the heart rate and mean arterial B.P were raised in immediate post-intubation period, was comparable in two groups. SPO_2 and ECG did not show any significant change in both the groups.

Table 3
Common Side Effects

Side effects	Palonosetron	Ondansetron
Headache	4(13.3%)	5(16.6%)
Dizziness	2(6.6%)	3(10%)
Constipation	3(10%)	2(6.6%)
Myalgia	1(3.3%)	0

The commonly observed adverse effects were headache, dizziness , constipation and myalgia. There was no instance of QT interval prolongation (QTc >40 milliseconds) in either of the study groups. All adverse effects were of mild to moderate severity and settled spontaneously without any treatment.

Discussion:
The incidence of PONV after laparoscopic surgery is high. The etiology is complex and dependent on a variety of factors including age , obesity, surgical procedure, anesthetic technique and post operative pain[7,8].

$5\text{-}HT_3$ receptor stimulation is the primary event in the initiation of vomiting reflex [9]. Anesthetic agents trigger this reflex by stimulating central $5\text{-}HT_3$ receptors in the medullary chemoreceptive trigger zone (CTZ) and also by releasing serotonin from the enterochromaffin cells of the small intestine and subsequent stimulation of $5\text{-}HT_3$ receptors on vagus nerve afferent fibers [10].

Ondansetron was the first $5\text{-}HT_3$ receptor antagonist and has frequently been used to control PONV [11]. Palonosetron is a second generation $5\text{-}HT_3$ antagonist. It has unique structural, pharmacological and clinical properties that distinguish it from other $5\text{-}HT_3$ receptor antagonists. It is a first approved for the prevention of chemotherapy induced nausea and vomiting. It has greater binding affinity and longer biological half time than ondansetron [12]. The mechanism of its action on PONV is similar to ondansetron.

In this study groups were comparable with respect to patient demographics, type and duration of surgery, anaesthesia regimen and antibiotics and analgesics used post operatively.

Kovac et al [13] found that 75 µg palonosetron is more effective dose for the prevention of PONV after major gynecological laparoscopic surgery than 25µg or 50 µg dose. So we selected dose of palonosetron of 75 µg.

Aspinall and Goodman[14] found that in randomized controlled trial day care surgery, single pre-induction iv dose of palonosetron 75 mcg proved to be superior to ondansetron 4mg in terms of numbers of subjects experiencing PONV episodes and the dose of rescue antiemetic required .

In our study we found that Palonosetron has a similar safety profile to other $5\text{-}HT_3$ antagonists and no difference was found in the incidence of adverse effects between both groups . The number of complete responders (no PONV episodes, no rescue medicine) were 16 (53%) in group-A and 14 (46%) in Group –B.

Conclusion:
So, we conclude that this randomized, controlled ,single blind study has shown that antiemetic efficacy of palonosetron is similar to that of Ondansetron for preventing PONV during the first 24 hrs after laparoscopic cholecystectomy.

Volume : 2 | Issue : 10 | October 2013 • ISSN No 2277 - 8179

REFERENCE

(1) Turkistani A ,Abdullah K,Manna E ,Delvi B,Khairy G,Abdulg,Ghani B,et al Effect of fluid preloading on postoperative nausea and vomiting after laparoscopic cholecyctectomy. Saudi J Anaesth 2009;348-52 | (2) Grover VK ,Mathew PJ ,Hegde H. Efficacy of orally disintegrating ondansetron in preventing postoperative nausea and vomiting after laparoscopic cholecystocomy: A randomized ,double-blind placebo controlled study. Anaesthesia 2009;64:595-600 | (3) Kloth DD. New pharmacologyc findings for the treatment of PONV and PDNV. Am J Health Syst Pharm 2009;66(1 suppl 1):S11-8. | (4) Navari RM. Palonosetron : A second generation 5-HT3 receptor antagonist. Future Oncol 2006;2:591-602 | (5) Baisakhi Laha et al. Evaluation of antiemetic effect of intravenous palolosetron versus intravenous ondansetron in laparoscopic cholecystectomy; A randomized controlled trials. Indian Journal of Pharmacology;February 2013;vol 45; Issue 1. | (6) Gan TJ. Mechanisms underlying postoperative nausea and vomiting and neurotransmitter receptor antagonist based pharmacotherapy.CNS Drugs 2007;21:813-833 | (7) Koivuranta M ,Laara E,Snare L,Alahuhta S. A survey of postoperative nausea and vomiting. Anaesthesia 1997;52:443-9 | (8) Bunce KT ,Tyres MB . The role of 5-HT in postoperative nausea and vomiting. Br.J Anaesth 1992;69 (7 supple 1):60S-2. | (9) Watcha MF.White PF .postoperative nausea and vomiting. Its etiology, treatment, and prevention. Anaesthesiology 1992;77:162-8 | (10) Habib AS , Gan TJ: Evidence-based management of postoperative nausea and vomiting : a review . Can J Anaesth 2004;51:326-341. | (11) Rojas C,Stathis M ,Thomas AG,Massuda EB,Alt J,Zhang J , et al. palonosetron exhibits unique molecular interactions with the 5-HT3 receptor . Anaesthe Analg 2008;108:469-78 | (12) Kovak al .Eberhart L,Kotasari J,Clerici G ,Apfel C. a randomized double blind study fo evaluate the efficacy and safety of three different doses of palonosetron versus placebo in preventing post operative nausea and vomiting over a 72 hrs period. Anaesth Analg 2008;107:439-44 | (13) Aspinall RL,Goodman NW. Denial of effective treatment and poor quality of clinical Information in placebo controlled trials of ondansetron for postoperative nausea and vomiting A review of published trials.Br Med J 1995;311:844-6 | (14) Park SK,Cho EJ.A randomized double blind trial of palonosetron compared with ondansetron in Preventing postoperative nausea and vomiting after gynaecological laparoscopic surgery. J IntMed Res 2011;39:399-407. | |