

Postoperative Nausea and Vomiting: Palonosetron with Dexamethasone vs. Ondansetron with Dexamethasone in Laparoscopic Hysterectomies

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ABSTRACT

Objectives: Postoperative nausea and vomiting (PONV) is the most common complication seen following laparoscopic surgery. Our study sought to evaluate the efficacy of the newer drug palonosetron with that of ondansetron, in combination with dexamethasone, for PONV in patients undergoing laparoscopic hysterectomies. **Methods:** A total of 90 patients, aged between 30–50 years old, posted for elective laparoscopic hysterectomies under general anesthesia belonging to the American Society of Anesthesiologist (ASA) physical status I and II were included in the study. Patients were randomly divided into one of two groups (n=45). Before induction, patients in the first group (group I) received 0.075mg palonosetron with 8mg dexamethasone and patients in the second group (group II) received 4mg ondansetron with 8mg dexamethasone. Postoperatively, any incidences of early or delayed vomiting, requirement of rescue antiemetic, and side effects were recorded. Patient's hemodynamics were also monitored. Statistical analysis was done using Student's *t*-test, chi-square test, and Fisher's exact test. **Results:** Preoperative, intraoperative, and postoperative heart rate, mean arterial pressure, peripheral capillary oxygen saturation were statistically not significant ($p>0.050$) in either group. In group II, eight patients had nausea in the first two hours and three patients had nausea in the two to six-hour postoperative period. In group I, three patients experienced nausea in the first six hours period. Eight patients in group II had vomited in the first two-hour period compared to one patient in group I ($p=0.013$). The requirement of rescue antiemetic was greater in group II than group I (20% vs. 4%). No side effects of antiemetic use were observed in either group. **Conclusion:** The combination of palonosetron with dexamethasone is more effective in treating early, delayed, and long term PONV compared to ondansetron with dexamethasone in patients undergoing elective laparoscopic hysterectomies under general anesthesia.

Postoperative nausea and vomiting (PONV) is the most common distressing symptom occurring after surgery.¹ Despite the advances in anesthetic and surgical techniques, PONV is still persistent. Various factors contributing to PONV include patient characteristics, anesthetic technique, type of surgery, and postoperative care.² Women undergoing laparoscopic surgeries are particularly at risk.³

Various pharmacological and non-pharmacological methods have been tried, but none has been 100 percent successful.^{4,5} The introduction of 5-hydroxytryptamine 3 (5-HT₃) receptor antagonists was a major advancement in the prevention of PONV because it had minimal side effects. Ondansetron is an example of a widely-used selective 5-HT₃ receptor antagonist.⁶ Palonosetron

is a recently introduced 5-HT₃ receptor antagonist and has better antiemetic properties, and a 5-HT₃ receptor binding affinity at least 30-fold higher than other 5-HT₃ receptor antagonists.⁷

When used in combination with ondansetron and palonosetron, dexamethasone⁸⁻¹¹ 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.¹

Our study sought to compare the effectiveness of 0.075mg palonosetron plus 8mg dexamethasone¹²⁻¹⁶ with that of 4mg ondansetron plus 8mg dexamethasone¹⁷⁻²¹ for PONV in patients undergoing laparoscopic hysterectomies. We also wanted to study the incidence of early or delayed vomiting, and the requirement of rescue antiemetics, and any side effects of these.

METHODS

This randomized, double-blind, prospective study was performed in the KVG Medical College and Hospital, India, after obtaining the ethical committee clearance. Patients were randomized into two groups of 45 patients each according to the sealed envelope technique. Patients aged between 30–50 years old, with an American Society of Anesthesiologist (ASA) physical status of I or II who were posted for elective laparoscopic hysterectomies under general anesthesia were selected for inclusion in the study.

Patients were excluded from the study for various reasons including: procedure refusal, receiving antiemetics, steroids, or psychoactive medications within 24 hours of study initiation, vomiting or retching in the 24 hours prior to surgery, having cancer chemotherapy within the last four weeks, ongoing vomiting from gastrointestinal diseases, allergy to NSAIDs, and if they had bronchial asthma.

All patients were evaluated for fitness for anesthesia one day prior to surgery. Clinical examination of the patient was performed including general physical examination and systemic examination. All patients were informed about the anesthesia technique and gave informed consent. Patients were kept nil per os (NPO) for eight hours prior to surgery. All patients were given diazepam tablet (5mg orally) the night before surgery and another 5mg in the morning.

Patients basal heart rate (HR), mean arterial pressure (MAP), peripheral capillary oxygen saturation (SpO₂) and electrocardiogram (ECG) were recorded. An intravenous line was secured with an appropriate sized cannula in all patients were preloaded with 500ml lactated Ringer's solution over 30 minutes.

Patients were premedicated with glycopyrrolate 0.2mg intravenous (iv) injection and midazolam 1mg iv injection. Group I received 0.075mg palonosetron along with 8mg dexamethasone and group II received 4mg ondansetron and 8mg dexamethasone before induction. All patients were preoxygenated for three minutes and were induced with anesthesia and 5mg/kg (2.5%) thiopentone sodium and 0.1mg/kg vecuronium 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.

Anesthesia was maintained with nitrous oxide (N₂O), oxygen (O₂), isoflurane, and controlled ventilation with the appropriate fresh gas flow. Analgesics were administered based on requirements. At the end of surgery, when patients had respiratory attempts, the residual neuromuscular blockage was reversed with neostigmine injection and glycopyrrolate. Recovery assessed and extubation was done after thorough throat suction. After complete clinical recovery, patients were shifted to the post-anesthesia care unit.

The occurrence and severity of nausea and vomiting were assessed using the visual analog scale (VAS) where a VAS score of zero indicated no nausea and a score of 10 indicated the most severe nausea. A four-point severity score was also used indicating no symptoms, mild nausea, severe nausea or up to two incidences of vomiting, and more than two incidences of vomiting.¹ Rescue antiemetic drug use was monitored immediately after surgery at zero to two hours, two to six hours, six to 24 hours and more than 24 hours postsurgery.

An episode of vomiting was defined as either vomiting (expulsion of stomach contents) or retching (an involuntary attempt to vomit but not productive of stomach contents). Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit.¹

Metoclopramide (10mg iv injection) was used as a rescue antiemetic when two episodes of PONV occurred or for a VAS greater than five where the patients requested treatment. A complete response was defined as the absence of PONV and no rescue antiemetic use.

Postoperative pain was treated with 75mg diclofenac intramuscular injection or 100ml paracetamol iv infusion.

Details of any adverse effects, including headache, dizziness, constipation, and myalgia, were recorded. The primary outcome measure of this study was the incidence of nausea and vomiting during the first 24 hours after anesthesia and up to 48 hours.

Statistical analysis was done using the Student's *t*-test, Fisher's exact test, and chi-square test with SPSS statistical software (SPSS Inc., Chicago, USA), version 17 and StatCalc software (AcaStat Software, USA). A *p*-value less than 0.050 was considered statistically significant.

RESULTS

A total of 90 patients were randomly assigned to receive either 0.075mg palonosetron or 4mg ondansetron with 8mg dexamethasone. Patients in the two groups had a similar demographic profile, and no patients were later excluded from the study. Baseline hemodynamic data were also similar in both groups. Table 1 and 2 shows age distribution and duration of surgery in both groups.

The four-point severity score^{1,22} showed that in group II, eight patients had nausea in up to two hours after surgery compared to zero patients in group I ($p=0.003$). Three patients had nausea in the two to six hours period in both groups I and II, which was not statistically significant. No patients had nausea after 24 hours.

The four-point severity score^{1,22} showed that in group II, eight patients had vomited up to two hours after surgery compared to one patient in group I ($p=0.013$). During the two to six hour and six to 24 hours postoperative period, seven patients in group II had vomited compared to three patients in group I ($p=0.179$). None of the patients vomited after 24 hours [Table 3].

Rescue medication (10mg metoclopramide iv injection) was given to 20% of the patients in group

II and only 4% of group I patients. Side effects were not observed in either group.

DISCUSSION

PONV is of multifactorial origin. The incidence of PONV after anesthesia is relatively high despite the advances in antiemetic therapy. We compared the effectiveness of palonosetron and ondansetron combined with dexamethasone in alleviating PONV in patients undergoing laparoscopic hysterectomies. Laparoscopic surgery was chosen because of the associated high incidence of PONV.²³⁻²⁷ Factors affecting PONV include patient factors (age, sex, phase of menstrual cycle), anesthesia-related factors (use of volatile agents, N₂O, opioid), and surgery-related factors (middle ear surgeries, ophthalmic surgeries, abdominal surgeries).² A higher incidence of PONV has been observed in female patients.^{2,3}

The incidence of nausea in our study was 8.8% for group I and 24.0% for group II. Eight patients in group II had nausea in the first two hours postoperatively compared to no patients in group I. During the two to six hour period, three patients in both groups had nausea. No patients had nausea after six hours and up to 48 hours in either group.

A study by Pueyo et al,¹⁷ observed that nausea and vomiting were more frequent in the first six hours postoperatively. The same results were observed in the study done by Fujii et al.²⁴ In our study, the incidence of vomiting was statistically significant in the first two hours ($p=0.013$) and not significant from then onwards. Rescue medication was also higher in group II than group I.

Our study suggests that palonosetron with dexamethasone is better than ondansetron with dexamethasone in preventing PONV. Even though ondansetron with dexamethasone was more cost effective, palonosetron with dexamethasone was more efficacious in preventing PONV.

Table 1: Age distribution in group I and II.

	Mean age (years)	SD	p-value
Group I	37.8	8.5	0.478
Group II	39.1	8.8	

SD: standard deviation.

Table 2: Duration of surgery in group I and II.

	Mean duration (minutes)	SD	p-value
Group I	119.7	24.8	0.712
Group II	118.0	18.3	

SD: standard deviation.

Table 3: Incidence of nausea and vomiting in group I and II.

Time (hours)	Nausea			Vomiting		
	Group I	Group II	p-value	Group I	Group II	p-value
0-2	0	8	0.003	1	8	0.013
2-6	3	3	1.000	3	7	0.179
6-24	0	0	NA	3	7	0.179
>24	0	0	NA	0	0	NA

NA: not applicable

In our study, which was done within 48 hours of operative intervention, the loss of follow-up was almost nil since each patient was monitored on an hourly basis. There were no deaths encountered in the study, so the question of censored data does not exist, and survival analysis was not performed. However, the limitation of the statistical method used was that we could not determine if those patients with nausea in the zero to two hours period were the same as those who had nausea in the two to six hours period. However, whenever patients had nausea, rescue antiemetic was given, so we can assume that the three patients in the two to six hour period were different from the eight patients in zero to two hours period. The same assumption applies to the other hourly groups (six to 24 hours and more than 24 hours).

CONCLUSION

Palonosetron when combined with dexamethasone, was more effective in preventing PONV compared to ondansetron with dexamethasone in patients undergoing laparoscopic hysterectomies under general anesthesia. The need for rescue medication is also minimal in patients given palonosetron compared to those given ondansetron. Thus, palonosetron is an effective alternative to ondansetron when combined with dexamethasone in preventing PONV.

Disclosure

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REFERENCES

- Christian c. Apfel, Post operative nausea and vomiting, Millers anesthesia. Chapter 86, 7th edition, 2010; 2739-40.
- Gold BS, Kitz DS, Lecky JH, Neuhaus JM. Unanticipated admission to the hospital following ambulatory surgery. JAMA 1989 Dec;262(21):3008-3010.
- Honkavaara P, Lehtinen AM, Hovorka J, Korttila K. Nausea and vomiting after gynaecological laparoscopy depends upon the phase of the menstrual cycle. Can J Anaesth 1991 Oct;38(7):876-879.
- Habib AS, Gan TJ. Evidence-based management of postoperative nausea and vomiting: a review. Can J Anaesth 2004 Apr;51(4):326-341.
- Gan TJ, Diemunsch P, Habib AS, Kovac A, Kranke P, Meyer TA, et al; Society for Ambulatory Anesthesia. Consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg 2014 Jan;118(1):85-113.
- Culy CR, Bhana N, Plosker GL. Ondansetron: a review of its use as an antiemetic in children. Paediatr Drugs 2001;3(6):441-479.
- Rojas C, Stathis M, Thomas AG, Massuda EB, Alt J, Zhang J, et al. Palonosetron exhibits unique molecular interactions with the 5-HT₃ receptor. Anesth Analg 2008 Aug;107(2):469-478.
- Aapro MS, Alberts DS. Dexamethasone as an antiemetic in patients treated with cisplatin. N Engl J Med 1981 Aug;305(9):520.
- Wang JJ, Ho ST, Liu YH, Lee SC, Liu YC, Liao YC, et al. Dexamethasone reduces nausea and vomiting after laparoscopic cholecystectomy. Br J Anaesth 1999 Nov;83(5):772-775.
- Rüsch D, Arndt C, Martin H, Kranke P. The addition of dexamethasone to dolasetron or haloperidol for treatment of established postoperative nausea and vomiting. Anaesthesia 2007 Aug;62(8):810-817.
- Bisgaard T, Klarskov B, Kehlet H, Rosenberg J. Preoperative dexamethasone improves surgical outcome after laparoscopic cholecystectomy: a randomized double-blind placebo-controlled trial. Ann Surg 2003 Nov;238(5):651-660.
- Maemondo M, Masuda N, Sekine I, Kubota K, Segawa Y, Shibuya M, et al; PALO Japanese Cooperative Study Group. A phase II study of palonosetron combined with dexamethasone to prevent nausea and vomiting induced by highly emetogenic chemotherapy. Ann Oncol 2009 Nov;20(11):1860-1866.
- Blitz JD, Haile M, Kline R, Franco L, Didehvar S, Pachter HL, et al. A randomized double blind study to evaluate efficacy of palonosetron with dexamethasone versus palonosetron alone for prevention of postoperative and postdischarge nausea and vomiting in subjects undergoing laparoscopic surgeries with high emetogenic risk. Am J Ther 2012 Sep;19(5):324-329.
- Ghosh S, Pal A, Acharya A, Biswas C, Ghosh TR, Ghosh S. Palonosetron and palonosetron plus dexamethasone to prevent postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy: A prospective, randomized, double-blind comparative study. Anesth Essays Res 2011 Jul-Dec;5(2):134-137.
- Park JW, Jun JW, Lim YH, Lee SS, Yoo BH, Kim KM, et al. The comparative study to evaluate the effect of palonosetron monotherapy versus palonosetron with dexamethasone combination therapy for prevention of postoperative nausea and vomiting. Korean J Anesthesiol 2012 Oct;63(4):334-339.
- Keith ACandiotti, Syed Raza Ahmed, David Cox, Tong J Gan BMC pharmacology and toxicology 2014, 15:4517.16. Keith A Candiotti., Syed Raza Ahmed, David Cox, Tong J Gan. BMC pharmacology and toxicology 2014, 15:45.
- López-Olaondo L, Carrascosa F, Pueyo FJ, Monedero P, Busto N, Sáez A. Combination of ondansetron and dexamethasone in the prophylaxis of postoperative nausea and vomiting. Br J Anaesth 1996 Jun;76(6):835-840.
- Rajeeva V, Bhardwaj N, Batra YK, Dhaliwal LK. Comparison of ondansetron with ondansetron and dexamethasone in prevention of PONV in diagnostic laparoscopy. Can J Anaesth 1999 Jan;46(1):40-44.
- Thomas R, Jones N. Prospective randomized, double-blind comparative study of dexamethasone, ondansetron, and ondansetron plus dexamethasone as prophylactic antiemetic therapy in patients undergoing day-case gynaecological surgery. Br J Anaesth 2001 Oct;87(4):588-592.
- Elhakim M, Nafie M, Mahmoud K, Atef A. Dexamethasone 8 mg in combination with ondansetron 4 mg appears to be the optimal dose for the prevention of nausea and vomiting after laparoscopic cholecystectomy. Can J Anaesth 2002 Nov;49(9):922-926.
- Song JW, Park EY, Lee JG, Park YS, Kang BC, Shim YH. The effect of combining dexamethasone with ondansetron

- for nausea and vomiting associated with fentanyl-based intravenous patient-controlled analgesia. *Anaesthesia* 2011 Apr;66(4):263-267.
22. Boogaerts JG, Vanacker E, Seidel L, Albert A, Bardiau FM. Assessment of postoperative nausea using a visual analogue scale. *Acta Anaesthesiol Scand* 2000 Apr;44(4):470-474.
 23. Klockgesthes-Radke A, Piorek V, Crozier TC, Kettler D. Nausea and vomiting after laparoscopic surgery: A comparison of propofol and thiopentone/halothane anaesthesia. *Eur J anaesthesiol* 1996 Jan;13:3-9.
 24. Fujii Y, Saitoh Y, Tanaka H, Toyooka H. Ramosetron vs granisetron for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. *Can J Anaesth* 1999 Oct;46(10):991-993.
 25. 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 Int Med Res* 2011;39(2):399-407.
 26. Laha B, Hazra A, Mallick S. Evaluation of antiemetic effect of intravenous palonosetron versus intravenous ondansetron in laparoscopic cholecystectomy: a randomized controlled trial. *Indian J Pharmacol* 2013 Jan-Feb;45(1):24-29.
 27. Kim YY, Moon SY, Song DU, Lee KH, Song JW, Kwon YE. Comparison of palonosetron with ondansetron in prevention of postoperative nausea and vomiting in patients receiving in-travenous patient controlled analgesia after gynecological laproscopic surgery. *Korean J Anaesthesia* 2013 Feb;64(2):122-126 .