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Study Comparing High Dose Palanosetron 0.05mg with Low Dose Palanosetron 0.025mg Plus 4mg Dexamethasone as Adjuvant for Prevention of Post-Operative Nausea and Vomiting in Laparoscopic Hysterectomies - A Double Blinded Study

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Abstract

Background: Post op nausea and vomiting is one of the most distressful complications after surgical procedure. The complication of same is very complex but laproscopic surgeries are one of the major reasons. Various agents have been found helpful to deal with this. But keeping in mind the long duration and late showing off of this side effect long acting 5HT3 acting antagonist were invented like palanosetron. But its high cost made its utility less common, so in order to cut down the cost without comprising on effect adjuvants like dexamethasone were used. The aim is to compare 0.05mg palanosetron with 0.025mg palanosetron with 4mg dexamethasone to prevent post op nausea and vomiting in lapros copic surgeries. **Material and Methods:** This study was a randomised, prospective, trial done on 100 adults, A.S.A. Grade I to II patients, age18– 65 years going for laparoscopic hysterectomy. They were sent to two groups which got either of the treatment regimens: Palanosetron 50 microgram (Gr P, number = 50) or dexamethasone four milligram plus palanosetron 25 microgram (Gr PD, number = 50). The main outcome was number of PONV cases in 24 hour and the secondary outcome included number of rescue antiemetic required. Student's t test used to analyze normally distributed data. Mann Whitney-U test applied for skewed data. Chi-square / Fisher exact test whatsoever was applicable was applied to Qualitative /categorical variables. All tests done were two-sided and performed keeping a significance level of 0.05. **Results:** There was no significant difference in the two groups (P>0.05) in terms of incidence of nausea, vomiting, retching, patient satisfaction and even side effects. **Conclusion:** 0.025mg palanosetron with 4 mg dexamethasone and 0.05mg Palanosetron are equally effective to prevent post op nausea vomiting plus more cost effective.

Keywords: PONV, Laproscopic, palanosetron, dexamethasone, 5HT3 antagonist, adjuvant.

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INTRODUCTION

One of the most upsetting side effects of anaesthesia and surgery, postoperative nausea and vomiting (PONV), affects an unacceptably high percentage of patients.[1] Due to its intricate mechanism and the careless behaviour of both patients and doctors, it has significantly raised the cost and toll of patient release delays. Unattended PONV increases the risk of cerebral hypertension, pneumothorax, stomach aspiration, wound dehiscence, postoperative haemorrhage, and electrolyte imbalance. In addition, it may cause the patient to feel more pain, be dissatisfied, experience dysphoria, and have a generally negative stay. PONV is described as nausea or vomiting that occurs within the first 24 hours of leaving the post-anesthesia care unit.

Every patient now chooses laparoscopic surgery because it results in a shorter hospital stay, an earlier return to work, and a return to regular activities with less pain from the smaller incision and less postoperative ileus.[2,3] Laparoscopic hysterectomies, for instance, have altered surgeons' operating and thinking styles in less than ten years since Phillipe Mouret performed the first one in Lyon, France, in March 1987. As a result, they have become the de facto method for removing uteruses. However, one of the most frequent and upsetting side effects is postoperative nausea and vomiting (PONV). According to surgical, anaesthetic, and patient-related risk variables, the incidence of PONV after LH ranges from 53% to 72%.[4] Therefore, the issue of PONV is

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increasingly necessary to be handled with with more recent drugs and modalities that are not only patient free but also patient pocket friendly due to the patients' rising need for laproscopic surgery.

The pathophysiology of PONV is complicated, and a review has revealed that a number of risk variables, including age, female gender, obesity, nonsmoking status, history of motion sickness, inhalational anaesthetics, length of operation, and anaesthesia, may be involved. Cholinergic (muscarinic), dopaminergic (D2), histaminergic (H1), and serotonergic (5-hydroxytryptamine type 3 [5-HT3]) receptors are some of the receptors on which antiemetics act. Palanosetron's inclusion in the class of 5-HT3 receptor antagonists was a praiseworthy achievement; it is a prospective longer-acting drug with a plasma half-life of around 40 hours and a substantially higher affinity for the 5-HT3 receptor than other "setrons".[5]

Palanosetron has been shown in recent studies to have a unique ability to increase the long-term internalisation of 5-HT3 receptors in neurons and to reduce the effects of substance P on NK1 receptors, most likely through indirect pathways. Due to the fact that palanosetron's effectiveness is dosage dependant, the dose was raised with the hope that it will further reduce the rate of PONV. However, as palonosetron is relatively pricey (138 Rs. for 25 microg), increasing the dose may result in higher costs for the patient. It is well known that multimodal antiemetic medication is more successful at treating PONV.[6,7]

As a result, we combined dexamethasone, which inhibits the release of arachidonic acid and the production of several inflammatory chemicals that sensitise the neurons that regulate emesis. Therefore, it was hypothesised that multimodal therapy, as compared to monotherapy utilising a larger dose of palanosetron, could achieve equal efficacy and cost less. Furthermore, research indicates that glucocorticoids have a direct inhibitory impact on 5-HT3 receptors[8], which accounts for their synergistic action when used in conjunction with 5-HT3 receptor antagonists. To avoid post-operative nausea and vomiting, the Society for Ambulatory Anaesthesia (SAMBA) recommendations advise using a 4 mg dose either alone or in combination with any other medication.

One ampoule of dexa costs Rs. 4.23/4mg. Dexamethasone and 25 microg of palanosetron were therefore coupled, greatly increasing the cost-effectiveness of the treatment. Studies on palanosetron with adjuvants [9] have found that combining two medications not only lengthens the duration of palanosetron's activity but also reduces the need for rescue antiemetics and improves patient satisfaction scores. There hasn't been any research comparing high dose palanosetron with dexamethasone or low dose palanosetron. We decided to use this combination in order to research how these medications interact with one another.

AIM and OBJECTIVES

AIM- To study comparison between 0.05mg palanosetron with 0.025mg palanosetron with 4mg dexamethasone as adjuvant to prevent post-operative nausea and vomiting

Objectives-

- To count incidence of nausea and vomiting at 30min, 2, 8, 24,36,48 h using four point scoring system
- To study patient satisfaction score.
- To calculate total dose of rescue antiemetics required.
- To study any side effects of drugs used.

Subjects and Approaches

We studied 100 individuals after receiving ethical permission from the institute and the patients' informed consent. American Society of Anesthesiologists (ASA) physical Status I and II patients between the ages of 18 and 65, weighing between 40 and 80 kg, and scheduled for an elective laparoscopic hysterectomy under GA meet the inclusion criteria. The investigation was prospective, randomised, and double-blind.

Among the exclusion criteria were:

- Kidney or gastrointestinal illness
- Who got emetogenic radiation within the previous eight weeks or cancer treatment within the last four weeks,
- Those who had ever felt queasy
- Epilepsy and cardiovascular impairment
- Patients who used antiemetic medicine within 24 hours of surgery were disqualified from the research.

METHODOLOGY

The patients were divided into two groups, P and PD, using computer-generated numbers contained within chits. Patients in Group P received 0.05 mg of palonosetron.

The dosage for Group PD was 0.025 mg palonosetron and 4 mg dexamethasone.

The medications were produced by a single physician who was not involved in the trial, using identical 20ml syringes that contained either 0.05 mg or 0.025 mg of palonosetron and 4mg of dexamethasone (total volume of

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20ml made with normal saline). It was already known that the study medications worked well together when combined and given right before anaesthesia was induced.
Senior anesthesiologist who administered general anaesthesia while using the research medicine was unaware of the substance's kind and declined to take part in the study.
All patients had general anaesthesia according to a set regimen that was used in the institute.
8 hours were observed when fasting.
Premedication Inj.Midazolam 1.5mg, Inj.glycopyrolate 0.2 mg, and
Inj.fentanyl 2 mcg/kg given by intravenous (IV) route, before start of the anesthetic procedure.
Monitoring – pulse rate, non-invasive blood pressure, electrocardiography ECG, oxygen saturation, and end-tidal carbon dioxide (ET CO2)
The study drugs were given slow IV, just before induction of anesthesia.
Patients were pre-oxygenated with oxygen for 3 min, Induction - IV Propofol 1.5mg/kg, followed by IV vecuronium 0.08 mg/kg and direct laryngoscopy with intubation by endo-tracheal tube of appropriate size.
Oro-gastric tube was introduced after intubation and suction through tube was done.
Maintenance- 33% oxygen with nitrous oxide with 0.5-1.5% isoflurane and 8 liters of total gas flow.
Inj vecuronium was repeated at 0.01mg/kg and Inj fentanyl 1 mcg/kg at 30-min interval.
Controlled - Ventilation was done to maintain ET CO2 at 30- 35 mm Hg. Intra-abdominal pressure was maintained below 15 mm Hg.
Analgesia - Inj tramadol 100 mg IV was given to all patients, 30 min before the end of surgery.
At finish of the operation, residual neuromuscular blockade was antagonized with Inj neostigmine 0.05 mg/kg with glycopyrolate (0.2 mg for each 1 mg of neostigmine).
After suctioning of the oropharynx and adequate recovery from GA as per clinical observation extubation was done. Patient conscious, oriented and responding was sent to post anaesthesia care unit (PACU) and oxygen was administered at 3 l/min. There was provision of rescue analgesic in the form of IV paracetamol 1 g (100 ml).
Patients were inquired about nausea, vomiting, retching and any side-effects, at 30min, 2, 8, 24, 36, 48 h by an investigator; who was blinded to the study.
PONV measurement scale-was measured on a four-point (1- 4) scoring system.
Score 1 = no nausea /retching;
2= complaining of nausea/ retching;
3= vomiting less than two times in 30 min;
4= vomiting more than an two times in 30 min.
Nausea was characterised as – unpleasant sensation characterized by gastrointestinal distress and an urge to vomit.
Retching was defined as the labored, spastic, rhythmic contraction of the respiratory muscles without the expulsion of the gastric contents.
Vomiting was defined as the forceful expulsion of gastric contents from the mouth. The number of patients in each category were recorded. If PONV score was 2 or more, IV ondansetron 4 mg was given as rescue anti-emetic.
Any need for rescue drug and side-effects like headache, dizziness and drowsiness were noted.

Statistial Analysis
The statistical analysis was performed with the SPSS 15.0 software. All quantitative variables were estimated using measures of central location and measures of dispersion. The normally distributed data were compared using Student's t test. For comparison of skewed data Mann Whitney-U test was applied. Qualitative or categorical variables were described as frequencies and compared with Chi-square or Fisher exact test whichever was applicable. All statistical tests were two-sided and were performed at a significance level of 0.05. Sample size was calculated on the basis of previous studies presuming at least 25% difference in the incidence of postoperative vomiting between groups, with α=0.05 and β=0.80 showed that 42 patients were required in each group. Thus, we took 50 patients in both group to take into account drop outs.

RESULTS
There was no significant difference between the two groups with respect to age, height, weight, PONV risk factors and ASA status.
In terms of the time spent in surgery and CO2 insufflation, groups were evenly matched. On the table, the hemodynamic parameters and the fluid presented were comparable. According to [Table 2], there was no discernible difference in the incidence of post-operative nausea and vomiting between the two groups. Age and gender did not significantly differ between the two groups when evaluated as risk variables. The amount of rescue antiemetic needed was comparable. [Table 3]. Group pD required fewer rescue analgesics than group P.

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Three patients in group P and one patient in group pD reported experiencing headaches and palpitations as a side effect, however this is likely due to their very worried personalities. As a result, both high dose palano (0.05 mg) and low dose palanosetron with dexa were equally effective in preventing postoperative nausea and vomiting.

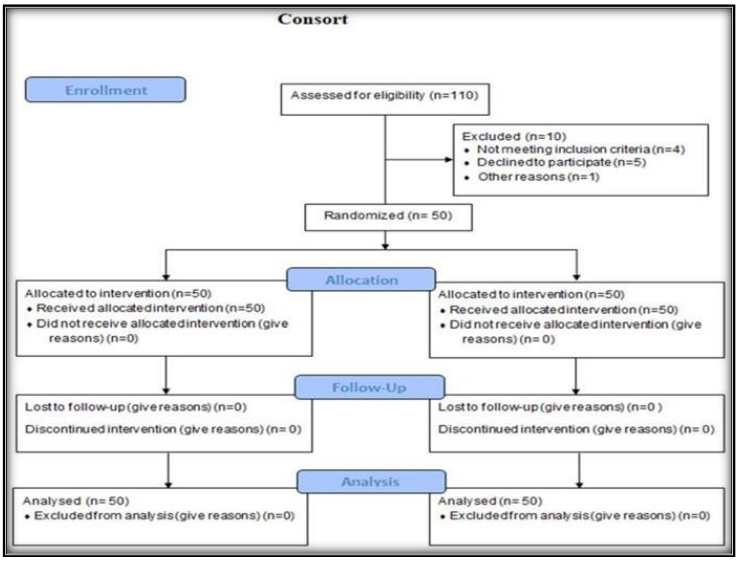

Figure 1: Consort Flow diagram

Table 1: Demographic data and intraoperative data.

Parameter	Group P (50)	Group D(50)	P value
PONV Immediately			
1	45(90%)	43(86%)	0.008
2	3(6%)	5(10%)	0.129
3	1(2%)	1(2%)	0.012
4	1(2%)	1(2%)	0.012
PONV 30min			
1	48(96%)	46(92%)	0.041
2	2(4%)	2(4%)	0.028
3	0	1(2%)	0.012
4	0	1(2%)	0.012
PONV 2hr			
1	49(98%)	48(96%)	0.045
2	1(2%)	1(2%)	0.012
3	0	1(2%)	0.033
4	0	0	
PONV 4hr			
1	50(100%)	49(98%)	0.046
2	0	1(2%)	0.012
3	0	0	
4	0	0	
PONV 8hr			
1	49(98%)	48(96%)	0.045
2	1(2%)	1(2%)	0.012
3	0	1(2%)	0.033
4	0	0	
PONV 16hr			
1	46(92%)	47(94%)	0.026
2	3(6%)	2(4%)	0.007
3	1(2%)	1(2%)	0.012
4	0	0	
PONV 32hr			

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1	43(86%)	44(88%)	0.014
2	3(6%)	3(6%)	0.032
3	3(6%)	2(4%)	0.007
4	1(2%)	1(2%)	0.012

Table 2: Comparison of incidence of post operative nausea and vomiting among the two groups.

Parameter	Group P	Group D	P value
Age(yr)	41.06+10	40.84+12	0.006
Gender (M:F)	10:40	12:38	0.128
Weight(kg)	63.02±11.70	59.67±7.05	0.009
Height(cm)	158.40± 3.46	160.02±4.69	0.101
ASA Grade	34:16	40:10	0.201
Durationof surgery(mins)	68.33±12.30	63.49±15.79	0.007
Duration of CO2 insufflation (min)	55.50±11.01	56.52±14.2	0.014

Table 3: Comparison between confounding factors for PONV and use of rescue antiemetics as well analgesics.

Parameters (PONV)	Group P	Group D	P value
Age<60yrs	4(45)	6(48)	0.076
Age>60yrs	3(5)	1(2)	0.089
Male	2(10)	1(5)	0.068
Female	5(40)	6(45)	0.097
Rescue antiemetics in 48hrs	10	12	0.065
Analgesic use	40	25	0.04
Adverse effects	1	2	0.09

Table 4: Showing patients satisfaction after both group drug.

Satisfaction score	Group P	Group D	P value
Satisfied	40	38	0.074
Neutral	3	5	0.082
Not satisfied	7	7	0.09

DISCUSSION

When no prophylactic antiemetic is given, the incidence of PONV in patients undergoing laparoscopic hysterectomy has been reported to be between 53 and 75 percent.[10] Although the exact cause of PONV is unknown, it is most likely caused by intraperitoneal CO2 insufflation, which stretches and irritates the peritoneum.[11] Compared to other 5-HT3 antagonists, palonosetron has a higher receptor affinity and stronger binding to 5-HT3 receptors. It also has a longer half life (40 hours). Additionally, palonosetron demonstrates antinauseatic properties.[12] The typical dosage for palanosetron is 0.05mg administered three times each day, making the overall cost relatively high.

In order to reduce the cost factor without compromising the effect of the treatment, we tried to add dexamethasone as an adjuvant to palanosetron at a dose of 0.025 mg and compare the results to those of high dose palanosetron.

Dexamethasone can potentiate the effect of other antiemetics by various mechanisms like, prostaglandin antagonism, release of endorphins and bradykinin reduction.

In individuals at high risk for PONV, combination therapy with dexamethasone and 5-HT3 antagonists, including ondansetron, granisetron, ramosetron, and dolasetron, appears to be more successful than single-drug prophylaxis.

Due to the lack of research comparing palanosetron at low and high doses, our study's findings were contrasted with indirect findings from other investigations. In a recent trial, ramosetron and dexamethasone combined were found to be superior to ramosetron alone, with 93% of patients in the combination group exhibiting a full response after 12–24 hours following laparoscopic cholecystectomy. In a second trial, between 0 and 24 hours, 18 (42.9%) patients in group P complained of nausea, while 5 (11.9%) patients in group DP experienced nausea and 6 (14.4%) patients reported vomiting. This is comparable to both of our groups, where about 5% of patients reported experiencing nausea and vomiting.

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nausea, while 5 (11.9%) patients in group DP experienced nausea and 6 (14.4%) patients reported vomiting. This is comparable to both of our groups, where about 5% of patients reported experiencing nausea and vomiting.

In a research by Chatterjee A,[13] overall incidences of PONV were 23.4% in the PD group, 27.2% in the P group, and 56.14% in the D group in the first 24 hours following surgery. In our investigation, neither low dose palanosetron with dexamethasone nor high dosage palanosetron significantly affected PONV in either group (at 16 hours, 8% in group P and 6% in group pD reported PONV). In the study by BALA I et al,[14] 33.3% of patients receiving only palanosetron reported vomiting during 0–24 hours, compared to 11.9% of patients in the group receiving palanosetron and dexamethasone together. Similar outcomes were observed in both of our groups, demonstrating no significant differences between the two groups, demonstrating the usefulness of dexamethasone and full-fledged use of low-dose palanosetron.

Dexamethasone was also added to palanosetron, which decreased the need for rescue antiemetic medication and was linked to higher patient satisfaction. There was no discernible difference in PONV between the groups in the Park et al,[15] study comparing palanosetron with palanosetron and dexamethasone 4 mg combination in gynaecological laparoscopic procedures. In the palanosetron and combination groups, the incidence of PONV was 9.8% and 14%, respectively. In patients undergoing outpatient laparoscopic surgeries, Blitz et al,[16] compared 0.075 mg palanosetron and 8 mg dexamethasone combination therapy with palanosetron monotherapy and reported low incidences of PONV in both groups (Pal+Dex, 1.7%; Pal, 6.8%), with no increase in side effects profiles due to the use of 8mg dexamethasone.

As a result of their non-smoking habits, gender, and laparoscopic surgery, our patients had a significant risk of PONV. All of these characteristics were, however, fairly distributed among the groups. In our investigation, there were no significant negative side effects in any patient group. Additionally, both groups used rescue analgesia at similar rates. Both patient groups reported feeling equally satisfied. One encouraging finding from our trial was that patients who received dexamethasone required fewer rescue analgesics than those who did not, which may be related to its anti-inflammatory properties.

CONCLUSION

As both the groups one receiving 0.05mg palanosetron andother using 0.025mg palanosetron plus 4mg dexamethasone had similar effects thus addition of adjuvant to low dose of palanosetron cuts down the cost three times but leads to no compromise on patients comfort as well as no adverse effect.

REFERENCES

1. Halliday TA, Sundqvist J, Hultin M, Walldén J. Postoperative nausea and vomiting in bariatric surgery patients: An observational study. Acta Anaesthesiol Scand 2017;61:471-9.
2. Choi PW. Pneumomediastinum, Pneumothorax, and Subcutaneous Emphysema Caused by Colonoscopic Perforation: A Report of Two Cases. J Emerg Med. 2017 ;52(4):e117-e122.
3. Elias S, Kuint R, Levy I, Ben-Yehuda A, Berkman N, Muszkat M. Massive subcutaneous emphysema in a long-term ventilated patient. QJM. 2015 ;108(1):67-8.
4. Larsson S, Lundberg D. A prospective survey of postoperative nausea and vomiting with special regard to incidence and relations to patient characteristics, anesthetic routines and surgical procedures. Acta Anaesthesiol Scand 1995;39:539□45.
5. Yoo JH, Jeon IS, Chung JW, Ryoo JH, You GW, Kim SI. Comparison of palonosetron and ondansetron to prevent postoperative nausea and vomiting in women using intravenous patient-controlled analgesia. Anesth Pain Med (Seoul). 2020 Jan 31;15(1):28-34.
6. Rajnikant K, Bhukal I, Kaloria N, Soni SL, Kajal K. Comparison of Palonosetron and Dexamethasone with Ondansetron and Dexamethasone to Prevent Postoperative Nausea and Vomiting in Patients Undergoing Laparoscopic Cholecystectomy. Anesth Essays Res. 2019 ;13(2):317-322.
7. Jo YY, Lee JW, Shim JK, Lee WK, Choi YS. Ramosetron, dexamethasone, and their combination for the prevention of postoperative nausea and vomiting in women undergoing laparoscopic cholecystectomy. Surg Endosc 2012;26:2306- 11.
8. Weibel S, Rücker G, Eberhart LH, Pace NL, Hartl HM, Jordan OL, Mayer D, Riemer M, Schaefer MS, Raj D, Backhaus I, Helf A, Schlesinger T, Kienbaum P, Kranke P. Drugs for preventing postoperative nausea and vomiting in adults after general anaesthesia: a network meta-analysis. Cochrane Database Syst Rev. 2020 19;10(10):CD012859.
9. Feo CV, Sortini D, Ragazzi R, De Palma M, Liboni A. Randomized clinical trial of the effect of preoperative dexamethasone on nausea and vomiting after laparoscopic cholecystectomy.Br J Surg 2006;93:295-9.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 06, 2023

10. Mitchell C, Cheuk SJ, O'Donnell CM, Bampoe S, Walker D. What is the impact of dexamethasone on postoperative pain in adults undergoing general anaesthesia for elective abdominal surgery: a systematic review and meta-analysis. Perioper Med (Lond). 2022 . 24;11(1):13.
11. Cho HB, Park SY, Kim N, Choi SJ, Song S, Yoo JH, Kim MG, Chung JW. Effect of anesthetics on postoperative nausea and vomiting after peripheral vascular surgery in end-stage renal disease patients: A retrospective observational study. Front Surg. 2022 Nov 23;9:1054670.
12. Dey S, Chanu SM, Dev P, Borthakur M, Karim HMR, Yunus M. Antiemetic Efficacy of Palonosetron Compared with the Combination of Ondansetron and Dexamethasone for Prevention of Postoperative Nausea and Vomiting in Patients Undergoing Laparoscopic Gynaecological Surgery. Rom J Anaesth Intensive Care. 2022 Sep 25;28(1):19-24.
13. Chatterjee S,Rudra A, Sengupta S.Current concepts in the management of postoperative nausea and vomiting.Anesthesiol Res Pract.2011;2011:748031.doi:10.1155/2011/748031.Epub 2011 Nov 3.
14. Bala I, Bharti N, Murugesan S, Gupta R. Comparison of palanosetron with palanosetron – dexamethasone combination for prevention of postoperative nausea and vomiting in patients undergoing laproscopic cholecystectomy.Minerva Anestesiol.2014;80:779-84.
15. Park JW ,Jun JW, Lim YH, Lee SS, Yoo BH, Kim KM, et al.The comparative study to evaluate the effect of palanosetron monotherapy versus palanosetron with dexamethasone combination therapy for prevention of postoperative nausea and vomting.Korean J Anesthesiol.2012;63:334-39.
16. Blitz JD, Haile M, Kline R, Franco L, Didehvar S, Pachter HL, et al.A randomised double blind study to evaluate efficacy of palanosetron with dexamethasone versus palanosetron alone for prevention of postoperative and postdischarge nausea and vomiting in subjects undergoing laproscopic surgeries with emetogenic risk.Am J Ther.2012;19:324-29.