Comparative study between ondansetron vs Palonosetron for controlling postoperative nausea and vomiting.

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Abstract

Postoperative nausea and vomiting (PONV) is a major complication in patients who undergo surgery under general anaesthesia. Various drug regimens and antiemetic interventions have been tried from time to- time for prevention of PONV but with a variable success rate. The aim of the study is to compare between ondansetron vs Palonocstron for controlling postoperative nausea and vomiting. In this prospective study, 100 patients aged 18-60 years of ASA GRADE-I and II scheduled for undergoing surgery under general anaesthesia after taking informed written consent at a tertiary care hospital, were randomly divided into two groups of 50 each .Group-A was given palonosetron 75 µg and Group–B was given ondansetron 4 mg. At 72 hours, nausea and vomiting were statistically significant between ondansetron and palonosetron groups. Postoperative side-effects such as headache, dizziness and drowsiness were not statistically significant between ondansetron and palonosetron groups. In conclusion, the antiemetic efficacy of palonosetron is similar to that of Ondansetron for preventing PONV during the first 24 hours after patients who undergo surgery under general anaesthesia. But after 72 hours, nausea and vomiting were statistically higher in ondansetron group than palonosetron group.

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Introduction

Post-operative nausea and vomiting (PONV) is commonly seen in female patients undergoing abdominal surgeries under general anaesthesia.[1] Postoperative nausea and vomiting (PONV) is a major complication in patients who undergo surgery under general anaesthesia. Various drug regimens and antiemetic interventions have been tried from time to- time for prevention of PONV but with a variable success rate. This study compares the safety and efficacy of ondansetron and palonosetron in preventing PONV in such patients.[2] 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 hours) following laparoscopic cholecystectomy.[3,4]

PONV is defined as any nausea, retching or vomiting occurring during the first 24-48 hours after surgery in inpatients. Though often temporary, it is unpleasant, with reported incidences of 30% in all post-surgical patients

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and up to 80% in high-risk patients.[5] In the recovery room 20% of patients suffer with nausea and 5% with vomiting while even thereafter, 50 % suffer with nausea and 25% with vomiting.[6]

Methods

In this prospective study, 100 patients aged 18-60 years of ASA GRADE-I and II scheduled for surgery under general anaesthesia after taking informed written consent at a tertiary care hospital, were randomly divided into two groups of 50 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 hours 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, ETCO2, 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 O2, N2O and sevoflurane. Muscle relaxation was maintained with intermittent dose of Inj. Atracurium. Ventilation was controlled and adjusted to maintain the ETCO2 between 35-40 mm of Hg. A nasogastric tube was inserted to make the stomach empty of air and other contents. All patients were received Inj. Diclofenac sodium 75 mg IM 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 number of PONV episodes in the 24 hours period following conclusion of surgery. Visual analogue score (as assessed using a 10 cm Nausea severity scale) at 2, 6 and 24 hours 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. Safety of the study drugs was assessed by monitoring vital signs, O2 saturation, ECG and examination and asking the patients for adverse events for 24 hours following surgery. The results were expressed in mean±SD and number (%).

Result

Age, sex, ASA grade, weight, duration of surgery and duration of anesthesia were not statistically significant between ondansetron and palonosetron groups (Table 1). At 72 hour, nausea and vomiting were statistically significant between ondansetron and palonosetron groups (Table 2). Postoperative side-effects such as headache, dizziness and drowsiness were not statistically significant between ondansetron and palonosetron groups (Table 3).

Table-1 : Demographic characteristic of the study patients

Demographic characteristics	Ondansetron (n=50)		Palonosetron (n=50)		p value
Sex (Male/ Female)	8	/42	6	/44	$^{a}0.56^{ns}$
ASA grade (I/II)	40	/10	42	/8	$^{a}0.60^{ns}$
Age in years (Mean±SD)	38.4	±10.4	40.3	±12.1	$^{b}0.40^{ns}$
Weight in kg (Mean±SD)	61.0	±9.4	58.2	±10.7	$^{b}0.16^{ns}$
Duration of surgery in mins (Mean±SD)	64.9	±33.8	66.7	±32.9	$^{b}0.78^{ns}$
Duration of anesthesia in mins (Mean±SD)	110.3	±29.4	114.7	±32.9	$^{b}0.48^{ns}$

ns= not significant
[a]P value reached from chi square test
[b]P value reached from unpaired t-test

Table-2: Incidence of postoperative nausea and vomiting (PONV) and need for rescue antiemetics.

Demographic characteristics	Ondansetron (n=50)		Palonosetron (n=50)		p value
0-2 hour					
Nausea	10	20.0	7	14.0	0.424^{ns}
Vomiting	2	4.0	2	4.0	0.691^{ns}
PONV	12	24.0	7	14.0	0.202^{ns}
Rescue antiemetics	4	8.0	3	6.0	0.500^{ns}
0-24 hour					
Nausea	18	36.0	9	18.0	0.043^{s}
Vomiting	7	14.0	4	8.0	0.338^{ns}
PONV	21	42.0	13	26.0	0.091^{ns}
Rescue antiemetics	10	20.0	9	18.0	0.799^{ns}
0-72 hour					
Nausea	25	50.0	15	30.0	0.041^{s}
Vomiting	11	22.0	4	8.0	0.049^{s}
PONV	27	54.0	19	38.0	0.108^{ns}
Rescue antiemetics	15	30.0	14	28.0	0.826^{ns}

s= significant, ns= not significant
P value reached from chi square test

Table-3: Incidence of adverse events.

Adverse events	Ondansetron (n=50)		Palonosetron (n=50)		p value
Dizziness	12	24.0	8	16.0	0.31^{ns}
Headache	10	20.0	7	14.0	0.42^{ns}
Drowsiness	5	10.0	6	12.0	0.74^{ns}

ns= not significant
P value reached from chi square test

Discussion

In present study observed that the age, sex, ASA grade, weight, duration of surgery and duration of anesthesia were not statistically significant between ondansetron and palonosetron groups. In study of Singh et al.[7] observed that the baseline demographic profile and clinical characteristics were comparable between both the groups with no statistically significant difference between them (p-value >0.05). 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.[8,9] These factors were comparable between both groups in the present study. Singh et al.[10] there were no statistically significant differences between the two groups in terms of demographic characteristics namely age, sex, weight, ASA status, duration of anaesthesia and surgery. The duration of anaesthesia and surgery has a bearing on post operative nausea and vomiting as prolonged duration of surgery will increase the incidence of post operative nausea and vomiting, hence increasing the requirement of antiemetic.[11,12]

In this study observed that at 72 hours, nausea and vomiting were statistically significant between ondansetron and palonosetron groups. Antiemetic efficacy of palonosetron is similar to that of Ondansetron for preventing PONV during the first 24 hours after laparoscopic cholecystectomy. 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.[13] The mechanism of its action on PONV is similar to ondansetron. Kovak et al.[14] 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[15] 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. The probable cause of early postoperative vomiting could be the use of volatile general anaesthetics.[12] Vomiting in these patients could be due to longer surgical procedures under volatile general anaesthetics and nitrous oxide leading to prolonged exposure to them.[11] Moon et al.[16] study observed that overall, PONV incidence during the 24 hour after surgery was lower in the palonosetron group compared with the ondansetron group (42% vs 62%, P=0.045). There was no significant difference between the groups during the first 2 hour after surgery. On the other hand, the incidence of nausea

and vomiting was significantly lower in the palonosetron group than in the ondansetron group 2–24 hour after surgery. Laparoscopic surgery has decreased the morbidity associated with cholecystectomy and has become an accepted procedure for symptomatic cholelithiasis.[17] However, high incidence of PONV (53–72%) is still been reported in patients undergoing this procedure.[18] Singh et al.[7] found that the incidence of nausea was significantly lower in the palonosetron group than in the ondansetron group during the 12-24 hour and over all 0– 24 hour time interval ($p<0.05$). The frequency of vomiting was also less during the 12-24 hour and overall 0– 24 hour time interval although not statistically significant. The overall incidence of nausea (PONV Score 1) in 24 hours was more in ondansetron group than palonosetron group, this difference was statistically significant ($p=0.037$). The incidence of post operative vomiting more than once in 24hours (PONV Score 3) was not statistically significant ($p=0.313$) among group O & group P. Only 40% in group O while 73.3% in group P showed complete response (no nausea vomiting) to the study drug ($p=0.009$), statistically significant. This is comparable with previous studies done by Nupur Chakravarty et al.[19] and Shadangi et al.[20]. Requirement of rescue antiemetic was in 6 (20%) patients in group O and in only 1 (3.3%) patient in group P ($p=0.044$), statistically significant.[10]

In present study revealed that postoperative side-effects such as headache, dizziness and drowsiness were not statistically significant between ondansetron and palonosetron groups. Prakash et al.[2] revealed that the rescue antiemetic (ondansetron 4 mg IV + dexamethasone 5 mg IV), was given to 9 (30%) patients in group O whereas to 5 (16.6%) patients in group P. But no significant statistical difference was observed between both the groups ($p >0.5$). The main side effects of 5-HT3 antagonists in the dosages used for PONV were headache and dizziness.[21] There was no significant statistical difference between both the groups regarding safety profile of study drugs ($p >0.05$). The effectiveness of ondansetron is comparable with palonosetron could be due to active metabolites of ondansetron (7-hydroxy or 8-hydroxyondansetron) contributing to prolonged action of the drug.[22] Risk factors for nausea and vomiting after laparoscopic surgery include a long period of carbon dioxide insufflation,[23] gall bladder surgery,[18] female sex[24] and postoperative use of opioids. A single dose of palonosetron (250 mcg) was found to be a superior antiemetic to ondansetron (8 mg) in complete prevention of PONV after middle ear surgery during the first 24hour postoperative period.[25] In a randomized controlled trial in day care surgery, single pre-induction I/V dose of palonosetron (75 mcg) proved to be superior to ondansetron (8 mg) in terms of the number of subjects experiencing PONV episodes and the dose of rescue antiemetic required.[26] The incidence of PONV has been found to be significantly lower with palonosetron than with ondansetron in gynecological laproscopic surgeries, although there were no significant differences in VAS scores for nausea.[27] Singh et al.[7] found that 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 0-24 hour time interval ($p<0.05$). Incidence of adverse effects and patient satisfaction were comparable between the two groups. Singh et al.[10] study showed that both palonosetron and ondansetron are known to have no serious adverse effects like short duration headache, constipation, dizziness. 2 (6.6%) patients in both groups complained of headache, and 1 (3.3%) patient in each group complained of dizziness. This difference was not significant statistically ($p=1.000$). Apart from this no side effects were observed in patients of both the groups.

Conclusion

In conclusion it is revealed that antiemetic efficacy of palonosetron is similar to that of Ondansetron for preventing PONV during the first 24 hours after patients who undergo surgery under general anaesthesia.But after

72 hour; nausea and vomiting were statistically higher in ondansetron group than palonosetron group.

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