http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v8i3.102

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Comparative Study of Palonosetron versus Ondansetron-Dexamethasone Combination for Prevention of Post-Operative Nausea and Vomiting in Patient Posted for Laparoscopic Cholecystectomy under General Anaesthesia

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Abstract
Background: *The incidence of PONV is as high as 60-70% encountering after laparoscopic cholecystectomy under general anaesthesia. It causes unexpected hospital stay and patient's morbidity.*
Aim: *To compare the efficacy of intravenous Palonosetron(0.05mg) and Ondansetron (4mg)-dexamethasone (8mg) combination for prevention of post-operative nausea and vomiting following laparoscopic cholecystectomy.*
Methods: *This is prospective, double blind study comprising of sixty patients of ASA grade I and II of either sex, aged 20-50 years and weight between 40 to 70 kilograms scheduled for laparoscopic cholecystectomy under general anesthesia. Patients were randomly divided into Group P (Intravenous Palonosetron 0.05 mg) and Group OD (Intravenous Ondansetron 4 mg+ Intravenous Dexamethasone 8 mg). The drug was administered just before the induction. All the vital parameters of patients were observed during intraoperative period. Episodes of nausea, vomiting, retching and any side effects were noted for 24 post-operative period. Intravenous Metoclopramide was administered as rescue antiemetic in a patient who experienced two or more episodes of vomiting and severe retching.*
Result: *Incidence of nausea and vomiting as well as requirement of rescue antiemetic was more or less same in both groups*
Conclusion: *Intravenous Palonosetron(0.05mg) was as potent as intravenous Ondansetron(4mg)-Dexamethasone(8mg) combination.*
Keywords: *Laparoscopic cholecystectomy, PONV, Palonosetron, Ondansetron, Dexamethasone.*

Introduction

Post-operative nausea and vomiting (PONV) is most common complication encountered after laparoscopic cholecystectomy under general anaesthesia.[1] It often causes pulmonary aspiration electrolyte imbalance, dehydration and esophageal rupture.[2]

The incidence of PONV is as high as 60-70% and is influenced by various patient related factors, anaesthesia technique, type of surgery, drugs used and post-operative factors such as pain, dizziness, ambulation etc.[3-6]

We have modified our anaesthetic techniques to secure more rapid and smooth recovery as a result of improved pre-operative and post-operative

medication, refinement of operative techniques and identification of patient's predictive factors.[7-8]

The management of nausea and vomiting has been improved in last couple of years with the introduction of 5 Hydroxytryptamine ($5\text{-}HT_3$) receptor antagonists. Ondansetron is a prototype of $5\text{-}HT_3$ receptor antagonist and commonly used drug. Ondansetron is considered as a gold standard drug for treatment of PONV.[9] Palonosetron is a recently developed second generation $5\text{-}HT_3$ receptor antagonist with a strong receptor binding affinity and has longer half life (40 hours) due to its unique chemical structure.[10] It is highly effective in PONV, Chemotherapy and radiotherapy induced vomiting. Dexamethasone is very potent and highly selective long lasting glucocorticoid. It causes prostaglandin antagonism serotonin inhibition in Gut and release of endorphins that elevates mood and stimulates appetite.[11] It augments efficacy of other primary antiemetic drugs like Ondansetron.[12]

We tried to find out an alternative regimen to prevent PONV due to high cost of new anti-emetics and Side effects associated with the traditional anti-emetics. In our study, We used intravenous Palonosetron (0.05 mg) and compared its efficacy with intravenous Ondansetron (4 mg)-Dexamethasone(8mg) combination to prevent PONV following laparoscopic Cholecystectomy under general anaesthesia.

Aims

To compare the efficacy of Palonosetron (0.05mg) and Ondansetron (4mg)-dexamethasone (8mg) combination for prevention of post-operative nausea and vomiting following laparoscopic cholecystectomy.

Materials and Methods

This prospective randomized double blind study was conducted following approval from our Institutional Ethical Committee (67/IAFC/IEC). Sixty patients of ASA grade I and II of either sex, aged 20-50 years, weight 40-70 kilograms scheduled for elective laparoscopic cholecystectomy under general anesthesia in department of anesthesiology, RIMS Ranchi, after obtaining written informed consent. The study was carried out from March 2018 to September 2019.

Pre-operative Assessment

After taking detailed history and systemic examination, Standard pre-anaesthetic check-up with relevant investigations was done. Patients were included or excluded for the study on the basis of following criteria:

Inclusion Criteria: Male or Female patients aged between 20-50 years, ASA physical status I and II, Weight-40-70 kilograms and Patients scheduled to be hospitalized for at least 72 hours after completion of surgery.

Exclusion Criteria: ASA physical status III and IV, Diabetic patient**,** H/O gastro-esophageal reflux, Use of antiemetic drugs within 72 hours prior to surgery and Patient on dexamethasone

After obtaining written informed consent and confirming inclusion and exclusion criteria, Sixty patients were randomly divided into two groups. Each group contains thirty patients.

Randomization was done by allocating patients using closed envelop method carried out by anesthesia technician. Group P (n=30) patients received intravenous Palonosetron (0.05mg) and Group OD (n=30) patients received intravenous Ondansetron (4mg)- Dexamethasone (8mg) combination.

Anesthetic Technique: All patients were kept nil per oral for 8-10 hours prior to surgery. 18G intravenous cannula was secured in non-dominant hand on the day of surgery. All patients were premedicated with inj. Ranitidine (50mg IV) and inj. Glycopyrrolate (0.2 mg IV) 30 minutes before induction. In the operation theatre, Standard anaesthesia monitors including ECG, NIBP and pulse oximeter were attached and baseline reading was obtained. Patients of group P were given intravenous Palonosetron 0.05mg just before induction and patients of group OD were given intravenous Ondansetron 4mg and intravenous

Dexamethasone 8mg combination just before induction. Patient were induced with propofol 2-2.5 mg/kg following preoxygenation with 80-100% oxygen for 5 minutes and haemodynamic variables were recorded. Loss of consciousness was confirmed and intubation was faciliatated with inj. Succinylcholine 2mg/kg with appropriate size endotracheal tube. Proper placement of endotracheal tube was confirmed by capnography and bilateral auscultation of chest and endotracheal tube was secured. Anaesthesia was maintained with IPPV and N_2O 50% + Oxygen O_2 50% + Isoflurane. Neuromuscular blocking agent intravenous Atracurium was administered and Nasogastric tube was inserted. Pulse rate, blood pressure, SpO_2 and ETO_2 were monitored throughtout perioperative period. After the completion of surgery, neuromuscular block was reversed by inj. Neostigmine 0.05 mg/kg and inj. Glycopyrrolate 0.5 mg. Afterthat, Patient was extubated and transferred to PACU. Postoperative analgesia was maintained by intramuscular inj. Diclofenac sodium.

Patients were monitored for nausea, retching and vomiting upto 24 hours post-operative period. Data was collected immediately after surgery, then at the interval of 0-2 hours, 2-4 hours, 4-8 hours, 8-16 hours and 16-24 hours. The episodes of nausea, retching and vomiting were noted using ordinal scale. Rescue antiemetic intravenous Metoclopramide 10 mg was given in a patient who experienced two or more episodes of vomiting or retching. All patients were observed for Side effects such as headache, abdominal discomfort for 24 hours post-operative period.

0= No nausea/ No Vomiting

1=Nausea

2=Retching/Vomiting

Statistical Analysis: All data were expressed as mean +/- standard deviation. Demographic data was analyzed using unpaired 't' test. The incidence of PONV and efficacy of drugs was compared using chi square test. P value < 0.05 was considered significant.

Results

Demographic data of both groups were comparable. There were no statistically significant differences between the groups with respect to age and body mass index (Table No-1). Duration of surgery of both groups were comparable.

Table No-1: Demographic data and duration of surgery

PARAMETERS	GROUP P	GROUP OD	P value
Age(years)	36.56±8.26	38.40±10.33	0.45
BMI	22.94±3.84	24.50±3.79	0.11
Duration of surgery(min)	73.46±11.95	76.06±12.11	0.40

Five patients (16.67%) of group P and nine patients(30%) of group OD experienced nausea. The result was not significant statistically with P value of 0.22 (P value >0.05). Three patients (10%) of group P and five patients(16.66%) of group OD experienced vomiting. The result was not significant statistically with P value of 0.45 (P value >0.05). (Table No-2)

Table No-2: Nausea and Vomiting over 24 hours

Parameters	Group P (n=30)		Group OD (n=30)		P value
	Number of patients	Percentage	Number of patients	Percentage	
Nausea	5	16.67	9	30	0.22
Vomiting	3	10	5	16.66	0.45

No patient from either groups reported PONV immediately and within first 2 hours after surgery. Incidence of PONV was 3.33% in group P and 10% in group OD with P value of 0.30 within 2-4

hours post-operative period. Incidence of PONV was 13.33% and 20% in group P and group OD, respectively with P value of 0.49 within 4-8 hours post-operative period. Incidence of PONV was 10% in group P and 16.67% in group OD with P value of 0.45 within 8-16 hours post-operative period. No patient of either group had PONV after 16 hours post-operatively. There was no significant difference statistically between the two groups in the terms of incidence of PONV with the post-operative duration. (Table No-3) or (Figure No-1)

Table No-3: Relation between PONV with post-operative time duration

Time in hours	Group P (n=30)		Group OD (n=30)		
	No. of patients	percentage	No. of patient	Percentage	P value
Immediately	0	0	0	0	
0-2 hours	0	0	0	0	
2-4 hours	1	3.33	3	10	0.30
4-8 hours	4	13.33	6	20	0.49
8-16 hours	3	10	5	16.67	0.45
16-24 hours	0	0	0	0	
Total	8	26.66	14	46.67	

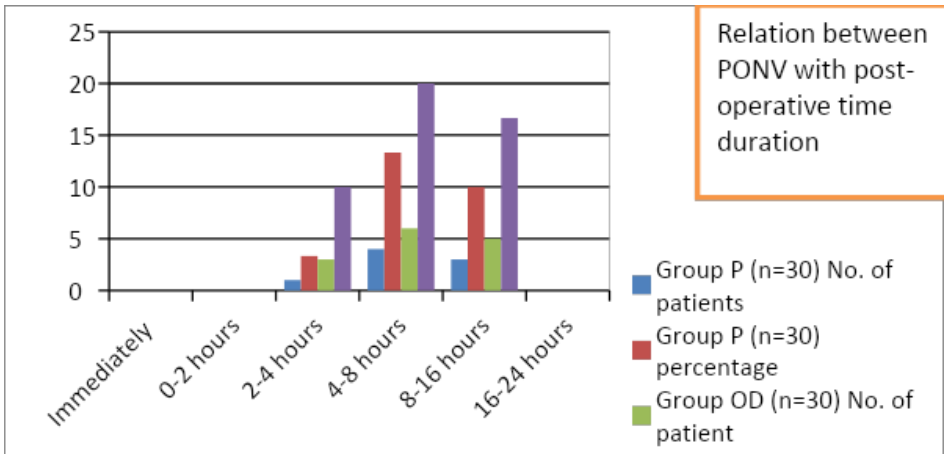

Figure No-1

Incidence of PONV was 3.33% in group P and 10% in group OD in the surgeries of duration 30-60 minutes. Incidence of PONV was 10% in group P and 16.67% in group OD in the surgeries of duration 61-90 minutes. Incidence of PONV was 13.33% in group P and 20% in group OD in the surgeries of duration 91-120 minutes. As duration of surgery increased, the incidence of PONV increased. Duration of surgery had no significant effect on incidence of PONV with P value of 0.11 (>0.05). (Table No-4) or (Figure No-2)

Table No-4: PONV in relation to duration of surgery

Duration of surgery in minutes	Group P (n=30)		Group OD (n=30)		P value
	No. of patients	percentage	No. of patients	percentage	
30-60 min	1	3.33	3	10	0.11
61-90 min	3	10	5	16.67	
91-120 min	4	13.33	6	20	
Total	8	26.66	14	46.67	

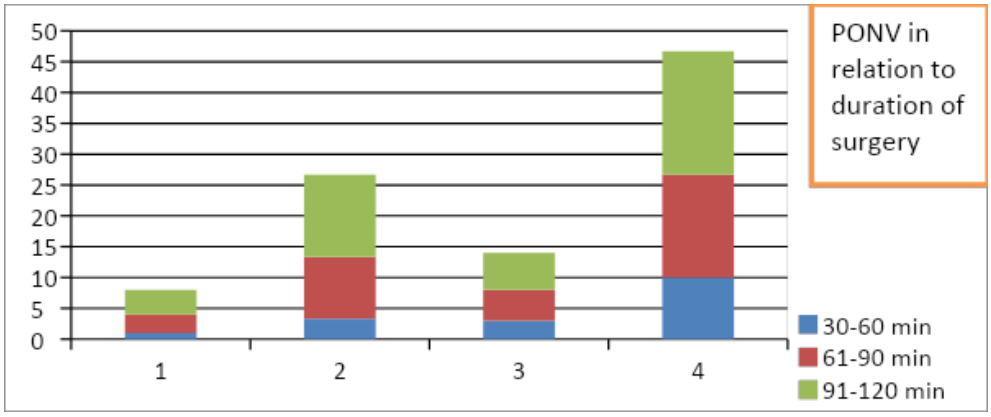

Figure No-2

Twenty two patients(73.33%) of group P and sixteen patients(53.33%) of group OD had shown complete response(no nausea, no vomiting).Five patients (16.67%) of group P and nine patients (30%) of group OD had score 1(only episodes of nausea) Three patients(10%) of group P and five patients(16.67%) of group OD had score 2 (retching or vomiting). There was no significant difference statistacally between two groups with the P value of 0.15(>0.05).(Table No-5) or (Figure No-3)

Table No-5: PONV Score

PONV Score	Group P (n=30)		Group OD (n=30)		P value
	No. of patients	percentage	No. of patients	Percentage	
Complete response(0)	22	73.33	16	53.33	0.15
Only nausea(1)	5	16.67	9	30	
Vomiting (2)	3	10	5	16.67	
Total	30	100	30	100	

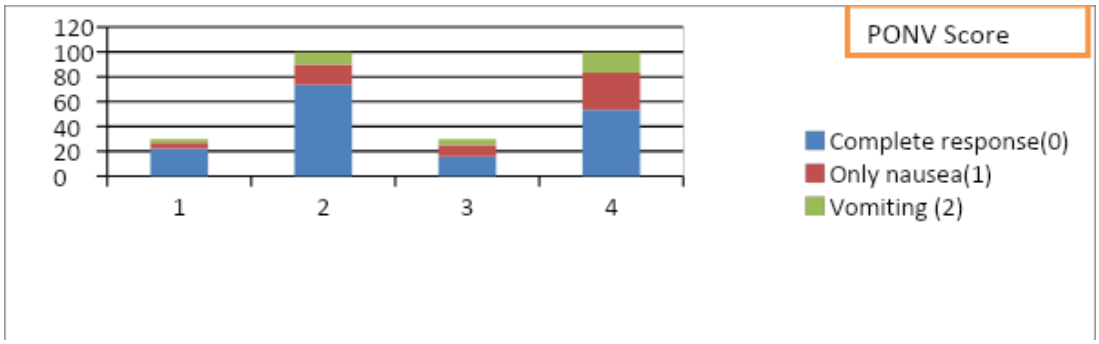

Figure No-3

When patient experienced severe nausea and vomited more than once, intravenous inj. Metoclopramide 10 mg I.V was administered as rescue antiemetic drug. It was observed that one patient (3.33%) in group P and three patients (10%) in group OD required rescue antiemetic drug. There was no significant difference stastically in two groups with P value 0.30 (>0.05). (Table No-6) or (Figure No-4)

Table No-6: Requirement of rescue antiemetic drug

Rescue antiemetic drug	Group P (n=30)		Group OD (n=30)		P value
	No. of patients	Percentage	No. of patients	Percentage	
Yes	1	3.33	3	10	0.30
No	29	96.67	27	90	
		100		100	

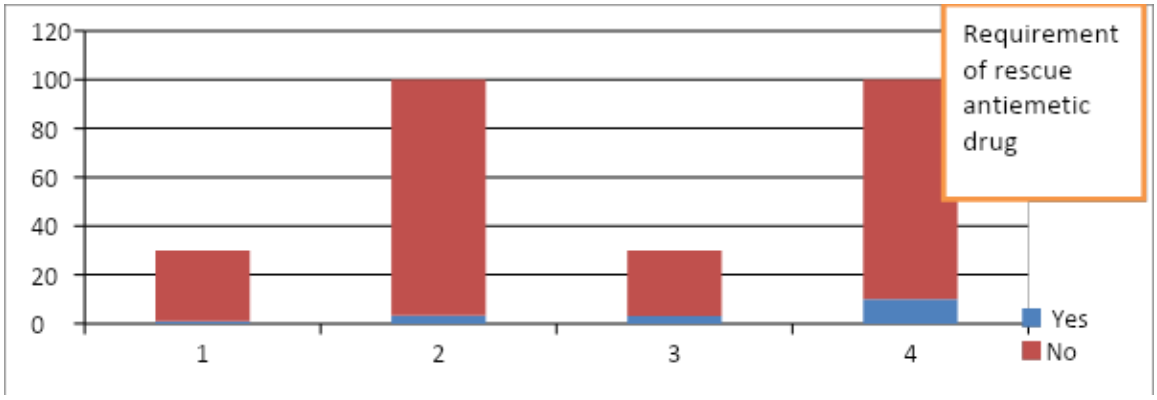

Figure No-4

In group P, one patient experienced headache. On other hand in group OD, two patients experienced headache and one patient experienced abdominal discomfort. (Table No-7)

Table No-7: Side effects

Side effects	Group P (n=30) No. of patients	Group OD (n=30) No. of patients
Headache	1	2
Abdominal discomfort	0	1
Nil	29	27
Total	**30**	**30**

Discussion

Post-operative nausea and vomiting is one of the common sequalae of general anaesthesia. Laparoscopic cholecystectomy itself is one of the risk factors causing PONV. Ondansetron was the first accessible 5-HT_3 receptor antagonist for the management of PONV. Extensive clinical researches have been carried out to prevent PONV in last couple of years. Palonosetron is second generation 5-HT_3 receptor blocker having highest affinity for 5-HT3 receptor. In 1961, Dexamethasone was first reported as an effective antiemetic agent in patients underwent cancer therapy. Some studies have shown that dexamethasone and other steroids are effective significantly in preventing nausea and vomiting associated with chemotherapy. Corticosteroids reduce 5-hydroxytryptophan level in neural tissue by decreasing its precursor tryptophan. The anti-inflammatory property of corticosteroid prevents the release of serotonin in the gut and it potentiate the main effect of other antiemetics by sensitizing the pharmacological receptor. Several studies have been done for PONV so far. A study reported that single dose Palonosetron was more powerful in high risk patient who underwent laparoscopic surgery. Some authors found that Dexamethasone was more impressive than Ondansetron in preventing post-operative nausea after 4-6 hours of laparoscopic surgeries in their studies. Bala I et al[13] reported that Palonosetron-Dexamethasone had greater efficacy as compared to Palonosetron on other hand Astha srivastava et al[14] reported that addition of Dexamethasone to

Palonosetron did not cause any added advantage over Palonosetron. Some authors found that Dexamethasone was more impressive than Ondansetron in preventing post-operative nausea after 4-6 hours of laparoscopic cholecystectomy in their studies. Shilpa Tiwari et al[15] reported that Palonosetron and Palonosetron-Dexamethasone combination both were effective in the treatment of post-operative nausea and vomiting in female underwent laparoscopic surgery. Arindam charatterjee et al[16] reported that Dexamethasone was least effective among Dexamethasone, Palonosetron and Palonosetron-Dexamethasone combination. In this study, We found that Palonosetron was as impressive as Ondansetron-Dexamethasone combination in preventing post-operative nausea and vomiting following laparoscopic cholecystectomy. However, Palonosetron required less rescue antiemetic as compared to Ondensetron-Dexamethasone combination but that was not significant statistically.

Conclusion

Intravenous Palonosetron (0.05mg) is as potent as intravenous Ondansetron(4mg)-Dexamethasone (8mg) combination for the prevention of post-operative nausea and vomiting in laparoscopic cholecystectomy under general anesthesia. Both groups have nominal headache and abdominal discomfort as side effects. There is no episode of post-operative nausea and vomiting instantly after surgery. Intravenous Ondansetron (4mg)-dexamethasone (8mg) combination may be used as alternative regimen in low socio-economic group patient due to low cost effective or easy availability.

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