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COMPARISON OF EFFECTIVENESS OF INTRAVENOUS PALONOSETRON VERSUS ONDANSETRON IN PREVENTION OF POST-OPERATIVE NAUSEA AND VOMITING IN LAPAROSCOPIC SURGERIES UNDER GENERAL ANAESTHESIA: A RANDOMISED DOUBLE BLIND INTERVENTIONAL STUDY

Anaesthesiology

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ABSTRACT

Introduction: Post-operative Nausea and Vomiting (PONV) is the most common distressing symptom following surgical procedures which can lead to medical complications and impose economic burden on the patients with psychological effects in patients experiencing anxiety about undergoing further surgery.

Purpose: The purpose of the study was to compare the efficacy of intravenous palonosetron versus ondansetron in preventing PONV in laparoscopic surgeries.

Materials and Methods: A randomized,double-blind interventional study was conducted in the Department of Anaesthesiology,SMS Medical College and Hospital,Jaipur,Rajasthan,India.100 adult patients were divided into two groups of 50 each,randomized to receive 0.075 mg of palonosetron and 4 mg of ondansetron before induction.The occurrence of nausea, vomiting and severity of nausea according to a visual analog scale were observed immediately after the end of surgery at 0-2hrs,2-6hrs,6-12hrs and12-24hrs.Injection metoclopramide was used as a rescue antiemetic.Details of any adverse events were recorded.

Results: The incidence of postoperative nausea and overall PONV were lower in Group P than Group O, which was statistically significant ($P < 0.05$).

Conclusion: Palonosetron 0.075 mg IV produced a lower incidence of PONV compared with ondansetron 4 mg IV in patients undergoing laparoscopic surgeries.

KEYWORDS

Adverse events,Nausea,Rescue antiemetics,Vomiting

INTRODUCTION

Post-operative Nausea and Vomiting (PONV) is the most common distressing symptom following surgical procedures. This can lead to medical complications and impose economic burden with psychological effects in patients experiencing anxiety about undergoing further surgery[1].PONV is the most, complication of surgery and anaesthesia[2].

PONV causes extended hospital stays, increased bleeding and aspiration pneumonia and even reopening of surgical wounds as result of the involuntary muscular contraction associated with vomiting. It also imposes economic burden on the health care system due to time spent for cleaning up, potential delays in recovery & discharge and increased medical care [3]. In ether era incidence of PONV was 75-80%. In second half of the century, the incidence of PONV is decreased by 50% [4]. The incidence of PONV after general anaesthesia in outpatients has been reported to be 37%.

Laparoscopic surgery is one condition, where risk of PONV is particularly high.Despite the minimally invasive nature of laparoscopy, high incidence of PONV remains a major cause for morbidity.Post-operative nausea and/or vomiting (PONV) can be defined as nausea and/or vomiting within 24 hrs of surgery.

Risk factors for PONV can be patient risk factors, pre-operative risk factors, intra-operative risk factors, anaesthesia related risk factors [5], procedural factors, post-operative factors.Most predictive factors are female gender, history of motion sickness, history of PONV, non-smoker and post-operative use of opioids among all the factors.

Pharmacological approach by use of antiemetics are the main stays of therapy for PONV.The first and second line pharmacological anti-emetics for PONV in adults include $5HT_3$ receptor antagonists, steroids like dexamethasone, phenothiazines (Promethazine Prochlorperazine),phenyl ethylamine (ephedrine), Butyroph enones,like droperidol, haloperidol, antihistaminics, diphenhydr amine, dimenhydrinate, anticholinergics like transdermal scopola mine, prokinetics like metoclopramide.[6]The 5-HT3 receptor antagonists,ondansetron, granisetron,ramosetron,tropisetron and palonosetron are most effective in prophylaxis of PONV [7].

Ondansetron was the first commercially available 5-HT3 receptor antagonist.

Palonosetron is new, potent, a second generation selective 5-HT3 (serotonin subtype 3) receptor antagonist with a strong binding affinity for this receptor and little or no affinity for other receptors.

In this study we aimed to compare the efficacy of palonosetron Vs ondansetron in prevention of post-operative nausea and vomiting in laparoscopic surgeries under general anaesthesia.

MATERIALS AND METHODS

A randomized double blind interventional study was conducted to compare the effectiveness of a single pre-induction dose of palonosetron (75µg) in Group A/P and ondansetron (4mg) in Group B/O after the approval from the institutional ethics committee.The sample size was calculated on the basis of the primary outcome measure. The required sample size was 50 cases in each group at 95% confidence and 80% power to determine the minimum difference of 34% in cases which were not developing PONV during first 24 hours postoperatively in both study groups.Patients belonging to the age group of 18-60 years of both sexes scheduled for elective laparoscopic surgeries were divided into two groups,Group A/P (palonosetron) and Group B/O (ondansetron) of 50 people each. Patients included were non-smokers,ASA grade I-II,no history of motion sickness or previous PONV.Randomization was done by computerized random number table method. Allocation was concealed by serially numbered sealed envelopes.100 adult patients were randomly divided into two groups.In the pre-anaesthetic room,IV line was secured and baseline vitals were recorded such as heart rate arterial pressure and oxygen saturation.All patients in Group P/A received 75 µg of palonosetron and Group O/B received 4mg of ondansetron before induction.Drugs were given by another anaesthesiologist not involved in this study.Patients were premedicated with injection glycopyrrolate 0.004mg/kg,injection midazolam 0.05mg/kg,injection fentanyl 2µg/kg and then adequately pre-oxygenated.Patients were induced by injection propofol 2mg/kg followed by injection atracurium 0.5mg/kg to facilitate laryngoscopy and intubation.Anaesthesia was maintained with 60%nitrous-oxide+40%oxygen,0.5-2%sevoflurane and inj. atracurium 0.1mg/kg sos. On completion of surgery, inj. neostigmine

0.05mg/kg and glycopyrrolate 0.004mg/kg given for reversal of neuromuscular blockade and patient extubated.Any occurrence of nausea and vomiting were observed at 0-2 hrs,2-6 hrs,6-12 hrs and 12-24 hrs post-surgery.Severity of nausea according to visual analog scale (VAS).Nausea is defined as subjectively unpleasant sensation associated with awareness of the urge to vomit by subject, whereas vomiting is defined forceful expulsion of gastric contents from the mouth.When one episode of PONV occurred or VAS >5 and patient requested for treatment, injection Metoclopramide was used as rescue antiemetic.Absence of PONV with no use of rescue antiemetic defined complete response.Adverse events like headache, dizziness and constipation were observed.

Data entered and analysed by using licensed SPSS software version 21.0 (Chicago, Illinois).The results were presented with the help of tables,text,bar-diagrams and pie-charts.Descriptive statistics were used to calculate frequencies of categorical variables and measures of central tendencies and dispersion were used to describe continuous variables.Bi-variate analyses was done using the Chi square test, to determine the association between various socio-demographic variables, clinical history and risk factors with laboratory outcomes.The level of significance was fixed at 0.05.

RESULTS

The study was conducted amongst 100 adult patients aged 18to 60 years and undergone for surgery in SMS Hospital, Jaipur for the analysis which was equal to the calculated sample size.The two groups were similar regarding age,weight and gender.In our study (Table 1), mean age in ondansetron group was 39.7 ± 11.4 years; and in palonosetron group was 38.67 ± 11.06 years and were statistically not significant (P = 0.66).In our study (Table 2), mean weight in ondansetron group was 59.02 ± 6.36 and in palonosetron group was 58.6 ± 6.43 and were statistically not significant (P = 0.76).In this study, (Table 3) 26% were males and 74% were females in group ondansetron and 32% were males and 68% were females in group palonosetron,suggesting that both the groups have comparable demographic characteristics. In our study (Table 4), the incidence of post-operative nausea was lower in palonosetron group compared to ondansetron group.This was found to be statistically significant in first 2 hrs (P = 0.017) and 0-24 h (P = 0.001).In our study, (Table 5),the incidence of post-operative vomiting was lower in palonosetron group compared to ondansetron group but they were not statistically significant.In our study (Table 6), the incidence of overall PONV was found to be statistically significant (P = 0.001).In our study, (Tables 7) 7 patients from ondansetron group and 4 patients from palonosetron group required rescue medication.This was statistically not significant.In this study, (Tables 8)the headache was found in 16% of ondansetron group and 12% of palonosetron group.Dizziness was found in 14% of ondansetron group and 14% of palonosetron group.Constipation was found in 8% of ondansetron group and 10% of palonosetron group.They were not statistically significant.

Table 1: Age wise distribution in both groups

Group	Mean ±SD	p-value
Group O	39.7±11.42	0.66
Group P	38.67±11.06	

Table 2:Weight wise distribution in both groups

Group	Mean ±SD	p-value
Group O	59.02±6.36	0.76
Group P	58.6±6.43	

Table 3: Gender wise distribution in both groups

Gender	Group O	Group P	p-value
Female	37	34	0.66
Male	13	16	
Total	50	50	

Table 4: Comparison of frequency of postoperative nausea episodes in both groups at different interval

Time	Occurrence	Group O	Group P	Total	P Value
0-2 Hrs	No	37	46	83	0.017
	Yes	13	4	17	
	Total	50	50	100	
2-6 Hrs	No	40	46	86	0.084
	Yes	10	4	14	
	Total	50	50	100	
6-12 Hrs	No	35	42	77	0.096
	Yes	15	8	23	
	Total	50	50	100	
12-24 Hrs	No	36	42	78	0.148
	Yes	14	8	22	
	Total	50	50	100	
0-24 Hrs	No	17	35	52	0.001
	Yes	33	15	48	
	Total	50	50	100	

Table 5: Comparison of frequency of postoperative vomiting episodes in both groups at different interval

Time	Occurrence	Group O	Group P	Total	P Value
0-2 Hrs	No	46	48	94	0.68
	Yes	4	2	6	
	Total	50	50	100	
2-6 Hrs	No	46	48	94	0.68
	Yes	4	2	6	
	Total	50	50	100	
6-12 Hrs	No	45	47	92	0.72
	Yes	5	3	8	
	Total	50	50	100	
12-24 Hrs	No	46	48	94	0.68
	Yes	4	2	6	
	Total	50	50	100	
0-24 Hrs	No	33	41	74	0.110
	Yes	17	9	26	
	Total	50	50	100	

Table 6: Comparison of frequency of overall PONV episodes in both groups

Occurrence	Group O	Group P	Total	P Value
No	17	33	50	0.001
Yes	33	17	50	
Total	50	50	100	

Table 7: Requirement of rescue medication in both groups

Requirement	Group O	Group P	Total	P Value
Yes	7	4	11	0.338
No	43	46	89	
Total	50	50	100	

Table 8: Comparison of adverse events in both groups:

Adverse Event	Occurrence	Group O	Group P	Total	P Value
Headache	Yes	8	6	14	0.56
	No	42	44	86	
	Total	50	50	100	
Dizziness	Yes	7	7	14	1.00
	No	43	43	86	
	Total	50	50	100	
Constipation	Yes	4	5	9	1.00
	NO	46	45	91	
	TOTAL	50	50	100	

DISCUSSION

PONV is a complication that causes discomfort and dissatisfaction in patients who undergo surgery.[8] Post- operative period is associated with the variable incidence of nausea and vomiting depending on the duration of surgery, the type of anaesthetic agents used (dose, inhalational drugs, and opioids), smoking habit etc.[9].5-HT3 receptor stimulation is the primary event in the initiation of vomiting reflex.[10]The use of prophylactic antiemetics is intended to prevent episodes of vomiting, eliminate or lessen the severity of nausea and minimize or remove the need for PONV rescue medications.[11]5-HT3 RAs are generally safe at the usual doses used to prevent or treat PONV, with no dose-related sedation or extrapyramidal reactions and no significant effects on vital signs.[12]

In our study mean age in group O was 39.7±11.42yrs while in group P was 38.67±11.06yrs. Mean weight in group O was 59.02±6.36kg while in group P was 58.6±6.43.M:F ratio was 13:37 and 16:34 in groups O and P respectively.P value for these was insignificant.

In our study, the incidence of post-operative nauseawas compared over 0-2 h, 2-6 h, 6-12 h, 12-24 h, and 0-24 h. The incidence was 13 in ondansetron group and 4 in palonosetron group in 0-2 h which was statistically significant (P = 0.017). Similarly, the incidence was 33 in ondansetron group and 15 in palonosetron group in 0-24 h which was

statistically significant (P = 0.001). In our study, post-operative vomiting was compared over 0-2 h, 2-6 h, 6-12 h, 12 24 h, and 0-24 h.The incidence was 17 in ondansetron group and 9 in palonosetron group over 0-24 h. Though the incidence was lower in palonosetron group than ondansetron group,they were not statistically significant (P = 0.110). In our study, overall PONV was compared between the two groups in 0-24 h. The incidence of overall PONV was 33 in ondansetron group and 17 in palonosetron group. This was statistically significant in 0-24 h(P = 0.001).

Schwartzberg and associates[13] demonstrated no significant difference between palonosetron and other 5HT3 antagonists during early post-chemotherapy period but significant difference was observed in delayed chemotherapy period. PONV episodes during first 48 hrs were 8 (13.76%) in palonosetron group and 20 (34.4%) in ondansetron group which was highly significant. Consistent results were also observed in previous study conducted by Kim[14] and associates where PONV incidence in palonosetron group was 22.2% and 77% in ondansetron group.Candiotti *et al*.[15] reported that palonosetron and ondansetron did not show differences in the primary efficacy endpoint of complete control during the 72 h after study drug administration.In the study by Gupta *et al*.,[16]the incidence of PONV was maximal during the first 4 h and was more in the patients of ondansetron group as compared to patients of palonosetron and granisetron group.

Adverse events with single IV dose of the study drugs were not serious.In our study, 3 adverse events headache, dizziness and constipation were compared.In O group headache was in 8 patients,dizziness in 7 patients and constipation in 4 patients. In P group headache was in 6 patients,dizziness in 7 patients and constipation in 5 patients. These were statistically not significant.In Study conducted by Sureshkumar et al[17] differences in the incidence of the headache, dizziness and constipation between the groups.

In our study,rescue antiemetics were required in 8% of palonosetron group and 14% of ondansetron group which was almost similar to study by Sureshkumar et al.

CONCLUSION

Thus from the current study we conclude that palonosetron was more efficacious than ondansetron in controlling PONV in patients postoperatively.

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