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"EVALUATION OF PALONOSETRON IN PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN ELECTIVE SURGERIES UNDER GENERAL ANAESTHESIA: A PROSPECTIVE, RANDOMIZED, DOUBLE BLIND STUDY"

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ABSTRACT

Background: Post operative nausea and vomiting (PONV) is one of the frequent and distressing postoperative complications in patients undergoing general anesthesia. Effective, longer acting anti-emetic treatment helps to improve postoperative recovery and early discharge.

Palonosetron, a selective 5-hydroxytryptamine type 3 (5-HT_3) receptor antagonists, exhibits greater receptor binding affinity, longer duration of action and fewer side-effects compared to Ondansetron.

Aims & objectives: To assess the efficacy and safety profile of Palonosetron in prevention of PONV in elective surgeries under general anesthesia.

Methodology: 60 patients (ASA grade I & II) between the age of 20-60 years of either sex undergoing general anaesthesia were randomly allocated into two groups; Group C (n=30) received normal saline and Group P (n=30) received inj. Palonosetron 0.075mg, 10 minutes before induction of anesthesia. In first 24 hours of postoperative period, all the patients were observed for nausea, retching, vomiting and need of any rescue anti-emetic. Adverse effects intra and postoperatively were also recorded.

Results: Palonosetron was highly effective in preventing PONV as compared to placebo ($p<0.05$). The incidence of nausea was significantly lower in group P compared to group C (16.7% vs. 73.3%, $p=0.0001$). Statistically significant difference ($p=0.009$) was observed between group C and P in prevention of vomiting in first 24 hours postoperatively.

Conclusion: The effectiveness of inj. Palonosetron 0.075mg in preventing PONV found to be significantly higher in patients undergoing general anesthesia.

KEYWORDS : Palonosetron, PONV, general anesthesia.

INTRODUCTION:

Despite having the better understanding knowledge about the pathophysiology of nausea and vomiting and use of more stable and effective anti-emetics like ondansetron, granisetron, the postoperative nausea and vomiting (PONV) continues to be the most disturbing complication following surgery and anesthesia.[1] The negative impact of PONV on patient's physical, metabolic and psychological condition not only delays discharge from or cause re-admission to hospital but also decreases the confidence level in future surgery and anesthesia. The incidence of PONV increases with definite risk factors including female gender, non-smokers, motion sickness, type and duration of surgery and use of peri-operative opioids. In addition, patient's anxiety prior to surgery, type of anesthetic medications and techniques also influence the incidence of PONV.[2-5]

With increased risk factors in a patient the chances of PONV may rise from 20% to 80%.

Second generation 5HT3 antagonist, palonosetron was initially approved for prophylaxis of nausea and vomiting in cancer patients, as it improves the prevention of chemotherapy induced nausea and vomiting[6] and proved superior to ondansetron in these patients. Because of its unique chemical structure, greater binding affinity with additional allosteric site binding property[7] and a substantially longer half-life of almost 40 hours made palonosetron suitable for its use in prevention of PONV.

AIM AND OBJECTIVES:

We designed this randomized double-blind study to evaluate the anti-emetic efficacy of newer and longer acting drug palonosetron for prevention of PONV.

METHODOLOGY:

After approval of the institute ethical committee and informed consent, this study was conducted on 60 patients between the age of 20–60 years of either sex of ASA Grade I or II scheduled for different surgeries requiring general anesthesia were included in this study.

Patients of ASA Grade III or more, pregnant and lactating women, patients with difficulty in communicating, those prone to nausea, vomiting or motion sickness, patients on opioids analgesics or anti-emetics within 24 hours before anesthesia, requiring continuous gastric suction for 24 hours in postoperative period were excluded from study.

Intervention plan and group allocation:

Patients were kept blinded by sealed envelope method and observer anesthesiologist was also uninformed of which drug was injected to which patient to avoid observer bias. The anesthesiologist who injected the study drugs took no further part in the study. Selected 60 patients were randomly allocated into two groups based on the study drug to be given:

Group C: 4ml of normal saline was given intravenously 10 minutes before induction of anesthesia.

Group P: Inj. palonosetron 0.075 mg diluted to 4 ml with normal saline given intravenously 10 minutes before induction of anesthesia.

Preanesthetic assessment:

All the selected patients were carried out with complete history, general examination, airway assessment, systemic examination along with routine investigations, ECG and CXR.

Premedication

All the patients were kept nil orally for at least 8 hours before procedure. Tablet Diazepam 10mg and tablet Pantoprazole 40mg were given night before surgery. Inj. Glycopyrrolate 0.2mg intramuscularly had given to all the patients as premedication, 30min before shifting the patient to Operation Theater.

Anesthesia management

After taking the patient in the operation theater, intravenous cannulation was done and ringer lactate (RL) infusion was started. Standard basal parameters had been recorded. Study drug was given by slow intravenous injection, 10 minutes before induction of anesthesia. Thereafter, preoxygenation with 100% oxygen was started and general anesthesia was induced with inj. fentanyl 2 µg/kg, inj. Thiopentone 3-5 mg/kg body weight. Propofol was avoided due to its anti-emetic property.

After securing mask ventilation inj. vecuronium 0.1 mg/kg body

weight administered intravenously for endotracheal intubation. Anesthesia was maintained with 50% oxygen in air and Isoflurane with intermittent doses of fentanyl and vecuronium, along with intermittent positive pressure ventilation. We avoided use of N2O so as to minimize the baseline risk factors for PONV during maintenance of general anesthesia.

After the completion of surgery, reversal done with combination of inj. Glycopyrrolate 0.01 mg/kg body weight and Neostigmine 0.05 mg/kg body weight.

Inj. Diclofenac sodium 75 mg was used intra-operatively and in the postoperative period for analgesia. After extubation and complete recovery, the patients were moved to postanesthesia care unit (PACU). In the PACU, every patient was watched and monitored for nausea, retching and vomiting at 30 min, 60 min, 2 hr, 6 hr, 12 hr and 24 hr. Any complications occurred perioperatively were noted and treated accordingly. All observed data are expressed as percentage and numbers.

Assessment of Nausea:
The incidence of nausea was assessed subjectively by intensity score, where 0=No nausea, 1=Mild nausea, 2=Moderate nausea and 3=Severe nausea.

Complete drug response (R) was considered as no PONV and if no use of rescue drugs to prevent or treat the PONV.

Statistical Analysis
Statistical analysis was carried out using SPSS version 19 (SPSS, IBM, Chicago, IL, USA). The study data were presented as mean±standard deviation. Student's't' test was used for inter-group comparison. P-value >0.05 and <0.05 were considered statistically insignificant and significant, respectively.

RESULTS:
In the present study, both the study groups were comparable on demographic pattern such as age, weight, and sex. (Table 1)

In our study, the incidence of complete response to prevent vomiting (no vomiting, no rescue medications) for control and palonosetron groups was 56.6% and 86.6% respectively. (P-value =0.009, highly significant). (Table 2)

Vomiting free patients in control group were 56.7% and in palonosetron group 86.6%, which was statistically highly significant at the end of 24 hours (p-value= 0.009). (Table 2)

The incidence of major adverse effects, e.g. headache, dizziness and drowsiness was comparable between all the study groups (Table 3).

Table 1: Demographic pattern of the study population

Parameters	Group C	Group P	P-value
Age (years)	41.4±12.7	39±9.68	0.413
Sex(male/female)	15/15	17/13	-

Table 2: Frequency of nausea and vomiting compared between groups and nausea and vomiting free patients

	Group C (n=30)	Group P (n=30)	P-value
30 minutes			
Nausea n (%)	10 (33.4)	3 (10)	0.02
Vomiting n (%)	5 (16.7)	2 (6.7)	0.22
60 minutes			
Nausea n (%)	10 (33.4)	3 (10)	0.02
Vomiting n (%)	10 (33)	2 (6.7)	0.009
120 minutes			
Nausea n (%)	17 (56.6)	5 (16.7)	0.001
Vomiting n (%)	7 (24)	2 (6.7)	0.07
8 hours			
Nausea n (%)	25 (83.3)	5 (16.7)	0.0001
Vomiting n (%)	6 (20)	2 (6.7)	0.12
24 hours			
Nausea n (%)	22 (73.3)	5 (16.7)	0.0001
Vomiting n (%)	13 (43.3)	4 (13.4)	0.009
Nausea free n (%)	5(16.6)	18 (60)	0.0005
Vomiting free n (%)	9 (30)	21 (70)	0.001

Table 3: Significant adverse effects observed in groups

	Group C (n=30)	Group P (n=30)
Headache	2 (6.6%)	2 (6.6%)
Dizziness	1 (3.3%)	1 (3.3%)
Drowsiness	1 (3.3%)	0 (0)

DISCUSSION:
In present study, we evaluated the response and efficacy of single intravenous dose of a new promising $5HT_3$ receptor antagonist, Palonosetron for prevention of PONV.

In our study, the dose selection was based on the recommendations of a previous study of single intravenous dose of 0.075 mg palonosetron. US Food and Drug Administration (FDA) approved a single dose of palonosetron 0.075 mg for preventing PONV for up to first 24 hours after the surgery.[8-10]

A stratified multicenter study[10] evaluated the dose response of the three different single intravenous doses of palonosetron and observed a linear trend in efficacy with increasing doses, with only the highest dose (0.075 mg) of palonosetron demonstrated a statistical significant treatment effect with complete drug response (no emesis, no rescue medication) was 43%.

In our study during 0 to 24 hours postoperatively the complete drug response was 83.3% with palonosetron which was statistically significant. We also found that a single dose of 0.075 mg palonosetron produced a considerable decrease in the incidence and severity of nausea than placebo in control group (16.7% Vs 73.3%, p=0.0001).

In our study, the incidence of adverse effects in Palonosetron group was comparable with control group, which was consistent with the previous study.[11]

Limitations and Scope of Future Studies:
In order to generalize such a study, one need to include regional anesthesia procedures, including use of neuraxial opioids. We exclusively enrolled patients who had had only general anesthesia. Further studies are required on palonosetron in larger study samples and in a wide variety of surgical procedures, especially involving high risk for PONV cases.

CONCLUSION:
We conclude that the second generation 5-HT3 antagonist, palonosetron is significantly effective against PONV. It has a particularly more pronounced and prolonged effect on postoperative nausea.

Conflict of Interest: Nil.
Source of Funding: Nil.

REFERENCES:
1. Gan TJ. Risk factors for post-operative nausea and vomiting. Anesth Analg 2006; 102: 1884-89.
2. Yoon JS, Kim KM, Kim YH. The effects of amounts of intra-operative intravenous fluid administration on post-operative Nausea and Vomiting during gynaecological surgeries. Korean J .Anesthesiol. 2008; 55: 166-170.
3. 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 post-operative nausea and vomiting. Korean J Anesthesiol 2012 Oct; 63(4): 334-9.
4. Sweeney BP. Why does smoking protect against PONV? Br J Anaesth 2002; 89(6): 810-813.
5. Onaka M, Yamamoto H. Comparison of analgesics used during balanced anesthesia on the incidence of PONV. Masui 2004 Feb; 53(2): 161-6.
6. Apro MS, Macciocchi A, Gridelli C. Palonosetron improves prevention of chemotherapy induced nausea and vomiting in elderly patients. J Support Oncol 2005; 3(5): 369-74.
7. Rojas C, Stathis M, Thomas AG, Massuda EB, Alt J, Zhang J, Rubenstein E et al. Palonosetron exhibits unique molecular interactions with the $5HT_3$ receptor. Anesth Analg 2008; 107: 469-479.
8. Tramer MR, Reynolds DJ, Moore RA, McQuay HJ. Efficacy, dose response and safety of Ondansetron in prevention of post-operative nausea and vomiting. A quantitative systematic review of randomized placebo-controlled trials. Anesthesiology 1997; 87: 1277-89.
9. Kovac AL, Eberhart L, Kotarski J, Clerici G, Apfel C. Palonosetron 04-07 Study Group. A randomized double blind study to evaluate the efficacy and safety of three different doses of palonosetron versus placebo for preventing post-operative nausea and vomiting over a 72-hour period. Anesth Analg 2008; 107: 439-444.
10. Candiotti KA, Kovac AL, Melson TI, Clerici G, Joo Gan T. Palonosetron 04-06 Study Group. A randomized double blind study to evaluate the efficacy and safety of three different doses of palonosetron versus placebo for preventing post-operative nausea and vomiting. Anesth Analg 2008; 107: 445-51.
11. Bajwa SS, Bajwa SK, Kaur J, Sharma V, Singh A, Singh A et al. Palonosetron: a novel approach to control post-operative nausea and vomiting in day care surgery. Saudi J Anaesth 2011; 5(1): 1924.