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A Comparative Study of Efficacy and Safety of Ondansetron versus Palonosetron for the Treatment of Post-Operative Nausea and Vomiting

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Abstract **Original Research Article**

The management of Post-operative Nausea and vomiting is an important consideration in surgical procedures. Inadequately treated PONV may result in prolonged post-operative care and increase the burden of treatment. We in the present study tried to evaluate the safety and efficacy of Ondansetron versus Palonosetron for the treatment of Post-Operative Nausea and Vomiting in elective surgical procedures. Methods: This cross sectional prospective study was conducted in the Department of Pharmacology, and Department of ENT, Government Medical College and Hospital, Rajnandgoan, CG. A total of n=79 were selected based on the inclusion and exclusion criteria. They were divided in two groups viz Group I (Ondansetron) n=40 and Group II (Palonosetron) and n=39. The Ondansetron Group (I) received Ondansetron 8mg IV in 10 ml normal saline over 30 seconds immediately before induction of general anesthesia and group (II) received inj. Palonosetron were given by 0.075mg IV. A standard anesthesia technique was followed endotracheal intubation was done with appropriate size cuffed endotracheal tube. In the monitoring room all the patients' recovery parameters were checked and any episode of nausea or vomiting (PONV) was recorded at an interval of 30 min, 2 hours, 6 hours and 24 hours. Frequencies of rescue medication given were noted. Results: In the group I 32 (80%) were belonging to ASA Grade I and 8(20%) belonging to ASA Grade II. In the group I the 26(66.66%) of patients with score 2 similarly in the Group II 22(55%) were with Apfel score 2. In the group I a total of n=13 patients were seen with nausea and in Group II n=7 patients were with nausea. The p values for the postoperative nausea between two groups were found to be <0.05 which is significant. The incidence of postoperative vomiting in group I was seen in 10(25%) out of the total 40 patients and most of the patients had vomiting between 6 -24 hours 6 (15%) had vomiting and 2(5.0%) between 0 – 2 hours and 2 – 6 hours. In the group II a total of 6 (15.38%) had vomiting equally in the duration between 2 – 6 hours and 6 – 24 hours. The p values were found to be <0.05 which was significant. Conclusion: it can be concluded that Palonosetron 0.075mgIV is more effective than ondansetron 8mg IV for prevention of post-operative nausea and vomiting in these group of patients. We recommend the use of palonosetron 0.075mg IV in patients with high risk of PONV with Apfel scores of 4.

Keywords: Ondansetron, Palonosetron, Post-Operative Nausea and Vomiting.

INTRODUCTION

Post-Operative Nausea and vomiting (PONV) is a problem encountered by the patients as well as the doctors [1]. Nausea is reported to occur in 20% of patients in recovery room and in 50% thereafter with vomiting in 5%- 25% respectively [2]. Although, the incidence of PONV following regional anesthesia is very less as compared to general anesthesia but if present its effect are equally distressing. PONV can increase the cost of patient care and can cause various complications like bleeding, wound dehiscence, electrolyte imbalance dehydration and aspiration pheumonitis [3]. Physical consequences includes sweating, Tachycardia, rupture of esophagus wound dehiscence, electrolyte imbalance and dehydration. Patients related risk factors for PONV includes female sex, history of PONV or motion sickness. Use of volatile anesthetics and intra-operative use of opioids and use of Nitrous Oxide [4-9]. There are a number of antiemetic drugs available; despite of their use the PONV is still a cause of concern post surgeries. Since there is no drug which is 100% effective in prevention of PONV sometimes combinations of various drugs are used which have lot of adverse effects [10]. Ondansetron is a $5HT_3$ receptor antagonist is supposed to be highly effective in treatment of PONV and other diseases associated with vomiting [11]. Ondansetron blocks the emetogenic impulses from both peripheral

origin and their central relay. It is cleared 60-70% by first pass metabolism and it is hydroxylated and conjugated and excreted [11]. Palonosetron is a selective second-generation 5-HT_3 receptor antagonist which has demonstrated efficacy in the management of CINV when administered both intravenously (IV) and orally [12]. It has prolonged duration of action with advantages over the other 5-HT_3 receptor antagonists for the prevention of CINV and PONV. Its binding affinity to the 5-HT_3 receptor is higher (approximately 100-fold) than other 5-HT_3 receptor antagonists [13]. In patients receiving moderate to highly emetogenic agents, the only 5-HT_3 receptor antagonist that has any effect in the prevention of delayed CINV is Palonosetron [14]. With this background we in the present study tried to evaluate the PONV in patients undergoing various elective surgical procedures.

Materials and Methods

This cross sectional prospective study was conducted in the Department of Pharmacology and Department of ENT, Government Medical College and Hospital, Rajnandgoan, CG. A total of n=79 were selected based on the inclusion and exclusion criteria they were divided in two groups viz Group I (Ondansetron) (n=40) and Group II (Palonosetron) and (n=39). Inclusion criteria were patients with ASA I and II categories, patients with no history of significant medical conditions. The excluded patients were patients receiving diuretics, antiarrhythmic drugs, pregnant or lactating females, those with history of motion sickness and those who have taken antiemetic 24 hours before surgery. The patients were randomly divided into two groups by a computer generated random number table into two groups. All routine investigations were done pre-operatively. All the patients were given tablet Alprazolam 0.25mg a night prior to the surgery and were kept NBM by mouth for 8 hours. The Ondansetron Group (I) received Ondansetron 8mg IV in 10 ml normal saline over 30 seconds immediately before induction of general anesthesia and group (II) received inj. Palonosetron was given 0.075mg IV. A standard anesthesia technique was followed endotracheal intubation was done with appropriate size cuffed endotracheal tube. The patients were connected to mechanical ventilator and anesthesia was maintained with N_2O and O_2 50%, isoflurane (0.2 – 1%) and inj. vecuronium 0.08mg/kg was used as a muscle relaxant as loading dose. In the monitoring room all the patients' recovery parameters were checked and any episode of nausea or vomiting (PONV) was recorded at an interval of 30 min, 2 hours, 6 hours and 24 hours. Frequencies of rescue medication given were noted.

Results

The mean age of the patients in Group I (Ondansetron) was 30.5 years and the mean age of the patients in the Group II (Palonosetron) was 32.5 years. The male to female ratio in Group I was 5:3 and similarly in the group II the ratio was 8:5. In the group I the 32 (80%) were belonging to ASA Grade I and 8(20%) belonging to ASA Grade II. In the group II the 30(76.92%) were belonging to ASA Grade I and 9 (23.08%) were belonging to ASA Grade II. The mean duration of surgeries in the Group I was 120 ± 10.5 minutes and in the group II was 130 ± 15.5 minutes (Table1).

Table-1: The Baseline characteristics of the patients involved in the study

	Group I (Ondansetron)	Group II (Palonosetron)
Mean Age in Years	30.5 ± 1.5	32.5 ± 2.5
Male/Female	25/15	24/15
Mean Weight in Kgs	58.10 ± 5.5	60.5 ± 4.0
ASA Grade I/II	32/8	30/9
Mean duration of Surgeries (mins)	120 ± 10.5	130 ± 15.5

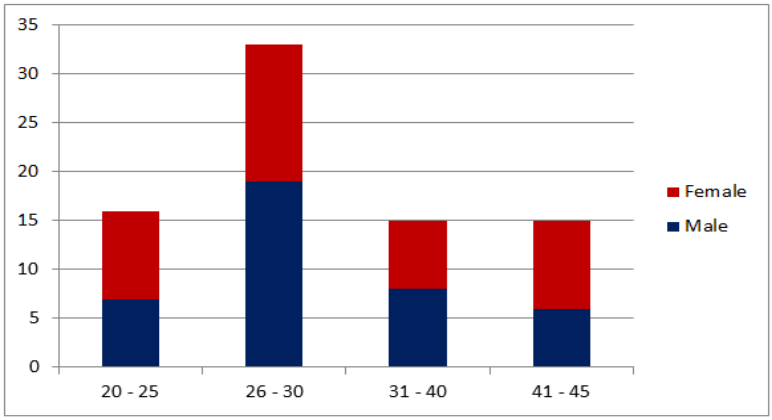

Fig-1: Showing the age wise and sex wise distribution of cases in the study

Apfel is a popular scoring system for identifying patients with high risk PONV [15]. PONV is defined as at least one episode of nausea or vomiting within the first 24hrs after the surgery. The scoring system is simplified to four item risk score which was defined as the number of predictors present. The predictors are female gender, nonsmoking status, PONV and post-operative use of opioids. If none, one, two, three or four present the risk was 10%, 21%, 39%, 61%, and 79% respectively. In the present study Apfel in group I 26(66.66%) of patients were with score 2. Similarly in the Group II 22(55%) were with Apfel score 2 the other distribution is as shown in the table 2.

Table-2: The Apfel Scores of the patients involved in the study

Apfel Scores	Group I (Ondansetron)		Group II (Palonosetron)	
	Total	Percentage	Total	Percentage
1	4	10.25	5	12.5
2	26	66.66	22	55.0
3	5	12.82	10	25.0
4	4	10.25	3	7.5

The incidence of Nausea was compared between both the groups. In the group I a total of 13 patients were seen with nausea and most of them had nausea between 2 – 6 hours post operatively. Similarly in the Group II the total number of cases of Nauseas postoperatively was in 7 patients and most of them had nausea between 2 - 6 hours after operation. The p values for the postoperative nausea between two groups were found to be <0.05 which is significant (table 3).

Table-3: The incidence of Postoperative Nausea in both groups

Hours	Group I (Ondanserton)	Percentage	Group II (Palonoserton)	Percentage	P values
0 – 2	2	5.0	1	2.5	<0.05*
2 – 6	6	15.0	4	10.25	
6 – 24	5	12.5	2	5.1	

* Significant

The incidence of postoperative vomiting in group I was seen in 10(25%) out of the total 40 patients and most of the patients had vomiting between 6 -24 hours 6 (15%) had vomiting and 2(5.0%) had vomiting between 0 – 2 hours and 2 – 6 hours. In the group II a total of 6 (15.38%) had vomiting equally in the duration between 2 – 6 hours and 6 – 24 hours respectively. The p values were found to be <0.05 which was significant (table 4).

Table-4: The incidence of postoperative Vomiting in both groups

Hours	Group I (Ondanserton)	Percentage	Group II (Palonoserton)	Percentage	P values
0 – 2	2	5.0	0	0.0	< 0.05*
2 – 6	2	5.0	3	7.69	
6 – 24	6	15.0	3	7.69	

* Significant

DISCUSSION

Post-operative nausea and vomiting is an important issue for the surgeon and its adequate management is vital for overall success of surgery. Although with invention of newer anesthetic agents and new surgical techniques the incidence of PONV is reduced. Ondansetron a 5 HT3 antagonist has been considered as the gold standard for prevention of PONV [16]. Since its introduction it has become a mile stone in antiemetic therapy caused by radiotherapy as well as chemotherapy and it has been widely used for prevention of PONV. In the present study we included patients only with ASA grade I/II and excluded patients with history of motion sickness as they have accentuated reflex arc for vomiting and are more prone to develop PONV. Also since the safety of the drugs is not clearly established in pregnancy and lactations therefore these patients were also excluded from the study. Palonosetron belongs to the second generation of 5-HT3 antagonist with unique pharmacodynamic characteristics. Since it is allosteric 5-HT3 receptor antagonist it causes conformational change in serotonin receptor and thereby inhibits the serotonin binding capacity indirectly [17]. Since palonosetron has greater affinity for 5-HT3 receptors, it has greater potency and longer duration of action [18]. In the present study we used the dose of Ondansetron 8mg IV before the induction of anesthesia in the Group I (Ondansetron). In

a similar study by Paventi *et al*. [19] found that the single dose of ondansetron 8mg is more effective for prevention of PONV. For the standard dose of palonosetron we followed the 2014 guidelines for PONV and used 0.075mg of palonosetron. Kovac Al *et al*. [20] finding the effect of different doses 0.025 mg, 0.05mg and 0.075mg of palonosetron found that the dose of 0.075 was superior to a placebo at all the points during the first 24 hours and it was also associated with longer median time to first emesis and the FDA has also approved the dose of 0.075mg as the minimum effective dose of palonosetron for PONV prophylaxis hence in the present study we utilized the same dose [21, 22]. The mean duration of surgery in the Group I was 120 ± 10.5 min and in group II it was 130 ± 15.5 minutes. It is generally noted that the duration of surgery has an impact on post-operative nausea and vomiting. As the duration of surgery prolongs there are greater chances of PONV and hence the requirement of antiemetic also increases [4, 23]. The present study has found that the incidence of PONV between the two drugs is statistically significant. The use of rescue antiemetic was lesser in palonosetron group as compared to the ondansetron group. Although, both groups did not have any adverse drug effects the subgroup analysis in the study found that the incidence of Nausea and vomiting in 0 – 2 hours, 2 - 6 hours, and 6 -24 hours found to be significant with lesser number of patients in the palonosetron group. In this study we found that the majority of patients were in Apfel scores of 2 and only 4 (10.25%) were with Apfel score 4 in group I and in group II 3(7.5%) were in Apfel score 4 which is considered as the high risk group for PONV. There were no major adverse reactions to both the drugs and minor complaints of headache, dizziness were present which were managed adequately in the patients.

Conclusion

Within the limitations of the present study it can be concluded that Palonosetron 0.075mgIV is more effective than ondansetron 8mg IV for prevention of post-operative nausea and vomiting in these group of patients. We recommend the use of palonosetron 0.075mg IV in patients with high risk of PONV with Apfel scores of 4.

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