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COMPARISON OF RAMOSETRON AND PALONOSETRON FOR CONTROL OF POST-OPERATIVE NAUSEA AND VOMITING IN TOTAL LAPROSCOPIC HYSTERECTOMY

Tamaskar Aparna Associate Professor, Department of Anesthesia L.N.Medical College & J.K. Hospital, Kolar Road, Bhopal

Patel Ashwini Assistant Professor, Department of Anesthesia L.N.Medical College & J.K. Hospital, Kolar Road, Bhopal Corresponding Author

Bhargava Sumit Professor, Department of Anesthesia L.N.Medical College & J.K. Hospital, Kolar Road, Bhopal

ABSTRACT

Background: Post-operative nausea vomiting (PONV) is a complaint which is not only distressing to the patient, but may cause complications in high risk patients and increase post-operative cost of stay as well as duration of stay.5-HT3 receptor antagonists have shown promising results in the prophylaxis of PONV.

Aim: This study has been undertaken in order to compare the effectiveness of Ramosetron versus Palonosetron in PONV following Total Laproscopic Hysterectomy .

Materials and Methods: The current study was conducted on 60 female patients aged 25 to 50 years of age falling under ASA I / II grades who were undergoing Laproscopic Hysterectomy Patients were divided into two groups; Group A received : Injection ramosetron 0.3 mg and Group B received : Injection palonosetron 0.075 mg (IV) made 2 ml were administered for prevention of PONV. The effect of both the drugs and their side effects were compared.

Results: In the present study, the complete response was observed in post operative period at 0 -2 h and 2 – 6 h was 83.3% and 86.66 % in Group A and 50 % and 53.33 % in Group B respectively. The incidence of PONV in 24 hours of post-operative period was 90.00 % in Group A and 100.00% in Group B.

Conclusion: Ramosetron was found to be an effective and better agent than Palanosetron for control of PONV in patients undergoing planned, total laproscopic hysterectomy under general anesthesia.

INTRODUCTION

With a reported incidence of 60 – 80% (1,2,3) PONV at times is more distressing than post-operative pain and can complicate post-operative care. The etiology of postoperative nausea and vomiting (PONV) remains unclear, but patients still suffer from PONV with increasing healthcare costs and decreasing satisfaction [4, 5]. The incidence of PONV when no antiemetics are administered is reported as high as 80%, and related to nearly all surgical procedures [6]. Therefore, numerous antiemetics, including antihistamines, anticholinergics, and dexamethasone, have been studied for the prevention and treatment of PONV. Among the available antiemetic drugs, palonosetron and ramosetron, which were both recently developed, are selective 5-hydroxytryptamine-3 receptor antagonists (5-HT3), which have a well-established role in the prophylaxis and treatment of PONV [7].

Post-operative nausea and vomiting (PONV) is a common complaint occurring in patients undergoing elective total laproscopic hysterectomy under general anesthesia.PONV not only causes distress to the patient but may lead to wound dehiscence, dehydration, fluid – electrolyte imbalance, increased pain at operation site, chances of aspiration, increased cost and duration of stay and possible delayed recovery. 5-HT3 antagonist drugs are very commonly used now , as they have a better safety profile and lack side effects of previous generation antiemetics like extrapyramidal syndrome, sedation and dysphoria.

The most commonly used drug for PONV is Ondansetron, either alone or in combination with other drugs. Compared to Ondansetron, Ramosetron is a newer drug which exhibits greater 5-HT3 receptor binding affinity and slower dissociation rate rendering it more potent in comparison to Ondansetron. Palanosetron is a 2nd generation 5-HT3 receptor antagonist, has a mean elimination half life of 40 hours, and a better receptor binding affinity compared to the 1st generation 5-HT3 antagonists. Compared to Ondansetron and Granisetron, Palanosetron binds to the receptor at a different allosteric site.

Extensive search revealed a number of studies comparing the efficacy of Ramosetron and Palanosetron on PONV, but the controversy regarding the best suitable drug still persists. As both the drugs are comparatively new and not much studies are done regarding their role following total laproscopic hysterectomy for PONV hence this study was undertaken.

MATERIALS AND METHODS

Approval from the Institutional Ethical Committee was sought and written informed consent was obtained from all patients undergoing this study. The current study was conducted on 60 female patients aged 25 to 50 years of age falling under ASA I/II grades who were undergoing elective, planned total laproscopic hysterectomy under general anesthesia at L.N.Medical College & J.K. Hospital, Kolar Road, Bhopal from April 2016 to March 2017. Patients with major systemic disorders like Cardiovascular disease, renal or gastro intestinal disorder, renal and hepatic disorder or diabetes mellitus were excluded from the study.

Pre-anesthesia check-up was routinely conducted for all patients . All patients were kept nil orally from midnight. Before coming to the operation theatre all patients had proper IV access with 20 gauge cannula and Ringer lactate 10ml /kg of bodyweight. Devices to monitor ECG, heart rate, oxygen saturation and end-tidal carbon dioxide were attached in the operation theatre.

Patients were randomly allocated in two groups of 30 patients each. Group A received Injection ramosetron 0.3 mg (IV) in 2 ml solution(Significantly fewer instances of PONV occurred in the group that received 0.3 mg of ramosetron than in the placebo group and Group B received Injection palonosetron 0.075 mg (IV) made 2 ml after adding 0.5 ml normal saline.

Patients were induced with IV Injection of Propofol 2mg / kg and IV Injection of Fentanyl 1micro g /kg. IV injection Vacuronium 0.1mg / kg was used to facilitate endotracheal intubation. A Ryle's tube was also passed after confirming the position of the ETT in place with the help of capnography. Anesthesia was maintained with nitrous oxide (66%) and isofluorane (1-2%) in oxygen. Intermittent doses of Injection Vacuronium were given in order to maintain intra-operative muscular relaxation. At the end of the procedure, intra muscular Injection of Diclofenac 75 mgs was given and IV injections of Neostigmine 0.05 / kg and Glycopyrrolate were used in order to effect reversal of neuro muscular blockade. Patients were extubated in a fully awake state after ensuring proper oral and nasogastric suction to avoid any kind of aspiration. Before transferring the patients from OT to the post-operative care unit , IV injection of either Ramosetron 0.3 mgs or Palanosetron 0.075mgs was administered. Opiods were

avoided in all patients for post operative analgesia. In the post operative care unit, in addition to vital signs and pain score patients were monitored for symptoms of nausea, retching and vomiting. An independent observer who was blinded to the study , monitored for complaints of any nausea, retching, vomiting any possible adverse effects and duly documented the same. Ondansetron 4-8 mgs IV was given as a rescue anti emetic.

Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit whereas retching was defined as the labored spasmodic, rhythmic contraction of the abdominal muscles without expulsion of gastric contents, and vomiting was defined as the forceful expulsion of gastric contents from the mouth. We made no distinction between vomiting and retching for treatment purpose. A trained nurse taking care of the patient recorded all episodes of PONV (nausea, retching, and vomiting) either by direct questioning or by spontaneous complaint by the patients during three periods within the first 48 h after anesthesia: 0-2 h in the PACU, 2-6 h in the PACU and then in the ward ward upto 24 hours. Nausea was scored on an 11-point verbal rating scale from 0 (no nausea) to 10 (worst possible nausea): Severity was scored as mild (1-3), moderate (4-6), or severe (7-10). Any side effects/adverse effects were recorded during the study period by the attending anesthesiologist and Gynecologist. Patient satisfaction regarding their satisfaction to be free of nausea and vomiting was performed on a four-point Likert scale (dissatisfied, neutral, satisfied, and highly satisfied) at the end of the study.

Statistical Analysis

The sample size was calculated from IBM SPSS statistical software package for windows was employed for statistical analysis. Independent sample t test was used for comparing variables with normal distribution and categorical data analysed by chi square test. The P < 0.05 was considered statistically significant.

OBSERVATIONS AND RESULTS

Table 1 – Demographic Data

Characteristics	Group A(Ramesetron) n-30	Group B(Palanosetron) n-30	P
Age – years	47.2	46.90	0.5160
Weight –kgs	54.30	58.00	0.6443
Duration of surgery(mins)	85.2	88.60	0.5714
ASA grade I/II	20/30	21/30	

Table 2 Incidence of post-operative nausea, vomiting, number of complete responders and use of rescue anti-emetics

Post-operative Time period	Incedence	Group A N-30	Group B N-30	P Value
0-2 Hours	1.Nausea	5 (16.67)	15 (50)	0.9981
	2.Vomitting	2 (6.6)	5 (16.7)	0.8849
	3.Retching	1	3	-
	4.Rescue anti-emetic	5 (16.67)	9 (30)	0.5398
	5.Complete responders	25 (83.3)	15(50)	0.9982
2- 6 Hours	1.Nausea	4 (13.33)	11 (36.66)	0.5832
	2.Vomitting	1 (3.3)	4 (13.33)	-
	3.Retching	2(6.6)	6(20)	-
	4.Rescue anti-emetic	4 (13.33)	8 (26.66)	0.5478
	5.Complete responders	26 (86.66)	16(53.33)	0.9987
6-12 Hours	1.Nausea	5 (16.6)	4 (13.3)	-
	2.Vomitting	2 (6.6)	1 (3.3)	-
	3.Retching	1 (3.3)	2 (6.6)	-
	4.Rescue anti-emetic	2 (6.6)	1 (3.3)	-
	5.Complete responders	26 (86.66)	24(80)	0.7549
12-24 Hours	1.Nausea	2 (6.6)	0	-
	2.Vomitting	0	0	-
	3.Retching	1 (3.3)	0	-
	4.Rescue anti-emetic	0	0	-
	5.Complete responders	27(90)	30 (100)	0.9582

P<0.05 – significant. Values expressed as numbers (%).n – number of patients

Table-3: Incidence of adverse events

Adverse events	Group A	Group B	P
Headache, n%	3 (10)	2 (6.6)	0.6404
Dizziness, n%	6 (20)	5 (16.6)	0.7386
Drowsiness, n%	0	2 (6.6)	-
Rash, n%	0	0	-

P<0.05 –significant. Values expressed as numbers (%).n – number of patients

Sixty patients were enrolled for this study and completed the same with none of the patients dropping out for any reason. Both groups had patients whose demographic data was comparable with respect to age, weight, ASA grade and duration of surgery [Table 1].

In the 24 hours post operative period the overall incidence of nausea and vomiting was found to be in 5 (16.6%) patients respectively in Group A i.e. Ramosetron group and 10 (33.3 %) patients in Group B i.e. Palanosetron group. This difference in figures for these two groups was statistically significant (0.9357).

The number of complete responders during 0–2 h and 2–6 h in Group A was 25 (83.3%) and 26 (86.66%) respectively whereas in Group B it was 15 (50%) and 16 (53.33%), respectively. This difference was found to be statistically significant (P = 0.9995). The incidence of post-operative nausea in Group A was 5 (16.6 %) and 4 (13.33%) respectively whereas in Group B it was 15 (50 %) and 11 (36.66 %) respectively, during 0–2 h and 2–6 h. This difference was found to be statistically significant (P = 0.01and P = 0.5832, respectively) [Table 2 and Figure 1]. The number of complete responders and post-operative nausea during 6–12 h and 12–24 h interval was not significant. The number of patients developing post-operative vomiting and retching, and the number of patients requiring rescue anti-emetics was also not significant during 0–24 h period [Table 2 and Figure 1]. Nausea severity score was comparable in both the groups during post-operative period [Figure 2]. Both the groups of patients had adverse effects such as headache and dizziness, but the incidence was statistically not significant [Table 3].

DISCUSSION

This present study showed that the 5HT3 receptor antagonist Ramosetron is more efficient than Palonosetron in preventing early PONV in patients undergoing total laproscopic hysterectomy under general anesthesia. Our study demonstrated the incidence to be much higher, i.e., as high as 45% which can be attributed to many risk factors in our patients such as female gender, young age (<50 years), non-smoking status, gynaecological surgery and duration of surgery lasting more than 30 minutes.

As both the drugs are comparatively new and not much studies are done regarding their role following total laproscopic hysterectomy for PONV, we decided to give Ramosetron and Palanosetron as monotherapy in these two groups of 30 patients each. According to the previous studies, a dose of 0.075 mg palonosetron given at the beginning of surgery was effective in reducing PONV[8,9] which has also been approved by FDA. Onset of action of palonosetron takes 30 min and so we decided to administer 0.075 mg of palonosetron.

De Leon A et al studied the role of palonosetron which is a second-generation 5-HT3 receptor antagonist for chemotherapy-induced nausea and vomiting. Palonosetron has the unique property of controlling 'delayed chemotherapy-induced nausea and vomiting' when compared to older serotonin antagonists. [10]

Kim EJ, Ko JS et al studied combination of antiemetics for the prevention of postoperative nausea and vomiting in high-risk patients Palanosetron is a selective 5-HT3 receptor antagonist that exhibits significantly greater binding affinity for 5-HT3 receptors

and a slower dissociation rate, resulting in more potent and longer action [11].

Song YK, Lee Cet al compared effects of ramosetron and dexamethasone on postoperative nausea, vomiting, pain, and shivering in female patients undergoing thyroid surgery.Our study showed that complete responders were more in ramosetron than in palonosetron group. Ramosetron reduced the incidence of PONV, pain and shivering in female patients undergoing thyroid surgery.[12]

Gan TJ, Diemunsch P et al formulated present guidelines that are based on the most recent data on postoperative nausea and vomiting (PONV) and an update on the 2 previous sets of guidelines published in 2003 and 2007. These guidelines were compiled by a multidisciplinary international panel of individuals with interest and expertise in PONV under the auspices of the Society for Ambulatory Anesthesia. These guidelines identify patients at risk for PONV in adults and children; recommend approaches for reducing baseline risks for PONV; identify the most effective antiemetic single therapy and combination therapy regimens for PONV prophylaxis, including nonpharmacologic approaches; recommend strategies for treatment of PONV when it occurs; provide an algorithm for the management of individuals at increased risk for PONV as well as steps to ensure PONV prevention and treatment are implemented in the clinical setting.

They showed that when different doses of palonosetron were compared with placebo, it has shown that the complete response in 0-2 h and 2-6 h in palonosetron (0.075 mg) group was 45% and 56% respectively which compares with our study. But that incidence was lesser when compared to ramosetron in our study which was 83.3% and 86.66% during 0-2 h and 2-6 h respectively.Our study demonstrated that the incidence of nausea was higher in palonosetron group than in the ramosetron group. This shows that palonosetron, a 5-HT3 antagonist has poor control on nausea like the older generation 5-HT3 antagonists.[13]

Kim WO et al reviewed 18 randomized controlled trials investigating the efficacy and safety of ramosetron in comparison with placebo or any other drugs . Ramosetron is effective and safe in children and adults without serious adverse effects compared with placebo or other active drugs, as shown in pooled data of RCTs, in terms of the prevention of PONV Adverse effects like headache and dizziness were comparable in both groups in our study. Significantly fewer instances of PONV occurred in the group that received 0.3 mg of ramosetron than in the placebo group [14]

The limitations of the present study were that the sample size was small. Further research is needed to know the efficacy of both the drugs with bigger sample size in prevention of PONV.

CONCLUSION

The 5HT3 antagonist Ramosetron was found to be more effective as compared to Palanosetron in reducing the incidence of PONV in patients undergoing total laproscopic hysterectomy under general anesthesia.

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