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Research Article

A Comparative Study of Ondansetron versus Ramosetron on Post Operative Nausea and Vomiting in Gynecological Surgeries

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Abstract: Postoperative nausea and vomiting (PONV) is one of the most unpleasant and distressing symptoms which follow anaesthesia and surgery and lead to serious postoperative complications. PONV commonly occurs within 24 hours after surgery and can occur following general, regional, or local anaesthesia. Patients undergoing major abdominal surgery are especially prone to PONV, with reported incidences of 50-75%. Ninety patients aged between 20-60 years with ASA class I and II, posted for elective abdominal surgeries under spinal anaesthesia were randomly allocated to three groups- Group O [n=30] - Ondansetron (4mg), Group R [n=30] - Ramosetron (0.3mg), Group C [n=30] - Normal saline(only rescue anti- emetic).The incidence of PONV in control group was 40%, while the incidence in Group O and Group R was 16% and 6% respectively. Complete response was observed in 60%, 84% and 94% of patients in Group C, Group O and Group R respectively. The need for rescue antiemetic was significantly reduced with both antiemetic groups compared to control group. Ramosetron was more effective than ondansetron in preventing postoperative nausea and vomiting in patients at high risk undergoing total abdominal hysterectomy.
Keywords: PONV, Ondansetron, Ramosetron, Total Abdominal Hysterectomy, Spinal Anaesthesia

INTRODUCTION

Postoperative nausea and vomiting (PONV) still is the most troublesome adverse event encountered in the recovery room, despite advances in prevention and treatment[1]. PONV as its occurrence may delay discharge[2] or cause unanticipated hospital admission[3]. Several different mechanisms may play a role in causing PONV in patients who receive regional anesthesia.

The consequences of PONV are surgical, physical and anesthetic complications for patients and financial implications for the hospitals or institutions. Of the many different modes of intervention to prevent PONV, antiemetic drugs play an important role in therapy of PONV. Presently, there is no single PONV antiemetic medication or technique that is 100% effective for all patients and a search for better drug continues. Anti-emetics acting on Dopamine, Cholinergic, Histamine, 5HT andNK1 receptors have been tried. Combination of 5HT3 receptor antagonists and Dexamethasone has been recommended for prophylaxis in patients at risk of PONV. Ondansetron and Ramosetron are known 5HT3 antagonists and used in combination with Dexamethasone for prophylaxis against PONV.

Since at least four major receptor systems are involved in the etiology of PONV, a better prophylaxis might be achieved by using a combination of agents acting at different receptor sites. The most common prophylactic antiemetic combination used to prevent PONV is Intravenous Ondansetron, a 5HT3 receptor antagonist. Ramosetron is a newly introduced selective serotonin 5-hydroxytryptamine type 3 (5-HT3) receptor antagonist and is more potent and has longer-lasting antiemetic effects than older agents because of a slower rate of dissociation from the target receptor and higher binding affinity

This study was done to compare combination of 5HT3 receptor antagonists ondansetron and ramosetron with dexamethasone in prevention of PONV in female patients undergoing elective major gynecological surgery under spinal anaesthesia

The objectives of the study is to compare the effectiveness of combination of ramosetron 0.3mg and dexamethasone 8mg v/s ondansetron 4mg plus dexamethasone 8mg in prevention of postoperative nausea and vomiting and to evaluate and record the

incidence of adverse events like headache, dizziness, drowsiness, flushing and sedation.

MATERIALS AND METHODS

The present study, entitled a comparative study of antiemetic –ramosetron0.3mg versus ondansetron 4mg in prevention of postoperative nausea and vomiting in patients undergoing elective gynecological surgeries performed under spinal anaesthesia conducted at MNR Medical College, Sangareddy, Telangana state.

The study is a prospective, randomized and double blind placebo controlled study. Pre anesthetic evaluation was done on the previous day of surgery and patients were assessed for risk factors for PONV. Written informed consent was taken from all patients selected for the study. A thorough history taking and general and systemic examination was done.

Basic laboratory investigations like hemoglobin level, total cell count, differential count, urine routine, screening of chest x-ray, ECG, RBS, blood urea, serum creatinine and thyroid function tests evaluated. Patients advised to remain nil orally for solids after 10 pm and 2 hours for clear fluids. All of them received alprazolam 0.25mg & Ranitidine hydrochloride 150mg orally on the night before surgery. In our study, patients with a history of motion sickness, migraine, renal, GIT disorders, liver disorders and previous PONV were excluded

After obtaining clearance from Hospital Ethical committee, Ninety patients aged between 20-60 years with ASA class I and II, posted for elective gynecological surgeries under spinal anaesthesia were randomly allocated to three groups- Group O [n=30] - Ondansetron (4mg), Group R [n=30] - Ramosetron (0.3mg), Group C [n=30] - Normal saline(only rescue anti- emetic). All patients were given spinal anaesthesia. Study drug was administered at two interval one given immediately before Spinal anaesthesia and other given 20 minutes before completion of surgery.

Group O [n=30] - Ondansetron (4mg) intravenously was given immediately before Spinal anaesthesia and 4 mg (2ml) was given 20 minutes before completion of surgery.

Group R [n=30] -Ramosetron (0.3mg) Intravenously was given immediately before Spinal anaesthesia and 0.3 mg (2ml) was given 20 minutes before completion of surgery.

Group C [n=30] - Normal saline (only rescue anti- emetic). For blinding process Normal saline 2 ml was given immediately before spinal anaesthesia and once again given

The incidence of nausea, retching and vomiting was studied for a period of 24 hours post operatively. All patients were assessed every hourly for the first 6 hours, 3 hourly for the next 6 hours and 6 hourly for subsequent 12 hours using the following PONV scoring system. The adverse effects were also studied.

The data was analyzed using the Predictive Analytics Software (PASW, version 18: Chicago, IL, USA). A repeated measure ANOVA (with Bonferroni correction) was used to compare the continuous variables and Chi-square test or Fisher's exact test was used for comparing categorical variables. Values were considered significant when $P < 0.05$.

RESULTS:

Ninety patients aged between 20-60 years with ASA class I and II, posted for elective gynecological surgeries under spinal anaesthesia were randomly allocated to three groups- Group O [n=30] - Ondansetron (4mg), Group R [n=30] - Ramosetron (0.3mg), Group C [n=30] - Normal saline(only rescue anti- emetic).

Based on previous studies we selected Ondansetron 4mg and Ramosetron 0.3mg for this study [4&5].

Demographic profile:

In our study the demographic profile was similar in all three groups with respect to age, sex weight and body mass index. There was no statistical significant difference noted in the above mentioned parameters.

Type and Duration of surgery:

Increase surgery duration increased baseline PONV risk by 60% [6]. PONV was more frequent during longer duration of surgery due to increased usage of emetic anaesthetic drugs [7]. All patients in our study underwent total abdominal hysterectomy with or without oopherectomy. The three groups were similar with respect to surgical procedures. The average duration of surgery was more than 90 minutes in all the three groups.

1.Complete Response

Complete response is defined as absence of nausea, retching, vomiting and no requirement of rescue anti-emetic. It is measured post operatively in 24 hours.

Table: 1. complete response of drugs in post operative period

Groups with Study drugs	% of patients showed complete response in			
	0-6hours	6-12hours	12-18hour	18-24hours
Ramosetron	94%	100 %	97%	100%
Ondansetron	90%	97%,	97%	97%
Control	67%	80%	90%	90%.

In our study in 24 hour period, overall complete response was 94% in Group R, while it was 84% in Group O and 60% in Group C.

Incidence Of PONV

Overall incidence of nausea was 16% in Group O and 40% in Group C while it was significantly less at 6% in Group R. Overall incidence of vomiting in Group O was 3%, Group R was 0% and Group C was 13%. Overall incidence of retching in Group C was 13% while it was 0% in Group O and Group R.

Table:2. Incidence of nausea in post operative period

Groups with Study drugs	% of patients showed nausea			
	0-6hours	6-12hours	12-18hour	18-24hours
Ramosetron	6%	3 %	3%	0%
Ondansetron	6%	3%,	3%	3%
Control	20%	10%	6%	6%.

Table:3. Incidence of vomiting in post operative period

Groups with Study drugs	% of patients showed vomiting			
	0-6hours	6-12hours	12-18hour	18-24hours
Ramosetron	0%	0 %	0%	0%
Ondansetron	3%	0%,	0%	0%
Control	10%	3%	0%	0%.

Requirement of rescue antiemetics

In our study, the requirement of rescue antiemetics in the postoperative period (0-24 hours) in the Ramosetron group and Ondansetron group was 0%. The requirement of rescue antiemetic in the early postoperative period 0-6 hours and 6-12hour in the Control group was 10% and13 % respectively.

Adverse Effects:

Most frequently reported adverse events were dizziness and headache, Perineal itching, dyspepsia and weakness [13]. In our study we did not observe any adverse effects in any of the three study groups.

Table 4: The summary of the present study

Parameter	Group O [n=30]	Group R [n=30]	Group C [n=30]
Age in years(sd)	39.03(5.37)	39.30(7.96)	39.77(6.86)
Weight in kgs(sd)	50.93(2.85)	51.30(6.78)	49.30(6)
Height in cms(sd)	152.53(3.608)	152.8(3.43)	153.20(5.48)
BMI kg/m2(sd)	9.87(1.38)	9.97(2.45)	9.07(2.36)
Duration of anaesthesia in minutes(sd)	103.6(19.77)	96.53(17.37)	103.70(18.20)
Incidence of PONV	16%	6%	40%
Complete response	84%	94%	60%
Rescue antiemetic	0%	0%	13%
Adverse events	0	0	0

DISCUSSION

We compared the prophylactic anti-emetic efficacy of ramosetron and ondansetron in patients at high risk for PONV undergoing total abdominal hysterectomy. Effective prophylaxis of PONV is invariably linked to the quality and the extent of pain relief in the post operative period.

The 5HT3 receptor antagonists suppress nausea and vomiting by inhibiting serotonin binding to the 5HT3 receptors present in several critical sites involved in emesis, including vagal afferents, the solitary tract nucleus (STN), and the area postrema. The highest concentration of 5HT3 receptors in the central nervous system (CNS) are found in the STN and chemoreceptor trigger zone (CTZ), and 5HT3 antagonists suppress nausea and vomiting by acting at these sites.

There was no statistical difference between the PONV scores in Groups O & Group R in any time period, suggesting that the two antiemetic combinations were effective in preventing PONV for over all, but there was a significant clinical difference in PONV scores noted between prophylactic groups and Control group.

In the first 6 hrs the incidence of nausea in the Control group in our study was 20% which has been effectively reduced in Group O and Group R to 6% and 6% respectively. The incidence of retching was 3% in Group C but retching was absent in both Groups O & R. The incidence of vomiting was reduced from 10% in control Group to 3% in group O and to 0% in Group R receiving prophylactic anti-emetics.

In this study ramosetron is proved to be more effective, as it has greater affinity to 5HT3 receptor leading to greater potency and longer duration. A similar study in patients undergoing gynecological surgery found ramosetron, 0.3 mg to be as effective as 8 mg ondansetron [8]. In a study performed on highly susceptible patients undergoing abdominal hysterectomy, ramosetron (0.3 mg) was found to be more effective in preventing delayed PONV which is understandable considering the fact that it has an elimination half-life of 9 h which is much longer than that of ondansetron (3.5 h) with a higher affinity and a slower dissociation rate for 5-HT $_3$ receptors compared with other 5-HT $_3$receptor antagonists [9]. Similarly, in a study of spine surgery with fentanyl patient controlled analgesia found ramosetron prophylaxis is as effective as ondansetron in reducing PONV [10]. In Knee replacement surgeries ramosetron is appeared to be more effective [11]. In a recent study of breast, parotid, thyroid or gynecological surgeries ramosetron and ondansetron were equally effective in reducing the PONV incidence [12].

CONCLUSION

The incidence of PONV in control group was 40%, while the incidence in Group O and Group R was 16% and 6% respectively. Complete response was observed in 60%, 84% and 94% of patients in Group C, Group O and Group R respectively. The need for rescue antiemetic was significantly reduced with both antiemetic groups compared to control group. Hence Ramosetron (0.3mg) is a better alternative to Ondansetron (4mg) in preventing PONV in high risk patients.

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