Original article:

Comparative study of ondansetron, granisetron and ramosetron for prevention of postoperative nausea and vomiting (PONV) in surgeries under general anaesthesia.

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Abstract:

Introduction: Prevention of postoperative nausea and vomiting (PONV) poses an anaesthetic challenge for surgeries under general anaesthesia. This study was aim to evaluate and compare the efficacy of ondansetron, granisetron and ramosetron as prophylactic antiemetic for surgeries under general anaesthesia.

Methodology : 90 patients of ASA grade I and II in the age group 20-65 years scheduled for surgery under general anaesthesia were studied. Patients were divided into three groups of 30 patients each according to computer generated random allocation. The patients received the following drugs intravenously. Inj. ondansetron 0.1mg/Kg (ondansetron group) Inj. granisetron 40µg/Kg (granisetron group)Inj.ranmosetron 0.3 mg (ramosetron group). All the drugs were diluted to 5ml volume in normal saline. The drugs were given 5 minutes prior to induction of anaesthesia. Postoperatively all episodes of nausea, retching and vomiting were recorded during 1st 24 hours. Efficacy of the drug was evaluated as a complete response – no nausea, retching or vomiting and no need for rescue medication. The observations obtained were tabulated and analysed using one way analysis of variance (ANOVA) or using chi-square test.

Results: During 0-3 hrs of postoperative period statistically non-significant difference were present in all the study groups ($P > 0.05$). During 3-24 hrs postoperative period, statistically significant difference was present between ramosetron and ondansetron groups ($P< 0.05$). However there was no significant statistical difference between granisetron and ramosetron group during the same period. ($P > 0.05$).

Conclusion: Based on this study it is concluded that upto 3 hrs postoperative period all the thre study drugs i.e. ondansetron, granisetron and ramosetron are comparable to each other for prevention of nausea, retching and vomiting. Both ramosetron and granisatron are better than ondansetronupto 24 hrs postoperative period.

Keywords: ondansetron, granisetron, ramosetron

Introduction:

Postoperative nausea and vomiting (PONV) is a distressing side effect of surgeries under general anaesthesia. PONV results in morbidity like wound dehiscence, bleeding, pulmonary-aspiration of gastric contents, fluid and electrolyte disturbances, delayed hospital discharge and decreased patient satisfaction. A variety of factors contribute to the occurrance of PONV. These are patient related, surgery related and anaesthesia related. Patients related factors are age,

weight, gender, pre-existing diseases, history of postoperative nausea and vomiting, anxiety and smoking. Interestingly non-smokers are two times prone to PONV as compared to smokers ([1]Apfel cc, 2005) A variety of drugs are being used for preventing PONV. These include traditional antiemetic agents like metoclopramide (Dopamine receptor anatagonists) as well as recently introduced group of antiemetic agents like ondansetron, granisetron and ramosetron (5HT receptor blockers). The prophylactic potency and the clinical efficacy of these drugs in the prevention of PONV is a keen subject of study in patients receiving general anaesthesia. We thus conducted this study to evaluate and compare the effect of ondansetron, granisetron and ramosetron for preventon of PONV in surgeries under general anaesthesia.

Methodology:

Following approval by the hospital ethics committee and a written informed consent 90 patients of ASA grade I and II in the age group 20-65 yrs scheduled for surgery under general anaesthesia were included in the study. Patients with history of motion sickness, pervious history of postoperative nausea vomiting, vestibular disease BMI (body mass index) > 30 and those who received antiemetic within 24 hrs prior to surgery were excluded from the study. After a thorough preanaesthetic check up all the patients were kept over night fasting and were advised to take tab alprazolam 0.5 mg on the night before surgery. Patients were divided into three groups of 30 each according to computer generated random allocation. The patients received the following drugs intravenously either Inj. ondansetron 0.1 mg/Kg (Ondansetron group) or Inj. granisetron 40 µg/Kg (granisetron group) or Inj.ramosetron 0.3 mg (ramosetron group). All the drugs were diluted to 5 ml volume in normal saline. The study drug was prepared by single person in 5ml syringe. The Investigator was not aware of the study drug used. After establishing the 1.V line in the preoperative area, the patient was taken to operation theatre and after attaching the monitors, each patient received 5ml of study drug 5 minutes prior to induction of anaesthesia. Standard induction was done in all three groups using Tramadol (0.5mg/Kg) propofol (2mg/Kg)rocuronin (0.6mg/Kg) to facilitate tracheal intubaten. Anaesthesia was maintained with N_2O : O_2 66% : 33% with halothane 0.5 – 1% and incremental doses of rocuronium.Supplemental analgesia was given in the form of Inj.diclofenac 75mg by infusion 30 minutes before the end of surgery. Perioperative monitoring consisted of continuous ECG, Blood Pressure, pulse rate, respiratory rate and pulse oxymetry. At the end of surgery residual neuromuscular blockade was reversed with Inj. neostigmine 50 µg/Kg I.V and Inj. glycopyrolate 10 µg/Kg I.V in all the patients. Patients were extubated after establishment of adequate spontaneous respiration and were transferred to recovery room. Postoperatively all patients were observed for every episode of nausea, vomiting and retching and recorded by persons who were unaware of the study drug. Rescue antiemetic was given in the form of Inj. metoclopramide 0.2 mg/Kg I.V. Nausea was defined as unpleasant sensation associated with the awareness of urg to vomit. Retching was defined as labored rhythmic contraction of abdominal muscles without expulsion of gastric contents. Complete response was defined as no nausea, retching or vomiting and no need of rescue medication. The results were tabulated

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and statistically analysed using one way analysis of variance (ANOVA) or using chi-square test.

Results:

Patients in all the three i.e. ondansetron, granisetron and ramosetron groups were statistically comparable as regards to age, body mass index (BMI) and duration of anaesthesia (P > 0.05) During 0-3 hrs of postoperative period the incidence of PONV was equal in all the three groups, nausea (N) = 13.3 % vomiting (V) = 13.3 % in ondansetrongroup N = 10 % V = 13.3 % in granisetron group, N = 3.3 % V = 6.7 % in ramosetron group. The percentage of patients who needed rescue antiemetic was 13.3 %, 13.3 % and 3.3 % in ondansetron, granisetron and ramosetron groups during the same period followed by 23.3 %, 10 % and 6.7 % in ondansetron, granisetron and ramosetron groups respectively during 3-24 hrs postoperatively. Statistically there was non-significant difference with regards to drug response in preventing nausea, vomiting, retching and need for rescue antiemetic in all the three study groups in 0-3 hrs postoperative period. Though it was statistically non-significant with regards to rescue antiemetic in ramosetron group but only 3.3 % patients needed rescue antiemetic. In ramosetron versus granisetronand ondansetron versus granisetron groups there was non-significant difference (P > 0.05) for prevention of nausea, vomiting retching and need for rescue antiemetic during 3-24 hrs interval postoperatively. However the difference was statistically significant (P < 0.05) in ondansetron versus ramosetron groups in prevention of nausea, vomiting and rescue antiemetic during the 3-24 hr period.

I Comparison of PONV, retching and rescue antiemetic in ondansetron, granisetron and ramosetron groups in 0-3 hr post-operative period.

Parameters	**Ondansetron Group N = 30**		**Granisetron Group N = 30**		**Ramosetron Group N = 30**	
	0-3 hr		**0-3 hr**		**0-3 hr**	
	Number	**Percentage**	**Number**	**Percentage**	**Number**	**Percentage**
Nausea	4	13.3 %	3	10.0 %	1	3.3 %
Vomiting	4	13.3 %	4	13.3 %	2	6.7 %
Retching	4	13.3 %	2	6.7 %	0	0.0 %
RescueAntiemetic	4	13.3 %	4	13.3 %	1	3.3 %

II Comparison of PONV, retching and rescue antiemetic in ondansetron, granisetron and ramosetron groups during 3-24hr postoperatively.

Parameters	Ondansetron Group N = 30		Granisetron Group N = 30		Ramosetron Group N = 30	
	3-24 hrs		3-24 hrs		3-24 hrs	
	Number	Percentage	Number	Percentage	Number	Percentage
Nausea	6	20.0 %	3	10.0 %	1	3.3 %
Vomiting	7	23.3 %	3	10.0 %	2	6.7 %
Retching	1	3.3 %	1	3.3 %	0	0.0 %
Rescue Antiemetic	7	23.3 %	3	10.0 %	2	6.7 %

III Complete drug response during 0-3 hrs postoperatively.
No nausea, No vomiting, No retching

Parameters	Ondansetron Group N = 30		Granisetron Group N = 30		Ramosetron Group N = 30	
	0-3 hrs		0-3 hrs		0-3 hrs	
	Number	Percentage	Number	Percentage	Number	Percentage
Compete drug response	24	80 %	25	83.3 %	28	93 %

IV Complete drug response during 3-24 hrs postoperatively.
No nausea, No vomiting, No retching

Parameters	Ondansetron Group N = 30		Granisetron Group N = 30		Ramosetron Group N = 30	
	3-24 hrs		3-24 hrs		3-24 hrs	
	Number	Percentage	Number	Percentage	Number	Percentage
Compete drug response	21	70.0 %	27	90.0 %	28	93.0 %

Discussion:

The etiology of PONV is multifactorial and depends upon a variety of factors which are related to patients surgery and anesthesia. The patient related factors are age, weight, gender, pre-existing disease, previous history of nausea and vomiting, anxiety and smoking. There is high incidence in surgeries such as strabismus surgery and middle ear surgery, use of drugs like opioids, ketamine and reversal agents like neostigmine increase the incidence of PONV. Patient movement, hypovolumia and early initiation of oral intake also increase patients risk for PONV. Overnight fasting, good sleep with tablet alprazolam 0.5 mg orally, smooth induction with propofol and

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adequate analgesia with Inj. diclofenac 75 mg IV infusion helped relieve preoperative anxiety and postoperative pain. The doses of drugs used in our study were based on previous reports of literature. The distribution of anthropometric parameters like height, weight and BMI (Body mass index) was not statistically significant across the three study groups. All the three study drugs are selective 5 hydroxytryptamine-3 antagonists and are effective for the treatment of patients with PONV. The 5HT-3 receptor antagonists which are regarded as the antiemetic gold-standard are used for prophylaxis against chemotherapy and radiotherapy – induced emesis. At equally effective doses, the 5HT-3 receptor antagonists have been shown to demonstrate broadly equivalent clinical antiemetic activity and safety. We found significantly less incidence of PONV with all the 3 drugsi.e. ondansetron, granisetron and ramosetrongroupsupto 3 hrs postoperative period. However beyond 3 hours upto 24 hours postoperative period, there was significant difference between and ondansetron and ramosetron groups. Similar results were reported by [2]HJBYON (2010) who showed that ramosetron was better than ondansetron for prophybaxis of PONV between 6-24 hrspostoperatively. Findings were also in accordance with that of [3]S.Haohm (2010). There was no statistically significant difference between granisetron and ramosetron groups upto 24 hrs postoperative period. The result being supported by [4]Yoshetaka Fuji (2001). They reported superiority of ramosetronover granisetron between 24-48 hrs after anaesthesia. Our study failed to get significant difference between granisetron and ramosetron groups since our study was limited upto 24 hrs only.

In conclusion, the prophylactic use of ondansetron, granisetron and ramosetron equally decrease the incidence of both postoperative nausea as well as vomiting upto 3 hrs. furtherramosetron is more effective than ondansetron for prophylaxis against PONV upto 24 hrs whereas the antiemetic efficacy of ramosetron and granisetron is almost comparableupto 24 hrs postoperative period. But still ramosetron scores over granisetron.

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