ORIGINAL RESEARCH PAPER

Anaesthesiology

KEY WORDS:

A COMPARATIVE STUDY OF INTRAVENOUS GRANISETRON AND ONDANSETRON FOR THE PROPHYLAXIS OF POST-OPERATIVE NAUSEA AND VOMITING FOLLOWING THE SURGICAL PROCEDURE UNDER GENERAL ANAESTHESIA USING INHALATIONAL AGENTS: A PROSPECTIVE, RANDOMIZED CLINICAL STUDY

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ABSTRACT

The objective is to evaluate the prophylactic profile, efficacy of granisetron and ondansetron to prevent postoperative nausea and vomiting (PONV) following the surgical procedure under General anaesthesia (GA). In a randomized, single blind trial, 100 patients following the surgical procedure under GA received either granisetron 1 mg or ondansetron 4 mg (n = 50 for each) intravenously before the end of surgery. A standard general anaesthetic technique was employed. Postoperatively, during the first 24 h after anaesthesia, the incidence of PONV, recovery score and adverse events were recorded. Incidence of nausea, vomiting and retching on 0-1 hrs, 1-3 hrs, 3-6 hrs and 6-12 hrs were between 0% -10 % in both the Groups. The incidence was more in patients receiving ondansetron as compared to those receiving granisetron. In postoperative period incidence of nausea, vomiting and retching on 12-24 hrs were higher in receiving ondansetron as compared to receiving granisetron, which was statistically significant (P>0.05). Use of rescue anti-emetic was more in patients receiving Ondansetron (26%) as compared to those who were given Granisetron (8%). ($p<0.05$). Granisetron is more efficacious and desirable drug than ondansetron for reducing the incidence of PONV in patients following the surgical procedure under General anaesthesia.

Introducton:

Post-operative Nausea and Vomiting (PONV) is one of the most important complain patients report following the surgical procedure under General Anaesthesia (GA). The consequences of PONV include delayed discharge from the Post-anaesthetic care unit, unanticipated hospital admission and increased incidence of pulmonary aspiration. PONV has also been associated with morbidity including dehydration, electrolyte abnormalities, wound dehiscence, bleeding, oesophageal rupture (Boerhaave's syndrome) and airway compromise. Without any prophylaxis, PONV occurs in upto 40% of all patients who undergo GA but can be as high as 80% in High-risk patients. Preventing PONV is easier than treating it. Several drugs are used to manage PONV including anticholinergics, dopamine receptor antagonists, antihistamines and phenothiazine derivatives. However, these drugs cause unwanted side effects such asdysphoria, extrapyramidal symptoms, dry mouth, restlessness, drowsiness, dizziness, fainting, irregular heartbeat and hot flushes.

The 5-hydroxytryptamine type 3 (5-HT3) receptor antagonists have been shown to devoid of such side effects and effective in the prevention and treatment of PONV. This study will be undertaken to compare the efficacy and safety of intravenous Granisetron 1 mg (1 mL) and Ondansetron 4 mg (2 mL) in preventing PONV in patients undergoing surgical procedures under GA.

Materials and Methods

After approval by an institutional ethical committee and written informed consent. This randomized study was performed at People's Hospital associated with People's College of Medical Sciences& Research Institute, Bhopal, during the period from December 2020 to May 2022.

100 patients aged between 18 and 60 years were randomized into two goups of 50 each belonging to ASA (American Society of Anaesthesiologists) class 1 and 2 weighing >40kg undergoing elective surgery under general anaesthesia using inhalational agents were selected. Those for emergency surgeries, History of motion sickness or previous PONV, Total intravenous anaesthesia or pregnant and lactating mothers excluded from study

Control group'O'(n=50): Inj. Ondansetron 100µg/kg over 15 min before end of surgery, then 8 hourly after first dose.

Study group'G'(n=50): Inj. Granisetron 40µg/kg over 30 seconds before end of surgery, Once a day.

METHODOLOGY-

One day before surgery, all patients received a pre-anesthetic evaluation by the anesthesiologist. The night before surgery, patients were kept nil per oral (nothing by mouth) after 10:00 p.m. Upon arrival in the operation theatre, patients were connected to the intravenous line and intravenous fluids was started; monitors for electrocardiogram, pulse-oximeter, and non-invasive blood pressure (NIBP) was also connected and set at monitoring mode. Patients were premedicated with an injection of midazolam (0.05 mg/kg) ,glycopyrrolate (0.2 mg) ranitidine (50mg) and fentanyl (2mcg/kg) Patients were randomly allocated into two groups, study groups and control groups (G and O) and in a single-blind manner. For induction injection Propofol (2-2.5mg/kg) was used. All patients received a suxamethonium (2 mg/kg) injection for relaxation and then were intubated with an appropriate size endotracheal tube with a throat pack. Anesthesia was maintained with nitrous oxide (N2O) (50%) and Isoflurane in oxygen. Patients were given intermittent positive pressure ventilation to maintain end-tidal carbon dioxide (EtCO2) between 35 and 45 mmHg. Parameters were monitored at 10

min intervals included heart rate (HR), BP, EtCO2, SpO2, and urine output (UO). Muscle relaxation was maintained with an injection of Vecuronium (0.05 mg/kg). Routine prophylaxis was performed with intravenous injection of Ceftriaxone (1 g). The anaesthesiologist administered one of the group of drugs intravenously 25 to 30 min before the end of surgery. Once the surgical procedure was completed, Isoflurane and nitrous oxide was discontinued and the patient was ventilated with 100% oxygen. The throat pack was then removed, oral suctioning was completed. Patients were reversed with injections of neostigmine (0.05 mcg/kg) and glycopyrrolate. They were extubated, then patients were transferred to a post-anesthetic care unit (PACU). In the PACU, patients were supplemented with oxygen. Monitors including a pulse-oximeter, electrocardiogram, and NIBP was attached and placed in monitoring mode. Once adequate recovery was achieved, the patients were transferred to the department wards.

Assessment Plan:

Postoperatively, all patients were assessed at the PACU and department wards for episodes of nausea, vomiting, retching and the need for rescue antiemetic at intervals of 0-1, 1-3, 3-6, 6-12 and 12-24 hours. Episodes of PONV were identified by spontaneous complaints from patients or by direct questioning. The patients were observed for 24 hours postoperatively for the incidence of complete response and side effects.

Statistical Analysis & Results

Statistical analysis was performed using the Statistical Package for Social Sciences software (SPSS) version 25.0 IBM. Parametric data were analyzed using the student ttest. Non-parametric data were analyzed using Mann Whitney 'U' test and Repeated measure of ANOVA. P value ofof <0.05 was considered as significant.

A prospective, randomized comparative clinical study of intravenous granisetron and ondansetron for the prophylaxis of post-operative nausea and vomiting following the surgical procedure under general anaesthesia was performed on 100 patients after dividing them in to Group G (n= 50; Inj. Granisetron 40µg/kg over 30 seconds before end of surgery, Once a day) and Group O (n= 50; Inj. Ondansetron 100µg/kg over 15 min before end of surgery, then 8 hourly after first dose). Based on the data collected, data analysis was performed and following observations were made.

Table 1: Comparing Nausea between two groups

Time points (hours)	Group				P value
	Granisetron		Ondansetron		
	Frequency	Percentage	Frequency	Percentage	
0-1	2	4	5	10	0.240
1-3	1	2	5	10	0.092
3-6	1	2	3	6	0.307
6-12	1	2	2	4	0.558
12-24	0	0	5	10	0.022

In postoperative period incidence of nausea on 12-24 hrs was 10.0% (n=5) in Group O as compared 0% (n=0) in Group G, which was statistically significant (P=0.022, P>0.05).

Rest all period of time no significant difference was obtained in terms of occurrence of nausea with both the intervention across the time points(P>0.005).

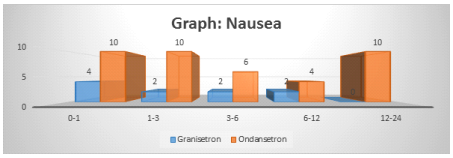


Table 2: Comparing Vomiting between two groups

Time points (hours)	Group				P value
	Granisetron		Ondansetron		
	Frequency	Percentage	Frequency	Percentage	
0-1	2	4	5	10	0.240
1-3	1	2	3	6	0.307
3-6	1	2	3	6	0.307
6-12	1	2	3	6	0.307
12-24	0	0	3	6	0.079

No significant difference was obtained in terms of occurrence of vomiting with both the intervention across the time points (P>0.005).

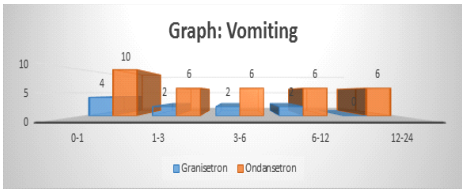


Table 3: Comparing Rescue Anti-emetic use between two groups

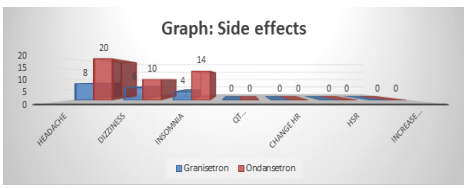
			Groups		Total	P value
			Granisetron	Ondansetron		
Rescue Anti-emetic	No	Count	46	37	82	0.017
		%	92.0%	74.0%	82.0%	
	Yes	Count	4	13	18	
		%	8.0%	26.0%	18.0%	

A significant difference in terms of use of rescue anti-emetic was obtained between the groups. Use of rescue anti-emetic was more in patients receiving Ondansetron (26%) as compared to those who were given Granisetron (8%). The p value for this comparison was 0.017 which is significant.

Table 4: Comparing side effects between two groups

Side effects	Group				P value
	Granisetron		Ondansetron		
	Frequency	Percentage	Frequency	Percentage	
Headache	4	8	10	20	0.084
Dizziness	3	6	5	10	0.461
Insomnia	2	4	7	14	0.081
QT prolongation	0	0	0	0	NA
Change HR	0	0	0	0	NA
HSR	0	0	0	0	NA
Increase transaminase	0	0	0	0	NA

Similar side effect profile was recorded between both the groups as revealed by the insignificant p value of >0.05. However numerically headache, dizziness and insomnia were more prevalent in patients receiving ondansetron as compared to those receiving granisetron.



DISCUSSION

Incidence of nausea, vomiting and retching on 0-1 hrs, 1-3 hrs, 3-6 hrs and 6-12 hrs were between 0% -10 % in both the

Groups. The incidence was more in patients receiving ondansetron as compared to those receiving granisetron, however the differences were statistically insignificant (P>0.05).

In postoperative period incidence of nausea, vomiting and retching on 12-24 hrs were higher in Group O as compared to Group G, which was statistically significant (P>0.05).

A significant difference in terms of use of rescue anti-emetic was obtained between the Groups. Use of rescue anti-emetic was more in patients receiving Ondansetron (26%) as compared to those who were given Granisetron (8%).(p<0.05)

Side effects like headache, dizziness and insomnia were more prevalent in patients receiving ondansetron as compared to those receiving granisetron with insignificant statistical difference (p>0.05).

CONCLUSION

In conclusion, granisetron at an intravenous dose of 1 mg was found to be safe, well tolerated, and more effective than a 4 mg intravenous ondansetron for antiemetic prophylaxis in patients receiving general anesthesia with less incidence of side effects and can be employed as routine antiemetic prophylaxis for PONV for patients undergoing surgeries, prophylactic use of anti-emetics should be considered.

This study concludes that the prophylactic intravenous administration of Safety profile is more with Granisetron and it is more potent than Ondansetron for controlling postoperative nausea and vomiting.

We observed minimal emetic and nauseating episodes in postoperative period in patients who had received i.v. Granisetron in comparison to i.v. Ondansetron, undergoing surgery under general anaesthesia However, on the incidence of early post operative nausea, vomiting and retching had not any significant difference of both the ondansetron and granisetron.

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