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COMPARISON OF ONDANSETRON AND GRANISETRON FOR ANTIEMETIC PROPHYLAXIS IN ELECTIVE SURGERIES UNDER GENERAL ANESTHESIA: A PROSPECTIVE, RANDOMISED, AND DOUBLE BLIND STUDY

Anesthesiology

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ABSTRACT

INTRODUCTION: To compare the efficacy of intravenous ondansetron (4 mg, 2 mL) and granisetron (2 mg, 2 mL) for preventing postoperative nausea and vomiting (PONV) in patients during surgical procedures under general anesthesia.
MATERIAL AND METHODS: A prospective, randomized, and double blind clinical study was carried out with 60 patients surgical procedures under general anesthesia. Patients were divided into two groups of 30 individuals each. Approximately 15 minutes before end of surgery, each patient received either 4 mg (2 mL) ondansetron or 2 mg (2 mL) granisetron intravenously in a double blind manner. Balanced anesthetic technique was used for all patients. Patients were assessed for episodes of nausea, retching, vomiting, and the need for rescue antiemetic at intervals of 0-6, 6-12, and 24 hours after surgery. Incidence of complete response and adverse effects were assessed at 24 hours postoperatively. Data was tabulated and subjected to statistical analysis using the chi-square test, unpaired t-test, A *P*-value less than 0.05 was considered statistically significant.
RESULTS: There was no statistically significant difference between the two groups for incidence of PONV or the need for rescue antiemetic. Both study drugs were well tolerated with minimum adverse effects; the most common adverse effect was headache. The overall incidence of complete response in the granisetron group (86.7%) was significantly higher than the ondansetron group (60.0%).
CONCLUSION: In conclusion, granisetron at an intravenous dose of 2 mg was found to be safe, well tolerated, and as effective as 4 mg intravenous ondansetron for antiemetic prophylaxis surgery patients receiving general anesthesia, and can be employed as routine antiemetic prophylaxis for PONV. It is a valuable alternative to ondansetron.

KEYWORDS

INTRODUCTION

Postoperative nausea and vomiting (PONV) remains a significant problem in modern anaesthetic practice, with an incidence of up to 80% in high-risk group patients.[1]Postoperative nausea and vomiting are one of the most common distressing symptoms occurring after surgery. These factors prevent patients returning home at the end of the day, after surgery and necessitating readmission to the hospital.

Patients often rate postoperative nausea and vomiting as worse than postoperative pain. It is not surprising, therefore, that prevention of postoperative nausea and vomiting improves satisfaction among patients who are likely to experience them.

Persistent nausea and vomiting may result in dehydration, electrolyte imbalance, tension on suture line, venous hypertension, increased bleeding under skin flaps and can expose the subject to an increased risk of pulmonary aspiration of vomitus, if airway reflexes are depressed from the residual effects of anaesthesia and analgesic drugs.

Traditional antiemetic drugs used for PONV include anticholinergics (e.g., scopolamine) phenothiazines (e.g.prochlorperazine), antihistamines (e.g.,promethazine), butyrophenones (e.g., droperidol), and benzamide(e.g., Metoclopramide).

Dimenhydrinate, a commonly used antihistaminic, has similar efficacy to 5-HT3 receptor antagonists. Its efficacy is presumably due to the high concentration of histamine and muscarinic cholinergic receptors within the vestibular system.[2]

Most of the anti-emetics used are dopamine receptor antagonists or antihistaminics. They have undesirable side-effects like excessive sedation, respiratory depression, dyspepsia, extrapyramidal syndrome, dysphoria, restlessness, etc and emesis potential of these drugs are of very short duration.

5-hydroxytrptamine subtype 3 (5HT-3) receptor antagonist produce pure antagonism of the 5-HT3 receptor. The introduction of this class of drugs in the 1960s represents a major improvement in the pharmacotherapy of chemotherapy and radiation therapy-induced nausea and vomiting. They have since proven to be highly effective in the prevention and treatment of postoperative nausea and vomiting. They are not effective in the treatment of motion induced nausea and vomiting. Their actions involve both central and peripheral mechanisms in the control of nausea and vomiting. Centrally, they bind competitively and selectively to serotonin receptors in the CTZ of the CNS. In addition to this central effect, they also block receptors in the gastrointestinal tract, which prevents the action of serotonin and inhibits emetic symptoms.[3]

Ondansetron, the first 5-HT-3 receptor antagonist to be introduced, is the most commonly used drug of this class. Others include Tropisetron, Dolosetron, Palanosetron and Granisetron.

Prophylactic therapy with intravenous Ondansetron has been evaluated for the prevention of PONV after middle ear surgery under general and local anesthesia and found that Ondansetron is effective in prevention of PONV after middle ear surgery.[2]

Granisetron is another recently introduced 5-HT receptor antagonist which has good potency and a longer duration of action against emesis. The optimal dose of granisetron in preventing PONV is 2 mg via an intravenous route.

The present study has been designed keeping in view the fact that the incidence of nausea and vomiting after surgery under general anaesthesia is high.

We hypothesized that Granisetron is more effective than Ondansetron for the long-term prevention of PONV. To test this hypothesis, we designed this prospective, randomized, double-blinded trial to assess the efficacy and safety of Ondansetron and Granisetron for preventing PONV after elective surgery under general anesthesia

MATERIALS AND METHOD

After approval from College and Hospital ethical committee and written informed consent from the patient and/or attendant , present study was carried out in 60 adult patients of ASA grade 1 & 2 between the age of 20-40 yrs. undergoing elective surgery under general anaesthesia in the Department of Anaesthesiology, Jhalawar medical college, Jhalawar. All the patients under the study subjected to detailed preaneasthetic check up, All patients in this study were subjected to detailed preanaesthetic evaluation and all investigations were done as a

protocol of the required procedure.

Inclusion criteria- Patients of ASA grade I & II within the age group of 20-40 years and body weight between 40 to 70 kg undergoing elective surgery (duration <3hrs) under balanced general anaesthesia are selected for the study. Only those patients who were not having any systemic disease and approved preaneasthetically were included.

This study was conducted on 60patients divided into 2 groups. Each group contain 30 patients. They have received either injection Ondansetron 2 ml (4mg) IV or injection Granisetron 2 ml(2 mg) IV 15 min. before end of surgery.All the patients were divided in two groups.

Group A (n = 30) injection Ondansetron 4mg IV in 2 ml
Group B (n = 30) injection Granisetron 2mg IV in 2 ml

Preoperatively: In the operation theatre after proper identification of patients, written informed consent was taken. Preoperatively pulse and BP was recorded after applying monitors and starting IV line with RL or other crystalloid fluids.All the patients were given pre anaesthetic medication with injGlycopyrolate 0.2 mg, inj. Midazolam 0.04mg/kg I.V. and injPentazocine 30 mg I.V. Preoxygenation of all the patients was done for 3 minutes in operation theatre before induction of anaesthesia.

Induction of anaesthesia was done with inj. Propofol 2 mg/kg IV slowly followed by inj. Succinylcholine 2mg/kg IV and IPPV with 100% oxygen was given. Intubation with proper size of disposable PVC cuffed endotracheal tube was done after muscle fasciculations pass off from hand muscles and complete muscle relaxation was achieved.

Maintenance of anaesthesia was done with 67 % Nitrus Oxide+33 % Oxygen and 1% to 2% halothane and nondepolarizing muscle relaxants (atracurium) and patients were mechanically ventilated to maintain ETCO2 (35 to 40mm of Hg).

Intraoperative period: Vital parameters eg pulse, blood pressure, spo2, ETCO2 and signs of inadequate plane of anaesthesiaeg. lacrimation, involuntary movements etc are noted and managed accordingly. No patient was given any other antiemetic drug during the intraoperative period. 15 min before the end of surgery the study drug was given by other person (blindly). So the observer does not know the name of drug and the person who injected the drug labeled the syringes as : A, and B.

Reversal: Patient given inj. Neostigmine 0.05 mg/kg IV with inj. Glycopyrrolate 0.01 mg/kg, as respiratory efforts begin.. After regaining muscle power to maintain spontaneous respiration and adequate tidal volume, patients were extubated after discontinuation of oxygen via mask, patients were observed for oxygen saturation if it remains above 97%, patients were shifted to recovery room and/or postoperative ward, where the patient was observed by some other observer for nausea & emetic episodes. Then drug was assumed and confirmed for putting the patient in group A, and B accordingly.

Postoperatively, all patients were assessed at the PACU and department wards for episodes of nausea, retching, vomiting, and the need for rescue antiemetic at intervals of 0- 6, 12, and 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 incidence of complete response and adverse effects.

"Complete response" was defined as the absence of nausea, retching, or vomiting and no need for rescue antiemetic during the 24 hour observation period. Rescue antiemetic in the form of an intravenous injection of metoclopramide 10 mg, was given in the event of one or more episodes of vomiting depending on the observer's discretion.

Observation

Table 1 Number Of Patients And Incidence Of Nausea And Retching

NAUSEA				RETCHING		
duration	GRP A	GRP B	P VALUE	GRP A	GRP B	P VALUE
0-6 hrs	2(6.66)	1(3.33)	0.195	0	0	0
6-12 hrs	2(6.66)	0	0.155	0	0	0
12-24 hrs	1(3.33)	0	0.321	1(3.33)	1(3.33)	1
total	5(16.66)	1(3.33)	0.082	1(3.33)	1(3.33)	1

Table 2 Incidence Of Vomiting And Rescue Medication

Duration	vomiting			Rescue		
	Grp A	B	P value	A	B	P value
0-6 hrs	2(6.66)	0	0.155	0	0	0
6-12 hrs	2(6.66)	1(3.33)	0.195	0	0	0
12-24 hrs	2(6.66)	0	0.155	1(3.33)	0	0.321
total	6(20)	1(3.33)	0.072	1(3.33)	0	0.321

Table No 3 Complete Response

	A	B	P value
No of pat.	18	26	0.021
percentage	60	86.7	

RESULT

The incidence of nausea was 16.7% (n=5) in group A and 3.3% (n=1) in group B over a 24-hour period (P>0.05).(Table 1) One patient in both groups had an episode of retching over a 24-hour period (P>0.05) (Table 1) .

Similarly, the results for vomiting when compared between the two groups were not statistically significant (P>0.05)(Table 2) When examining the need for rescue medication, only a single patient in the ondansetron group needed an injection of metoclopramide (10 mg) as compared to no patients in the granisetron group over the 24-hour period (P>0.05)(Table 2).

The incidence of complete response over a 24-hour postoperative period was 60.0% (n=18) in group A as compared to 86.7% (n=26) in group B, which was statistically significant (P=0.021, P<0.05).(Table 3)

Headache was the only adverse effect occurring more frequently in group A (n=3, 10.0%) as compared to group B (n=1, 3.3%); however, the result was statistically not significant (P>0.05).

DISCUSSION

In our study, we selected an intravenous dosage of 4 mg ondansetron based on previous studies by McKenzie et al.3, The intravenous 2 mg dosage of granisetron was based on the study by Bhattacharya and Banerjee4.

Postoperative assessment of nausea, retching, and vomiting at 0- 6, 12, and 24-hour intervals in both ondansetron and granisetron groups was found to be statistically insignificant (P>0.05). This finding is comparable to the study by Bestaset al.5, who compared the effects of ondansetron and granisetron on PONV in adult patients undergoing laparoscopic cholecystectomy and observed no significant differences in PONV between the active treatment groups.

In our study. At the 12- 24-hour interval, one patient out of 30 (3.3%) in the ondansetron group received rescue antiemetic in the form of intravenous metoclopramide (10 mg), while no patients in the granisetron group received rescue antiemetic. These results were not statistically significant and comparable to studies reported in the literature4,5.

Both drugs were relatively well-tolerated and had minimal adverse effects. In the ondansetron group, three patients (10.0%) complained of headache whereas as one patient (3.3%) reported similar in the granisetron group. These results were comparable to studies by Figueredo and Canosa6 that showed a 7.05% incidence of headache with ondansetron and studies by Fujii et al 7 that showed a 2% to 5% incidence of headache with granisetron. Dizziness, rashes, allergic reactions, and other adverse effects were not reported in the entire study population.

In our study, complete response occurred in 60% of the cases in the ondansetron group, which is comparable to the studies conducted by Naguibet al.8. (65.5%) and Kovacet al.9 (64%). The complete response in the granisetron group occurred in 86.7% cases, which is comparable to the work done by Fujiiet al.7 (85%). This result was statistically significant (P=0.021; P<0.05) and similar to the study by Bhattacharya and Banerjee2. However, the incidence of complete response in our study (complete response=60.0% in ondansetron group and 86.7% in granisetron group) was less than previously

reported by Bhattacharya and Banerjee4 (complete response=80% in ondansetron group and 93% in granisetron group). This may be explained by a difference in the type and duration of surgical procedures included in the present study, as tubal ligations were also included in their study.

CONCLUSION

In conclusion, granisetron at an intravenous dose of 2 mg was found to be safe, well tolerated, and as effective as 4 mg intravenous ondansetron for antiemetic prophylaxis surgery patients receiving general anesthesia, and can be employed as routine antiemetic prophylaxis for PONV. It is a valuable alternative to ondansetron.

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