Original Research Paper

Volume-10 | Issue-2 | February - 2020 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Anaesthesiology

COMPARISON OF EFFICACY OF ONDANSETRON AND GRANISETRON IN PREVENTION OF POST – OPERATIVE NAUSEA AND VOMITING AFTER TONSILLECTOMY AND MIDDLE EAR SURGERIES

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ABSTRACT **INTRODUCTION:** Postoperative nausea and vomiting are multifactorial in etiology. It remains a common problem after general anesthesia and contributes to patient dissatisfaction, especially in patients undergoing tonsillectomy and middle ear surgeries. So, we conducted a study to compare the efficacy of Ondensetron and Granisetron in the prevention of Post-operative nausea and vomiting.

AIM: Thisstudy compares the effect of Ondansetron and Granisetron in the prevention of post-operative nausea and vomiting in patients undergoing tonsillectomy and middle ear surgery and to evaluate the safety of the drugs by studying the incidence of side-effects.

METHODOLOGY: The present study was carried out in the Department of Anaesthesiology, Govt. Villupuram Medical College, Villupuram, Tamilnadu.A total of 60 patientsof ASA grade I & II posted for tonsillectomy and middle ear surgery under general anesthesia were included. After obtaining informed consent, patients were randomly assigned to one of the three treatment groups.Group (O) received Inj.Ondensetron 150 µg/Kg, Group (G) received Inj.Granisetron 40 µg/Kg, Group (P) received normal saline 2ml as placebo after induction of anaesthesia.

STATISTICALANALYSIS: Alldemographic parameters were evaluated by ANOVA test.Chi-square test was used to analyze categorical data.

RESULTS: Both ondansetron and Granisetron were effective in preventing nausea and vomiting with no clinically significant side effects.

CONCLUSION: Ondansetron and Granisetron were effective in preventing post – operative nausea and vomiting. There was a decrease in the requirements of rescue antiemetics, when these drugs were given. The side effects observed with these drugs were mild and clinically insignificant.

KEYWORDS : Post operative nausea and vomiting, tonsillectomy and middle ear surgeries, Ondansetron, Granisetron

INTRODUCTION:

Postoperative nausea and vomiting are multifactorial in etiology. It remains a common problem after general anesthesia and contributes to patient dissatisfaction. In a study conducted by Eberhart et al, nearly 50% of patients mentioned PONV as the postoperative side effect of greatest concern[1]. But, much importance has been given to post-op pain relief than to prevention of post-operative nausea and vomiting. When severe, post-op nausea and vomiting can lead to wound dehiscence, bleeding, dehydration, electrolyte imbalance, prolonged hospital stay and increased treatment cost to patients[2,3].

Among all the available antiemetic drugs, 5HT3 antagonists like Ondansetron and Granisetron play a significant role in the prevention of post operative nausea and vomiting.Ondansetron is a carbazole derivative developed to control chemotherapy and radiotherapy induced vomiting and PONV. Ondansetron blocks emetogenic impulses both at their peripheral origin and central relay. It does not block dopamine receptors. It has a weakgastro kinetic action due to $5HT_3$ blockade and a minor $5HT_4$ antagonistic action.Granisetron is an indazole derivative. The mechanism of action is similar to ondansetron, except that the weak $5HT_4$ blockade has not been detected. The present study was undertaken to compare the efficacy of Ondensetron and Granisetron in the prevention of post-operative nausea and vomiting in patients undergoing tonsillectomy and middle ear surgeries.

MATERIALS AND METHODS:

After getting Institutional Ethical Committee approval, 60 patients of either sex who underwent tonsillectomy and middle ear surgeries were included in the study.

Inclusion Criteria:

ASA physical status I and II
No history of motion sickness or prior PONV.

Exclusion Criteria:

ASA physical status III and IV
Patients with history of motion sickness
Any history of allergy to the study drugs

Study design

This is a prospective, randomized, double blinded study. Patients were systematically randomized into three groupsof 20each. All the patients received the following drugs after induction of anaesthesia

Group(O) Ondensetron - received Inj.Ondensetron 150µg/Kg,
Group(G) Granisetron - received Inj.Granisetron 40µg/Kg
Group (P) Placebo - received 2 ml of Normal saline

A standardized anesthetic technique was followed. Premedication was given with Inj. Glycopyrolate 0.05mg/kg and Inj. Pentazocine 0.5mg/kg I.M. 45 minutes before induction of anaesthesia.After pre-oxygenation with 100% O_2 for 3 minutes, patients were induced with Inj. Propofol 2mg/kg and Inj. Vecuronium 0.1mg/kg and intubated with appropriated sized endotracheal tubes. Patients were ventilated with IPPV with N_2O/O_2 in the ratio of 2:1 and Isoflurane 0.5 to 2%,neuromuscular paralysismaintained with Inj, Vecuronium 0.02mg/kg. Intra-operatively, pulse rate, non invasive BP, ECG and SpO_2 were monitored in all the patients. At the end of surgery, patients were reversed with Inj.Neostigmine 0.05mg/kg andInjGlycopyrolate 0.1mg/kg and extubated. Post-operatively patients were assessed for nausea and vomiting in the early post-op period (up to 1 hour), up to oral intake and up to 24 hours. Presence of any side effects and need for rescue anti-emetic (for more than 2 episodes of vomiting) was noted. Post-op pain was treated with Inj. Paracetomol 15mg/kg i.v infusion

OBSERVATION AND RESULTS:

The following data were collected in this study.

Demographic profile such as age in years, sex and weight in Kgs.

Nausea and vomiting were evaluated in three periods. Period 1 - immediatepost op period upto 1 hour, Period 2 - upto oral intake and Period 3 - upto 24 hours.

The presence of any side effects and the need for any rescue anti emetic were also recorded.

STATISTICAL METHODS:

All demographic parameters were evaluated by ANOVA test. Chi-square test was used to analyze categorical data. P value of greater than 0.05 is considered as significant.

RESULTS:

The two groups were comparable with respect to the age, weight and sex. There was no statistical difference between the two groups in demographic profile.The incidence of nausea and vomiting was

significantly less in Ondansetron and Granisetrongroups, when comparedwith Placebo group in all the periods except for the incidence of nausea inPeriod 2. There was no statistically significant difference in the incidence of any side effects.

TABLE 1.Nausea and Vomiting

		Group					
		Ondansetron		Granisetron		Placebo	
		n	%	n	%	n	%
sex	male	11	55.0%	8	40.0%	13	65.0%
	female	9	45.0%	12	60.0%	7	35.0%
surgery	Tonsil	14	70.0%	14	70.0%	14	70.0%
	Middle ear	6	30.0%	6	30.0%	6	30.0%
Nausea (period1)	no	15	75.0%	16	80.0%	8	40.0%
	yes	5	25.0%	4	20.0%	12	60.0%
Nausea (period2)	no	12	60.0%	14	70.0%	10	50.0%
	yes	8	40.0%	6	30.0%	10	50.0%
Nausea (period3)	no	17	85.0%	18	90.0%	8	40.0%
	yes	3	15.0%	2	10.0%	12	60.0%
vomiting (period1)	no	18	90.0%	20	100.0%	10	50.0%
	yes	2	10.0%	-	-	10	50.0%
vomiting (period2)	no	19	95.0%	18	90.0%	14	70.0%
	yes	1	5.0%	2	10.0%	6	30.0%
vomiting (period3)	no	19	95.0%	20	100.0%	13	65.0%
	yes	1	5.0%	-	-	7	35.0%
Rescue	no	20	100.0%	20	100.0%	13	65.0%
	yes	-	-	-	-	7	35.0%
headache	no	14	70.0%	15	75.0%	16	80.0%
	yes	6	30.0%	5	25.0%	4	20.0%
Abdominal discomfort	no	17	85.0%	19	95.0%	20	100.0%
	yes	3	15.0%	1	5.0%		
allergy	no	20	100.0%	20	100.0%	20	100.0%

TABLE 2.DATA ANALYSIS

	*x*2 test	P-value
nausea (Period 1)	8.4	0.02
nausea (Period 2)	1.7	0.43
nausea (Period 3)	14.9	0.001
vomiting (Period 1)	17.5	0.001
vomiting (Period 2)	5.5	0.06
vomiting (Period 3)	12.4	0.002
rescue	15.8	0.001
headache	0.5	0.77
abdominal discomfort	3.75	0.15

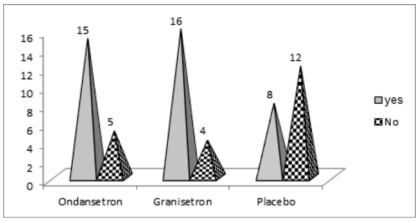

FIG.1 NAUSEA (Period 1)

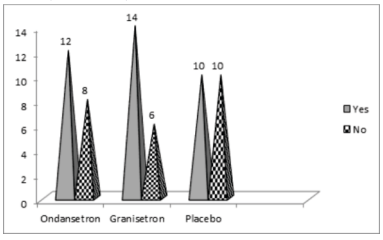

FIG.2 NAUSEA (Period 2)

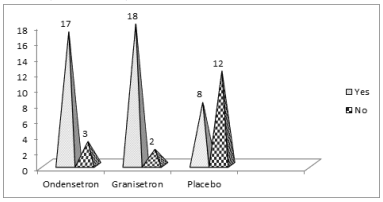

FIG. 3 NAUSEA (PERIOD 3)

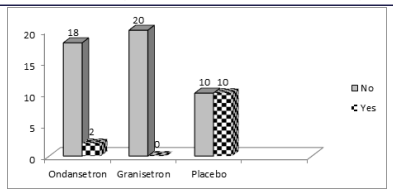

FIG.4 VOMITING (Period 1)

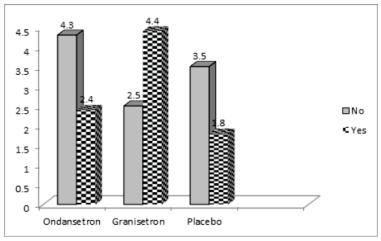

FIG.5 VOMITING (PERIOD 2)

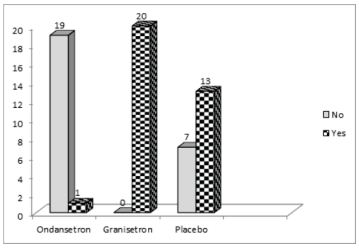

FIG.6 VOMITING (Period 3)

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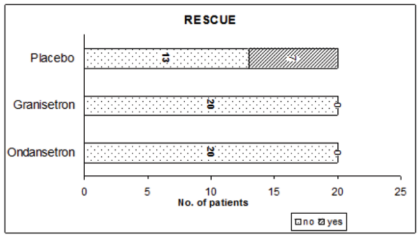
TABLE 3. ODDS RATIO

	Period 1	Period 2	Period 3
Ondansetron	1.00	1.00	1.00
Granisetron	0.00	2.11	0.00
Placebo	9.00	8.14	10.23

From the above values the odds ratio (Risk ratio) was calculated. The risk of getting nausea and vomiting is highest in placebo group and least in granisetron group

FIG. 7



No patient in the ondansetron and granisetron group needed rescue antiemetics, where as nearly 35% in the placebo group required rescue drug.

DISCUSSION

Nausea and vomiting are both unpleasant and distressing to the patient, surgeon and anaesthesiologist. Nausea is a subjective sensation of the desire to vomit, but without any attempt at expulsive movements. It is frequently accompanied autonomic phenomenon, resulting in objective signs such as secretion of saliva, sweating, increase in pulse rate, variations in rate, depth and regularity of respiration, pallor, and pupillary dilation.Retching and vomiting are active exclusive mechanisms, and are differentiated by the end result of the process. Vomiting results in forceful expulsion of gastric contents through the mouth, whereas retchingcausesnoexpulsion.

The factors affecting the incidence of post operative nausea and vomiting depends on both the individualpatient and the anaesthetic drugs[4,5]. The incidence is high in adults when compared to elderly, while in females the incidence is more during the ovulatory phase[6,7]. Among anaesthetic drugs, opioids are associated with increased incidence of PONV. Atropine has a centrally acting anti emetic effect, but it delays gatric emptying. Ketamine and etomidate based anaesthesia have been proposed to cause more PONV than

thiopentone. Propofol and midazolam have been shown to be associated with less PONV[8-11]. Nitrous oxide may cause increased PONV due to increase in middle ear pressure, bowel distention and sympathetic stimulation[12,13]. The incidence is less with newer fluorinated volatile anaesthetics than with ether.Neostigminemay increase PONV due to increased gut motility[14,15]. Benzodiazepines like midazolam decreases the incidence of PONV[16].

Numerous drugs have been used in the past in the prevention of post – operative nausea and vomiting, but they also have been associated with undesirable side effects. For example, metaclopramide results in extrapyramidal symptoms, droperidol produces restlessness and dysphoric reactions, antihistaminics result in sedation. The newer 5 HT3 antagonists like ondansetron and granisetron are very effective in preventing post-operative nausea and vomiting especially in laparoscopic surgery, day case surgery and in women undergoing ambulatory gynaecologic surgery[17-21]. They are generally well tolerated and the only common side effect is headache. Mild constipation, diarrhoea, abdominal discomfort, rashes and allergy (after IV injection) can occur.

Fuji Y et al have done two studies in patients undergoing tonsillectomy and middle ear surgery comparing granisetron and placebo. The incidence of PONV in their studies were 17% and 60% in tonsillectomies and 17% and 63% in middle ear surgeries. In our study it was 30% and 85% respectively.

Dua N et al compared granisetron and ondansetron for the prevention of nausea and vomiting in patients undergoing modified radical mastectomy and demonstrated that the incidence of PONV with ondensetron, granisetron and placebo were 25%, 20% and 70% respectively.

Khalil SN et al compared intravenous ondansetron and placebo for preventing post op emesis in paediatric patients after general anaesthesia and established the effectiveness of ondansetron in prevention of vomiting.

Morton NS et al compared ondansetron and placebo in patients undergoing tonsillectomy and demonstrated the superiority ofondansetron. The incidence of nausea was 36% and 49% and the incidence of vomiting was 40% and 53%. In our study it was 40% and 85% respectively. Our study findings concurred with this study with a slightly higher incidence, the figures being 40%, 30% and 85% respectively.No clinically significant side effects were noted with both these drugs during our study.

CONCLUSION

We compared the efficacy of ondansetron and granisetron in patients undergoing tonsillectomy and middle ear surgeries and found that both drugs were effective in preventing post – operative nausea and vomiting. There was a decrease in the requirements of rescue antiemetics, when these drugs were given. The side effects observed with these drugs were mild and clinically insignificant.

Conflict of interest: Nil

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