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Comparison Of Granisetron With The Combination Of Granisetron And Dexamethasone In The Prophylaxis Of Postoperative Nausea And Vomiting

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Abstract

Introduction: Post Operative Nausea and Vomiting (PONV), despite the advance in anesthetic care, is still a 'big little problem'1 within the anesthesia world.1 It is defined as nausea and/or vomiting that occurs within 24hrs after surgery and can occur following general, regional, or local anesthesia. It is their most distressing concern in the postoperative period. The incidence can be as high as 80% following certain procedures like ENT, Laparoscopic and gynecological surgeries. When severe, postoperative nausea and vomiting can lead to wound dehiscence, bleeding, dehydration, electrolyte imbalance, delayed discharge, and increased treatment cost.

Aim Of Study: This study aims to compare and evaluate the effect of granisetron and a combination of granisetron with Dexamethasone given prophylactically in the prevention of postoperative nausea and vomiting in patients undergoing elective ENT surgeries**.**

Materials And Methods: 90 Patients of (ASA Physical status 1) aged 15 - 50 yrs. with body weight ranging from 40 – 80kgs. scheduled for elective ENT surgeries were studied at the Sri Lalithambigai Medical College And Hospital Adayalampattu, Maduravoyal, Chennai, Tamil Nadu India in the year 2022. Patients with cardiovascular, respiratory, renal, or hepatic diseases, pregnant, lactating (or) menstruating women and those taking medications that would affect the study, those who had a H/o of motion sickness and or previous H/o of postoperative nausea and vomiting were excluded from the study. Premedication - Intramuscularly Pentazocine 0.5 mg/kg, Glycopyrrolate 0.2mg half an hour before surgery for all patients. Patients were randomly allocated into three different groups (30 in each group). Patients were given in a randomized, double-blind manner, a single dose of normal saline (placebo) 5ml, (or) Inj. Granisetron 40mcg/kg,(GROUP –II) (or) Inj. Granisetron 40mcg/kg with dexamethasone 8mg, (GROUP –III) intravenously. Study medications were prepared by personnel not involved in the study in identical 5 ml volumes. The study drugs were given just after intravenous cannulation, before Induction of anesthesia. The patients fasted for eight hours before surgery and on arrival to the operating theatre, routine monitoring devices were attached and basal HR, BP, ECG, and SPO2 were observed and also observed throughout the study period. Incidence Of nausea, retching (or) vomiting during the first 24 hrs was recorded.

Results: The results were scored like Belville et al. Grade 0 - No nausea /retching/vomiting, Grade 1 - Nausea/retching, Grade 2 – Vomiting. Patients were assessed for nausea, retching, and vomiting at 1,2,4,12 & 24 hrs. postoperatively. If two (or) more episodes of emesis occurred Inj. Metoclopramide 10mg iv. as rescue antiemetic was given. Results were statistically analyzed with t-test, chi–square test They were also enquired about adverse effects like Headache, sedation, abdominal discomfort, dizziness, etc., and noted.

Conclusion: Antiemetic prophylactic should be included in the anesthetic management of patients with a risk of postoperative nausea and vomiting undergoing general anesthesia. Granisetron is effective in preventing postoperative nausea and vomiting in the majority of patients. Granisetron plus Dexamethasone combination prophylaxis is highly effective in controlling postoperative nausea and vomiting with few side effects.

Keywords: Granisetron ; Dexamethasone ; Prophylaxis ; Post Operative Nausea ; Vomiting

Introduction

Pre-medication with opioids increases the incidence, by stimulating opioid receptors. Opioids predispose to postoperative nausea and vomiting by sensitizing the otic and vestibular areas to motion They prolong gastric emptying time by decreasing gastric and GI motility, However, if opioids are not given it still causes vomiting due to increased pain.[1] Benzodiazepam decreases the incidence of postoperative nausea and vomiting by decreasing the plasma level of catecholamines. Atropine causes relaxation of the sphincter and delays gastric emptying.[2]Post operative nausea and vomiting cause delay in ingestion of fluids, foods, and oral medication and causes accompanying pain and discomfort. post-operative nausea and vomiting cause interruption of diet, nutrition, oral drug therapy, aspiration of gastric contents electrolyte imbalance, dehydration, Tachycardia, cardiac dysrhythmias, increased intracranial tension, intraocular pressure, and blood pressure. [3]Surgical complications include visceral wound dehiscence, bleeding at the surgical site, disruption of vascular grafts and anastomoses, and oesophageal rupture (or) tears. Post Operative Nausea and Vomiting (PONV), despite the advance in anesthetic care, is still a 'big little problem within the anesthesia world. [4] It is defined as nausea and/or vomiting that occurs within 24hrs after surgery and can occur following general, regional, and local anesthesia. It is their most distressing concern in the postoperative period. [5] The incidence can be as high as 80% following certain procedures like ENT, Laparoscopic (or) gynecological surgeries. When severe, postoperative nausea and vomiting can lead to wound dehiscence, bleeding, dehydration electrolyte imbalance , delayed discharge and increased treatment cost.

Materials And Methods

90 Patients of (ASA Physical status 1) aged 15 - 50 yrs. with body weight ranging from 40 – 80kgs. scheduled for elective ENT surgeries were studied at the Sri Lalithambigai Medical College And Hospital Adayalampattu, Maduravoyal, Chennai, Tamil Nadu India in the year 2022. Patients with cardiovascular, respiratory, renal, or hepatic diseases, pregnant, lactating (or) menstruating women, and those taking medications that would affect the study, those who had a H/o of motion sickness and or previous H/o of postoperative nausea and vomiting were excluded from the study. Premedication - Intramuscularly Pentazocine 0.5 mg/kg, Glycopyrrolate 0.2mg half an hour before surgery for all patients. Patients were randomly allocated into three different groups (30 in each group). Patients were given in a randomized, double-blind manner, a single dose of normal saline (placebo) 5ml, (or) Inj. Granisetron 40mcg/kg,(GROUP –II) (or) Inj. Granisetron 40mcg/kg with dexamethasone 8mg, (GROUP –III) intravenously. Study medications were prepared by personnel not involved in the study in identical 5 ml volumes. The study drugs were given just after intravenous cannulation, before Induction of anesthesia. The patients fasted for eight hours before surgery and on arrival to the operating theatre, routine monitoring devices were attached and basal HR, BP, ECG, and SPO2 were observed and also observed throughout the study period. Incidence Of nausea, retching (or) vomiting during the first 24 hrs was recorded. Grade 0 - No nausea /retching/vomiting Grade :1 Nausea/retching, Grade:2 - Vomiting Patients were assessed for nausea, retching, and vomiting at 1,2,4,12 & 24 hrs postoperatively. If two (or) more episodes of emesis occurred Inj. Metoclopramide 10mg iv. as rescue antiemetic was given. They were also enquired about adverse effects like Headache, sedation, abdominal discomfort, dizziness, etc, and noted.

Volume 5, Issue 6; November-December 2022; Page No 656-662

Stastical Methods: Data were analyzed using the SPSS software version 25 and data were significantly described in terms of mean ± standard deviation. For comparing categorical data Chi-square test was used. Kruskal Wallis test was used for comparing more than 2 groups. Differences were considered statistically significant if the two-tailed p-value was less than 0.05.

Results

90% of the patients in group I and 23% in group II had nausea while it fell to 4% in group III. From the above-mentioned table, we see that the incidence of nausea is reduced significantly both in Group II and Group III. Among these two, grade 0 was in 96% of patients in Group III (P<0.05). Similarly, the incidence of retching was compared in all three groups. Group I shows an incidence of 80% group II shows 17% and group III shows only 4%. When the number of episodes was seen in group I it is 60%, in group II it is10% and none in group III have multiple episodes and the need for rescue antiemetic. complete response (no postoperative nausea and vomiting) occurred in 96% of group III and 77% in group II and 10% in group I . Thus a complete response was significantly more common in the patients who had received the drugs Granisetron and Dexamethasone. Incidence of some side effects which were not statistically significant among the groups.

Table – I: Group-Wise Comparison Of The Baseline Characteristics

Parameter	Group I (N = 30)	Group II (N = 30)	Group III (N = 30)	P value	Inference
Age (Years)	29.2 ± 8.04	29.8 ± 9.7	29.1 ± 9.8	0.951	NS
Weight (Kg)	56.3 ± 6.9	59.3 ± 9.89	61.23 ± 10.26	0.1188	NS
Sex (M:F)	14 ± 16	19 ± 15	16 ± 14	0.875	NS

P>0.05 indicates statistically not significant

Table – Ii Blood Pressure& Surgical Duration

Parameter	Group I (N = 30)	Group II (N = 30)	Group III (N = 30)	Pvalue	Inference
BP Systolic	122.4 ± 7.9	119.5 ±9.38	121.6 ±10.12	0.4598	NS
BP Diastolic	79 ± 7.12	77.4 ± 8.2	76.4 ± 6.8	0.396	NS
Surgical Duration(mins)	96.7 ± 20.5	93.67 ±19.8	94.17 ± 18.9	0.817	NS
Pulse Rate	82 ± 4.90	82.2 ± 6.8	79.8 ± 5.1	0.208	NS

P>0.05 indicates statistically not significant.

Volume 5, Issue 6; November-December 2022; Page No 656-662

Table Iii: Incidence Of Nausea According To Groups

Comparison of Nausea	P Value	Inference
Group I vs Group II	< 0.001	S
Group I vs Group III	<0.001	S
Group II vs Group III	<0.02	S

Table – Iv: Incidence Of Retching According To Groups (0-24 Hrs)

RETCHING	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
Presence	24	80	5	16.7	1	3.3
Absence	6	20	25	83.3	29	96.7
Total	30	100	30	100	30	100

Table V: Incidence Of Vomiting According To Groups (0-24 Hrs)

VOMITING	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
Presence	24	80	6	20	1	3.3
Absence	6	20	24	80	29	96.7
Total	30	100	30	100	30	100

Table: VI Comparison Of Vomiting

COMPARISON OF VOMITING	P Value	Inference
Group I vs Group II	< 0.001	S
Group I vs Group III	<0.001	S

Volume 5, Issue 6; November-December 2022; Page No 656-662

Group II vs Group III	<0.05	S

Table Vii: Distribution Of Incidence Of Vomiting According To Groups

Vomiting episodes	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
None	6	20	24	80	29	96.7
Single	6	20	3	10	1	3.3
Multiple	18	60	3	10	0	
Total	30	100	30	100	30	100

Table: Viii Distribution Of Patients According To Nausea Score

Grade 0	Grade 1	Grade 2
No Nausea/Vomiting	Nausea/Retching	Vomiting
No Rescues		

Table 1x: Group Wise Distribution Of Side Effects

Side effects	Group I		Group II		Group III		P Value
	No.	%	No.		%	No.	%
Headache	3	10	3	10	2	6.7	0.87
Sedation	1	3.3	1	3.3	2	6.7	0.76
Abdominal discomfort	1	3.3	1	3.3	1	3.3	1
Dizziness	2	6.7	1	6.7	2	6.7	0.80

Discussion

Post Operative Nausea and Vomiting are distressing and sometimes, the patients dread them more than post-operative pain. Various factors predispose a Patient to postoperative nausea and vomiting. It is more frequent in women, nonsmokers, Pts with a History of motion sickness, morning sickness, or postoperative nausea and vomiting, and with perioperative use of opioids.[6] The frequency of nausea and vomiting following middle ear surgery can be as high as 62%-80%. If the prophylactic antiemetic is not given in our study the incidence is a little bit higher about 90% in the control group.[7] Prophylactic administration of scopolamine, prochlorperazine, droperidol, $5HT_3$ antagonists, and a combination of antiemetics have been advocated for postoperative nausea and vomiting in middle ear

Volume 5, Issue 6; November-December 2022; Page No 656-662

surgery and ENT surgeries in various studies. Ondansetron has been less effective in preventing postoperative nausea and vomiting in middle ear surgery patients.[8] Granisetron alone (or) in combination with dexamethasone is highly effective in patients undergoing middle ear surgery as concluded by Dandee JW et al in various studies. In high-risk populations, the current mode of preventing postoperative nausea and vomiting is by multimodal therapy and commonly used combinations are $5HT_3$ receptor antagonist & Dexamethasone.' So in our present study, we tried to compare the efficacy of Granisetron 40 mcg/kg with Granisetron 40 mcg/kg plus Dexamethasone 8mg and found a statistically significant decrease in the incidence of nausea and vomiting between group I, group II and Group III. All factors which predisposed to increase postoperative nausea and vomiting like age, obesity, gender, durations type of surgery, and anesthetic technique are equally distributed among the groups and hence the difference in the incidence of complete response between groups and the requirement of rescue antiemetics between groups can be attributed to the difference in the anti-emetics tested. The possible mechanism of Dexamethasone action might be to decrease the level of prostaglandins in the central nervous system.[9] They regulate neurotransmitter concentrations, receptor densities signal transduction, and neuronal configuration. As concluded in many studies the granisetron plus Dexamethasone significantly reduce post-operative nausea and vomiting when given prophylactically. It is usually recommended that an anti-emetic be given prophylactically before surgery or chemotherapy to improve the efficacy of the drug. Hence, the study agents were administered intravenously before the commencement of surgery. They have suggested that 40 mcg/kg was the minimum effective dose for the prevention of postoperative nausea and vomiting following surgery.[10] The dose of dexamethasone used (8 mg) was based on the studies previously shown to decrease emesis when added as an antiemetic regimen. In the present study, therefore, the same dose of dexamethasone was added to granisetron. The precise mechanism by which dexamethasone increases the effectiveness of granisetron is not known. Granisetron produces antiemesis by blocking $5HT_3$ receptors.[11] Dexamethasone may inhibit stimulation of $5HT_3$ receptors and may also potentiate the other pharmacological receptors [12] The pro emetic effect was larger than another risk factor. In patients who are at high risk for postoperative nausea and vomiting, it would therefore be better to avoid inhalation anesthesia. In our study, the incidence of postoperative nausea and vomiting is high among female patients. Obesity increases the incidence of vomiting, in our study patients who weighed more than 60 kg had increased incidence.[13]Jhi-Joung wan et.al in their study to prevent nausea and vomiting following cancer chemotherapy concluded that both ondansetron and granisetron have similar antiemetic efficacy but the dose of granisetron is much less than ondansetron Iv. Moreover, ondansetron has a shorter half-life of 3 hrs, whereas granisetron has a half-life of 8-9 hrs, which is more effective in preventing nausea and vomiting. Granisetron is also a more selective 5HT3 receptor antagonist than ondansetron. In our study, the need for rescue antiemetic in group I is 60%, the group is 10% whereas in group III is nil. [14] The safety of intravenous and oral granisetron has been evaluated in more than 7,000 patients in the clinical trial, which have shown the drug to be well tolerated, with mild and transient side effects. There have been no reports of extrapyramidal side effects with either intravenous or oral granisetron for the prevention and treatment of chemotherapy-induced emesis and postoperative nausea and vomiting. In our study also patients tolerate the drug well with few side effects[15].In our study patients receiving a placebo stayed in the hospital more than patients receiving Granisetron with dexamethasone.

Conclusion

Antiemetic prophylactic should be included in the anesthetic management of patients with a risk of postoperative nausea and vomiting undergoing general anesthesia. Granisetron is effective in preventing postoperative nausea and vomiting in the majority of patients. Granisetron plus Dexamethasone combination prophylaxis is highly effective in controlling postoperative nausea and vomiting with few side effects.

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Volume 5, Issue 6; November-December 2022; Page No 656-662

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Volume 5, Issue 6; November-December 2022; Page No 656-662