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Research Article

To Study the Efficacy of Granisetron and Granisetron Plus Dexamethasone in Preventing the Incidence of Nausea and Vomiting in Patients Undergoing Laparoscopic Surgeries

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ABSTRACT

Background: Despite advances in anaesthesia care postoperative nausea and vomiting (PONV) remains a vexing problem. Objectives to determine the efficacy of Granisetron and Granisetron plus dexamethasone in preventing the incidence of PONV, also assess the requirement of rescue antiemetic and adverse effects in the postoperative period AIM: To determine the efficacy of Granisetron and Granisetron plus dexamethasone in preventing the incidence of Nausea and Vomiting in 70 patients undergoing Laparoscopic Surgeries.

Methods: Prospective, Randomized, Double Blind Study among 70 Patients aged between 18 to 50 years, ASA class Grade I and II was conducted. 35 patients were recruited in two groups using randomization method. Post operatively data was collected using a questionnaire at 4 hrs and 24 hrs. Episodes of PONV were recorded by three points ordinal scale (TPOS). Intensity of nausea graded verbally with an eleven-point score (0-10).

Results: In group G, at 0-4 hours 11.4% patients had nausea and 25.7% had vomiting/retching. In group G+D, 8.6% had nausea and 2.9% had vomiting/ retching. There was significant difference (p =0.018) on Three point ordinal scale (TPOS) between the two groups.

In group G, at 4-24 hours 5.7% patients had nausea and 20.0% had vomiting and retching. In group G+D 11.4% had nausea and there was no vomiting / retching. There was significant difference (p =0.017) on Three point ordinal scale (TPOS) between the two groups.

Conclusion: We concluded that Granisetron + Dexamethasone had lower incidence of PONV compared to Granisetron group alone in Laparoscopic surgeries.

Postoperative nausea and vomiting (PONV) is one of the most common complication after both general and regional anaesthesia. The incidence of postoperative emesis in large number of studies has been reported to be in the 20-30% range [1]. Laparoscopic surgeries carry high risk of PONV [2]. Although many treatment therapies are available for the management of PONV, none is entirely effective. Most of the published trials indicate an improved antiemetic prophylaxis when using a combination of agents acting at different receptor sites compared with monotherapy [3]. So, we decided to study the efficacy of a combination of two antiemetic drugs in preventing PONV, after surgeries with a high incidence of PONV.

Methods

After institutional ethical committee approval, a prospective randomized double-blind study was planned on 70 patients of physical status ASA class grade I and II

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of either sex, age group of between 18 to 50 years undergoing laparoscopic surgeries under general anaesthesia. Randomization was done by computerized randomization table

They were randomly allocated into 2 equal groups as below:

• Group G (n= 35): patients received Inj. Granisetron 40µg/kg.

• Group GD (n=35): patients received Inj. Granisetron 40µg/kg + Dexamethasone 0.1mg/kg.

Pre anaesthetic evaluation was done in all patients for any co-morbidities. Exclusion criteria was patients with liver disease or renal pathology, on chemotherapy/radiotherapy, non-steroidal anti-inflammatory drugs (NSAIDS), history of motion sickness. Preoperative risk scoring of PONV is done by simplified Apfel Scoring System which includes female gender, non-smoking status, postoperative use of opioids and previous h/o of PONV or motion sickness. Each risk is given a score of 1, total score being 4, score of 1 corresponds to 20%, score 2 to 40%, score 3 to 60%, and score 4 to 80% of incidence of PONV. Patient were kept nil per oral as per standard guidelines and tab. Ranitidine150mg given. Tab Diazepam 5mg will be given orally evening prior to surgery. Then patient was wheeled into operation theatre and monitors were attached (Pulse oximeter, NIBP, ECG, Et CO2) and baseline values were recorded. Anaesthesia was given with premedication iv Glycopyrrolate 0.2mg. iv midazolam 2mg, then induced with inj propofol 2-2.5mg/kg iv, inj fentanyl 2µg/kg iv and inj vecuronium bromide 0.1mg/kg iv for muscle relaxation. Inj Diclofenac sodium 75mg was an added analgesic through intravenous infusion. Proper sized cuffed oral endotracheal tube was inserted, anaesthesia was maintained with N2O 66%, O2 33%, sevoflurane 1-2% and intermittent doses of vecuronuim bromide. The intra-abdominal pressure was kept between 12-14 mmHg. A nasogastric tube was inserted and suction applied to empty the stomach after intubation and also before extubation. Reversal of muscle relaxation was done with inj Glycopyrrolate 0.01mg/kg iv and Neostigmine 0.05mg/kg iv and patient was extubated. Postoperative analgesia was provided with iv paracetamol.

All patients were observed in the recovery room for 24 hours and received supplementation of oxygen through the simple face mask for 6hours and were also observed closely for any adverse drug reactions. Episodes of PONV were recorded immediately after extubation, (0-4) hours and (4-24) hours. Episodes of PONV were recorded by three points ordinal scale (TPOS), defined as 0=none, 1=nausea, 2=vomiting/Retching. Rescue antiemetic was given with Metoclopramide 10mg iv, if patients had nausea/vomiting /retching. Intensity of nausea graded verbally with an eleven-point score (0-10), patients who scored their nausea as zero were termed nausea free and 10 being most severe.

Statistical analysis

Data was entered into microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data were represented in the form of frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Independent t-test was used as test of significance to identify the mean difference between two quantitative variables. Graphical representation of data MS Excel and MS word were used to obtain various types of graphs such as bar diagram. p value of <0.05 was considered as statistically significant after assuming all the rules of statistical tests. Statistical software MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) were used to analyze the data.

Results

Mean age of subjects in group G was 31.71 ± 7.839 years and in group G+D was 30.49 ± 6.573 years. There was no significant difference in age distribution between the two groups (Table 1).

In group G, mean Simplified APFEL Scoring System was 1.97 ± 0.17 and in group G+D, mean Simplified APFEL Scoring System was 1.97 ± 0.17. There was no significant difference in Simplified APFEL Scoring System between the two groups (Table 2).

In group G, at 0 to 4 hours, 11.4% had nausea and 25.7% had Vomiting / Retching. In group G+D, 8.6% had nausea and 2.9% had Vomiting / Retching. There was significant difference (p value 0.018) in Three Points Ordinal Scale (TPOS) between the two groups. In group G, at 4 to 24 hours, 5.7% had nausea and 20.0% had Vomiting / Retching. In group G+D, 11.4% had nausea and 0% had Vomiting / Retching. There was significant difference (p value 0.017) in Three Points Ordinal Scale (TPOS) between two group (Table 3, Figure 1).

Mean Eleven Point Verbal Numerical score in group G was 6.89 ± 1.844 and in group G+D was 3.50 ± 0.926. There was highly significant difference (p value 0.001) in Eleven Point Score Verbal Numerical Scoring between two groups (Table 4, Figure 2).

Mean time for rescue antiemetics at (0-4) hours in group G was 2.45 ± 0.82 hours and in group G+D was 3.75 ± 0.50 hours. There was significant difference (p value 0.012) in mean time for rescue antiemetics between two groups. Similarly mean time for rescue antiemetics at (4-24) hours in group G was 8.25 ± 1.67 and in group G+D was 16 ±2.31 hours. There was highly significant difference (p value 0.001) in mean time for rescue antiemetics between two groups (Table 5, Figure 3).

Table 1- Age Distribution between two Groups

		Group G* Count	%	Group G+D# Count	%
Age Group	≤ 20 Years	3	8.6%	0	0.0%
	21 - 30 Years	10	28.6%	17	48.6%
	31 - 40 Years	20	57.1%	15	42.9%
	> 40 Years	2	5.7%	3	8.6%
	Total	35	100.0%	35	100.0%
Mean ± SD		31.71 ± 7.839		30.49 ± 6.573	

*G – Granisetron
#G+D – Granisetron and Dexamethasone

Table 2- Mean Simplified APFEL Scoring System Comparison between two groups

	Group G Mean	SD	Group G+D Mean	SD	P value
Simplified APFEL Scoring System	1.97	0.17	1.97	0.17	0.984

Table 3- Three Points Ordinal Scale (TPOS) Distribution between two groups

		Group G n	%	Group G+D n	%	Chi Square
(0-4) hrs	None	22	62.9	31	88.6	P = 0.018*
	Nausea	4	11.4	3	8.6	
	Vomiting / Retching	9	25.7	1	2.9	
(4-24) hrs	None	26	74.3	31	88.6	P = 0.017*
	Nausea	2	5.7	4	11.4	
	Vomiting / Retching	7	20	0	0	

Table 4- Eleven Point Score Verbal Numerical Scoring System Distribution between two groups

	Group	N	Mean	SD	P value
Eleven Point Score Verbal Numerical Scoring System (0-10)	G	18	6.89	1.844	<0.001
	G+D	8	3.50	0.926	

Table 5- Mean time for rescue antiemetics given (hours). Comparison between two groups

Time for rescue antiemetics	Group G Mean	SD	Group G+D Mean	SD	P value
(0-4) hours	2.45	0.82	3.75	0.50	0.012*
(4-24) hours	8.25	1.67	16	2.31	< 0.001*

Figure 1- Bar Diagram Showing Three Points Ordinal Scale (TPOS) Distribution between two groups

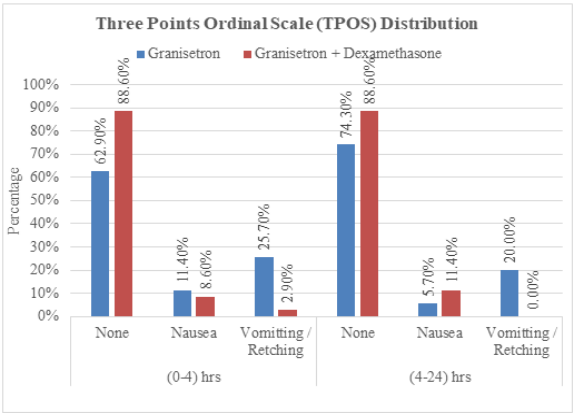


Figure 2- Bar Diagram Showing Eleven Point Verbal Numerical Scoring System Distribution between two groups

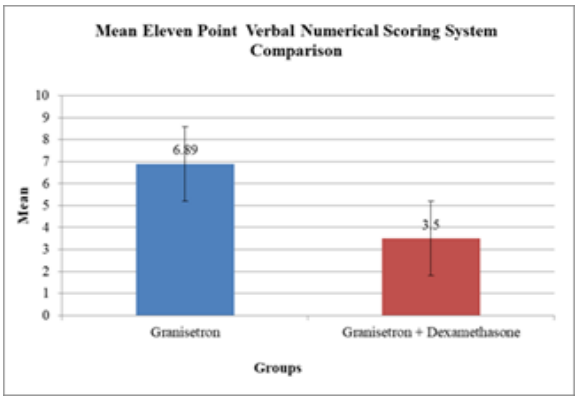
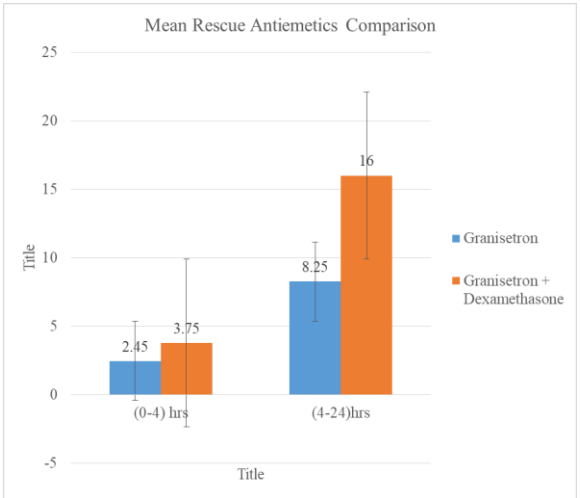


Figure 3- Bar Diagram Showing Mean Rescue Antiemetics Comparison between two groups



Discussion

Postoperative nausea and vomiting (PONV) are of multifactorial origin. The incidence of PONV after anaesthesia, despite the advances in antiemetic therapy in the last decades is still found to be relatively high. Most common causes for admission following day care surgery are pain, bleeding and intractable vomiting. Factors affecting PONV include patient related factors (age, sex, phase of the menstrual cycle), anaesthesia related factors (use of volatile anaesthetic agents, N2O, Opioid) and surgery related factors1. Female gender has been associated with higher incidence of PONV compared to male patient [4], Laparoscopic surgery was chosen because of high incidence of PONV associated with it. Naguib et al. [5] demonstrated that the incidence of PONV after laparoscopic surgery in their placebo group was remarkably high (72%). Andrews et al. [6] demonstrated that 5HT3 receptor antagonist drug Granisetron, is more potent and long acting than Ondansetron against emesis. Yoshitaka Fujii et al [7] in their study found that Granisetron administration was superior to Metoclopramide and placebo in the long term prevention of PONV after anaesthesia. Furue et al [8] found that the effective dose of Granisetron for treatment of emesis is between 40µg/kg and 80µg/kg. Yoshitaka Fujii et al [9] have also found that Granisetron 40 µg /kg was as effective as 60 µg /kg, and both doses had potent antiemetic effect than Granisetron 20 µg /kg. Fujii et al [10] have found that a high dose of Granisetron 40 µg /kg was more effective than Droperidol 20 µg/kg or Metoclopramide 0.2mg/kg for the treatment of established PONV after laparoscopic surgery. Dexamethasone has been reported to be effective in reducing the incidence of emesis in patients undergoing chemotherapy [11-12]. Dexamethasone has been found to have a prophylactic effect on PONV in patients undergoing various surgeries [13-15]. Dexamethasone may also inhibit stimulation of 5HT3 receptors [12]. Wang JJ et al [16] demonstrated the prophylactic antiemetic effect of Dexamethasone in women undergoing ambulatory laparoscopic surgery. The commonly used dose is 8-10 mg but the minimum effective dose is suggested to be 5mg as reported by Wang JJ et al. In another study demonstrated that Dexamethasone 8mg significantly reduced the incidence of nausea and vomiting after laparoscopic surgery.

Fujii et al. [17] demonstrated that prophylactic therapy with a combination of Granisetron and Dexamethasone was more effective than each antiemetic alone for the prevention of PONV after middle ear surgery. Elkahim et al [18], suggested that Dexamethasone 8mg and 16mg were equally effective, when combined with a 5HT3 receptor antagonist in preventing PONV after laparoscopic surgery. So in our study Dexamethasone 8mg was used in combination with Granisetron. The

present study was conducted to compare the postoperative antiemetic effects of Granisetron and combination of Granisetron with Dexamethasone.

In the present study Three Points Ordinal Scale (TPOS) in group G, at 0 to 4 hours, 11.4% had nausea and 25.7% had Vomiting / Retching and at 4 to 24 hours, 5.7% had nausea and 20.0% had Vomiting / Retching. In group G+D, at 0 to 4 hours 8.6% had nausea and 2.9% had Vomiting /Retching and at 4 to 24 hours, 11.4% had nausea and 0% had Vomiting / Retching. There was significant difference in Three Points Ordinal Scale (TPOS) between two groups at 0 to 4 hours and at 4 to 24 hrs. In the study by Rashmi Pal et al [19]. based on TPOS Scale, Overall incidence of PONV was 20% in Granisetron group, 16% in Granisetron plus Dexamethasone group and 76% in the control group. Although the incidence of PONV reduced with the addition of dexamethasone the difference was not statistically significant. Although there was no statistically significant difference in the PONV scores of group Granisetron and group Granisetron with dexamethasone, but on their comparison with control group both groups had the lower scores than control group which were statistically significant. The findings were similar to our study. Similarly, in the study by Rao V K et al [20], in Granisetron group, incidence of mild nausea was 20.1%, moderate nausea was 3.3% and severe nausea was 3.3% and no nausea was73.3%, in Granisetron plus Dexamethasone group, incidence of mild nausea was 3.3%, moderate nausea was 3.3% and no nausea in 93.4%. Incidence of mild vomiting in Granisetron group was 20.1% and moderate vomiting was 3.3% and incidence of mild vomiting was 3.3% in Granisetron with dexamethasone group. In the present study Mean Eleven Point Verbal Numerical score in group G was 6.89 ± 1.844 and in group G+D was 3.50 ± 0.926. There was significant difference in Eleven Point Score Verbal Numerical Scoring between two groups. In the study by Wadaskar DR et al [21] mean nausea score at which patients demanded rescue was 5 with range of 4-6 in both Granisetron40 µg/kg and Granisetron 20 µg/kg +Dexamethasone 160µg/kg groups. There was no significant difference in Eleven Point Verbal Numerical score for nausea between two groups. In the present study, mean time for rescue antiemetics in group G, at 0 to 4 hours, 2.45± 0.82 and in group G + D was 3.75± 0.50 hours. There was significant difference in mean time for rescue antiemetics between the two groups at 0-4 hours and at 4-24 hours. In study by Wadaskar DR et al [21] cumulative frequencies of rescue antiemetic required in first 24hours were found to be 1(3.33%) in Granisetron 40µg/kg with dexamethasone160µg/kg group and 5(16.67%) in group Granisetron 20µg /kg with dexamethasone 160µg/kg while in group Granisetron 40µg /kg it was 8(26.67%).There was a statistical difference between group Granisetron 40µg/kg with dexamethasone 160µg/kg and group Granisetron 40µg/kg but statistically insignificant in groups Granisetron 40µg/kg with dexamethasone160µg/kg versus groups Granisetron 20µg/kg with dexamethasone 160µg/kg and groups Granisetron 20µg/kg with dexamethasone 160µg/kg versus Granisetron 40 µg /kg. Wang et al [16] stated that they were unable to find any report on side effects associated with a single dose of Dexamethasone. Less than 24 hour of Dexamethasone therapy is considered safe and almost without adverse effects. In our study also, no adverse events were noted in the postoperative period in the combined group where Dexamethasone was used. In study by Wadaskar DRt al [21]. there were no significant differences in incidence of adverse effects between the groups.

Conclusion

From the study it can be concluded that the combination (Granisetron plus Dexamethasone) was found to have better efficacy in attaining a complete response to prevent PONV in comparison to Granisetron alone.

LIMITATIONS: Since the Study was conducted on Laparoscopic surgeries, the results cannot be generalized to other surgeries, serial measurement of vital parameters was not done in the present study.

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