Evaluation of the efficacy of Granisetron over Droperidol in the prevention of Postoperative Nausea and Vomiting following open Cholecystectomy

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ABSTRACT

BACKGROUND: Post operative nausea and vomiting (PONV) continue to be frequent occurrences, even when conventional antiemetics are prophylactically used.

OBJECTIVE: To compare the efficacy of Granisetron over Droperidol in the prevention of PONV in patients undergoing elective open cholecystectomy under general anesthesia.

MATERIAL & METHODS: In this double blind randomized study, 100 adult patients with physical status ASA I and II, (age, 20-60 years), were randomly allocated into two groups, X or Y, to receive either injection Granisetron hydrochloride (3 mg i/v) or Droperidol (2.5 mg i/v), 5 min prior to induction of general anesthesia. The incidence of nausea and vomiting was recorded every six hourly for a period of 24 hour after the surgery.

RESULTS: 6 (12%) patients in the granisetron group and 20 (40%) patients in the Droperidol group reported an emetic episode, ($p = 0.002$); the incidence of PONV in the total 24 hr period after the surgery, 54% in the granisetron group and 76% in Droperidol group ($p = 0.022$)

CONCLUSIONS: It was found that granisetron is superior to Droperidol in the prevention of postoperative nausea and vomiting. JMS 2011;14(1):11-14

Keywords: Postoperative nausea and vomiting(PONV), retching, droperidol, granisetron, cholecystectomy

Postoperative nausea and vomiting is the most frequent side effect after anesthesia, occurring in about 30% of unselected inpatients and up to 70% of high risk patients during the first 24 hours after emergence¹. Although Post operative nausea and vomiting is almost always self limiting and non fatal, it can cause significant morbidity including dehydration, electrolyte imbalance, suture tension and wound dehiscence, venous

hypertension and bleeding, esophageal rupture and life threatening airway compromise, although the more severe complications are rare. Each vomiting episode delays discharge from the recovery room by approx. 20 min.¹

A large study reported rates of 37% for nausea and 20% for vomiting in patients undergoing general anesthesia.² There are, however, considerable variations in the reported prevalence of PONV.^{3,4,5} which can be attributed to a number of factors. In the UK, it has been estimated that PONV affects between one and two million patients every year.^{6,7} A number of drugs have been used to control PONV which include butyrophenones (droperidol), benzamides (metoclopramide), histamine receptor antagonists (dimenhydrinate), muscarinic receptor antagonists and 5-HT₃ receptor antagonists (ondansetron, granisetron), all with different efficacy and side effects.

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Droperidol is inexpensive and very effective in small doses and is often considered the gold standard when it comes to comparing the efficacy of other medications. In 2001, FDA issued a black box warning about Droperidol citing concerns of QT prolongation and torsades de pointes. With over 20 reported cases in 30 yrs of torsades, it appears that the ECG abnormalities are dose related side effects (in excess of 50mg in a 24 hour period) and that in low doses; Droperidol is not a significant risk.⁸

Granisetron, the most recently approved 5-HT₃ receptor antagonists for the indication of PONV, lags significantly behind in published trials to prove its efficacy. An i.v dose as low as 0.04mg/kg is effective in the prevention of post operative nausea and vomiting. Headache, dizziness, and constipation are the most common reported side effects.⁹ This study had been undertaken to compare the efficacy of Granisetron over Droperidol in the prevention of post operative nausea and vomiting following open cholecystectomy.

Methods

Hundred adult patients with physical status ASA I and II, age between 20 to 60 years, undergoing elective Open Cholecystectomy under general anesthesia were taken up for the study in a double-blind randomized fashion. Patients with some neurological problems like history of motion sickness, migraine, muscular dystrophy or who received anti emetics within 48 hours before surgery or pregnant/lactating females were excluded.

After taking the informed written consent and approval of the institutional ethics committee, the patients were randomly allocated into two groups, X or Y, to receive either injection Granisetron hydrochloride 3 mg i/v or Droperidol 2.5 mg i/v 5 min prior to induction of general anesthesia. Study medications were prepared by technologist in charge operation theatre who did not reveal the nature of drug to any one till the completion of study. He also maintained a register documenting the particulars of each patient and code of the drug.

The incidence of nausea and vomiting was recorded every six hourly for a period of 24 hour after the surgery (retching event was considered as a vomiting event). PONV was evaluated on a 3 point scale, i.e., 0 = none, 1 = nausea, 2 = vomiting. Rescue anti-emetic medication was administered as and when required in the form of injection metoclopramide, and dose repeated in case of severe nausea, or more than three emetic episodes within a period of 15 mins or if the patient asked for it.

At the end, all the data collected was decoded, patients allocated to their respective groups and subjected to statistical analysis using Students t-test, Man Whitney U test, Chi Square test and Kruskal- Wells Test.

Results

There was no significant difference between the groups in age, gender and weight ($p = 0.761, 0.826$ and 0.563 respectively). Also the duration of anesthesia and surgery was statically

Table 1: Demographic characteristics of patients in Granisetron (X) and Droperidol (Y) groups

Characteristics	Group X (Granisetron)	Group Y (Droperidol)	p value	Remarks
Age (years)	40.4 ± 11.0*	39.7 ± 11.3	0.761	NS
Weight (kg)	68.2 ± 10.7	67.0 ± 10.7	0.563	NS
Duration of anesthesia(min)	66.9 ± 12.1	63.4 ± 9.9	0.116	NS
Duration of Surgery(min)	59.3 ± 11.9	58.1 ± 9.3	0.600	NS

* mean ± SD

Table 2: Comparison of rescue anti emetics used in the two groups during 0-24 hour study period

Group	Number/Percentage of Patients with PONV		p value
	N	%	
X Granisetron (n=50)	3	6	0.003 (Sig)
Y Droperidol (n=50)	14	28	

3(6%) patients in group X and 14 (28%) patients in group required rescue anti emetic

insignificant ($p = 0.116$ and 0.600). In the group X (granisetron), a complete response (PONV Score 0) was observed in 44 (88%) during 0-6 hours of the study. In the subsequent time intervals, i.e. 6-12hrs, 12-18 hrs, and 18-24 hrs, a lesser response was seen with score 0 being present in 39(78%), 38(76%) and 41(82%) patients respectively. (Fig. 1)

Figure 1: PONV Score at different time intervals in group X (Granisetron)

Episodes of nausea were observed in more number of patients with increasing time. During the first 6 hrs, it was seen in 4 patients (8%) and the number increased to 7 (14%), 9 (18%), and 8 (16%) in the next three 6 hr intervals. Out of 50, 2 (4%) patients suffered vomiting in the first 6hr, where as it was seen in 4 (8%), 3 (6%), and 1 (2%) patients in the subsequent intervals.

Taking together emetic episodes (nausea + vomiting) were seen in 6(12%), 11(22%), 12(24%), and 9(18%) patients in the 0-6, 6-12, 12-18, and 18-24 hr interval. Intra-group comparisons of emetic episodes at different time intervals revealed a non-significant variation ($p=0.252$). In the Droperidol group, a complete response i.e. score 0, was seen in 30 (60%) of patients in

Figure 2: PONV Score at different time intervals in group Y (Droperidol)

Figure 3: Comparison of incidence of nausea and vomiting between Granisetron and Droperidol group

the initial 6hrs of postoperative period. In the subsequent 6 hr interval, it was found in 31 (62%), 27 (54%) and 28 (56%) patients.

Nausea was seen in 13 (26%), 14 (28%), 19 (38%) and 15 (30%) of study subjects in the four 6 hourly time interval taken in increasing order. Out of 50 patients, 7 (14%) suffered from vomiting episodes in the first 6 hours after surgery, where as this number was 5 (10%), 4 (8%), and 7 (14%) in the subsequent six hour intervals.

Taking nausea and vomiting together i.e. emetic episodes were seen in 20 (40%), 19 (38%), 23 (46%) and 22 (44%) patients in the similar time frames taken in the increasing order. Again, as seen in the other group, no statically significant difference ($p=0.910$) was seen on intra group comparison of incidence of emetic episodes in the different time frames.

During the first 6 hrs after anesthesia, 6 (12%) patients in the Granisetron group and 20 (40%) patients in the Droperidol group developed an emetic episode, the variation was statically

significant ($p = 0.002$). At 6-12 hrs after anesthesia, 11 (22%) of patients in the Granisetron group suffered an emetic episode compared to 19 (38%) patients in the Droperidol group. However, this difference was found to be statically insignificant ($p = 0.104$). A statically significant difference ($p = 0.030$), was found when the incidence of emetic episodes was compared between the two groups in the 12-18 hr time frame i.e. 12 (24%) patients in the Granisetron group were found to have nausea/vomiting compared to 23 (46%) patients in the Droperidol group. At 18-24 hrs, emetic episode was seen in 9 (18%) patients in the Granisetron group compared to 22 (44%) patients in the Droperidol group. The difference was statically significant ($p = 0.003$). 3 (6%) patients in group X (Granisetron group) and 14 (28%) patients in group Y (Droperidol group) required rescue anti emetic medication during the 24 hour study period. The difference between the two groups was found to be statistically significant ($p = 0.003$).

Discussion

Post operative nausea and vomiting (PONV) are considered as very unpleasant side effects of anaesthesia, causing distress and dissatisfaction to patients. After laparoscopic cholecystectomy its incidence has been reported to be as high as 40-70%. The main patient related factors are age, gender, history of motion sickness, previous post operative nausea and vomiting and pregnancy. The incidence on females has been reported to be very high.⁷ Women are more sensitive to emetic stimuli. The mechanism of post operative nausea and vomiting in them is complicated by prevailing hormone status.⁸ The management of post operative nausea and vomiting is based primarily on treatment rather than prevention.

In our study, we found that during the first 6 hrs after anesthesia, 6 (12%) patients in the Granisetron group and 20 (40%) patients in the Droperidol group reported an emetic episode, with significant variation between the two (p value 0.002). This shows that a complete response i.e. no nausea and vomiting was seen in 88% and 60% patients in Granisetron and Droperidol groups respectively.

Our results are at par with Fujii Y, Tanaka H *et al* in 1999, who found a complete response in 90% and 55% of patients in the Granisetron and Droperidol group, they studied, during the first 3 hrs after surgery. Saitoh Y, Tanaka H *et al* in 1999, while comparing the two drugs for treating PONV also reported a complete response in 78% and 56% patients during first three hours and 80% versus 52% during 3-24 hrs postoperatively in the Granisetron and Droperidol groups respectively.^{10,11} Also, D'Angelo R, Philip B, Gan TJ *et al* (2005) reported a complete response in >90% of patients when Granisetron was given as a prophylactic measure for postoperative nausea and vomiting.¹² In another study by Fujii Y, Tanaka H (1995), the incidence of emetic episodes was reported to be same i.e., 12% in both the drug groups, during the first 3 hrs after surgery. However, in the subsequent 21 hrs, there was a decrease in emetic episodes to 8% in the Granisetron group only depicting that the said drug is

superior to Droperidol in controlling PONV during 24 hrs postoperatively.¹³

Taking together the four time frames, the incidence of postoperative nausea and vomiting in the total 24 hr period after the surgery, we found that 27(54%) patients suffered emetic episodes in the granisetron group compared to 38 (76%) patients in Droperidol group. This difference was statically significant ($p = 0.022$). In a similar comparison by Fujii Y, Toyooka H, *et al* in 1998, 16% of patients reported an emetic episode in the granisetron group where as it was 46% in case of Droperidol group.¹⁴ Contrary to this study, Contreras-Domínguez V and Carbonell-Bellolio P studied the efficacy of low dose Droperidol (0.625 mg) in comparison to Granisetron and other drugs for the same purpose. They reported 4% incidence of emetic episodes in the Droperidol group as compared to 12% in the granisetron, concluding low dose Droperidol to be more effective.¹¹

In our study 3(6%) patients in Granisetron group and 14 (28%) patients in Droperidol group required rescue anti emetic medication during the 24 hour study period. The difference between the two groups was found to be statistically highly significant (p value 0.003).

In conclusion, our observations suggest that Granisetron, at a dose of 3mg i/v 5 min prior to the induction of anesthesia is a better choice in treating PONV during first 24 hrs post-operatively. However, in order to get rid of this unwanted problem following general anesthesia and surgery and to achieve the goal of '0' PONV score for patient safety and comfort, further scientific work and research is needed in this field.

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