

Original Research Article

Dexamethasone combined with other anti-emetics for prophylaxis after laparoscopic cholecystectomy

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Abstract

Background: Following surgery and anesthesia, post-operative nausea and vomiting (PONV) are two of the most common side effects. Dexamethasone has been reported to be effective in reducing the incidence of emesis in patients undergoing chemotherapy.

Aim: The aim of the study was to compare the effectiveness of granisetron and dexamethasone in combination with ondansetron and dexamethasone in combination for prophylaxis after laparoscopic cholecystectomy.

Materials and methods: This is a prospective study on patients undergoing laparoscopic cholecystectomy consisted of 200 patients. 164 patients completed the study. 82 patients in group 1 and 82 patients in group 2. Patients were randomised in two groups, namely group 1 received granisetron and dexamethasone while group 2 received ondansetron and dexamethasone.

Results: Out of 200 patients who initially signed the informed consent form, 164 patients (82 in group 1 and 82 in group 2) completed the study. In this study, Granisetron + Dexamethasone was found to be as effective as when compared to ondansetron + Dexamethasone as at 0-1 hour, 100% of patients in group 1 had no vomiting and 97.56% of patients had no vomiting in group 2. Total response was present in 97.56% in group 1 and 95.12% in group 2. The percentage of patients who received metoclopramide was 8.53% in both the groups. At 1-7 hour, 97.56% of patients in group 1 had no vomiting and 100% of patients had no vomiting in group 2. Total response was present in 96.34% in group 1 and 93.90% in group 2. The percentage of patients who received metoclopramide was 4.87% in group 1 and 2.43% in group 2. At 7-24 hour, 97.56% of patients in group 1 had no vomiting and 100% of patients had no vomiting in group 2. Total response was present in 95.12% in group 1 and 95.12% in group 2. The percentage of patients who received metoclopramide was 2.43%

in both the groups. 4 out of 82 patients complained of dizziness in group 1 and 4 out of 82 patients complained of dizziness in group 2. 6 out of 82 patients complained of headache in group 1 and 6 out of 82 patients complained of headache in group 2 in the post anaesthesia care unit. Pain scores in group 1 were at 0-1 hr was 6 ± 2.4 , at 1-7 hour was 5.4 ± 0.7 and at 7-24 hour was 3.5 ± 0.9 . Pain scores in group 2 were at 0-1 hr was 7 ± 2.3 , at 1-7 hour was 5.9 ± 2.7 and at 7-24 hour was 4.5 ± 0.2 . In between the two groups, there was no significant difference in the side effects and pain scores. **Conclusion:** The combination of dexamethasone with either granisetron or ondansetron after induction of anesthesia in patients undergoing laparoscopic surgery showed no statistically significant difference in antiemetic efficacy with minimal side effects and excellent patient satisfaction.

Key words

Granisetron, Ondansetron, Laparoscopic cholecystectomy.

Introduction

Following surgery and anesthesia, post-operative nausea and vomiting (PONV) are two of the most common side effects [1]. Dexamethasone has been reported to be effective in reducing the incidence of emesis in patients undergoing chemotherapy. The antiemetic effect was found to be equal to or better than the 5HT₃ receptor antagonists like ondansetron and granisetron. Dexamethasone was also reported to be effective in reducing the incidence of postoperative nausea and vomiting. PONV was seen in 11% of patients and severe PONV in 2% of patients despite prophylaxis with dexamethasone, ondansetron and the use of total intravenous anaesthesia technique in a review on postoperative recovery profile after laparoscopic cholecystectomy [2, 3]. Dexamethasone has also been effective in paediatric patients undergoing strabismus repair, tonsillectomy and adenoidectomy in reducing postoperative nausea and vomiting and also in women undergoing major gynaecological surgery. High incidences of PONV have been reported in patients undergoing laparoscopic cholecystectomy for cholelithiasis i.e. 53-72% [4]. Therefore dexamethasone has been evaluated in combination with other anti-emetics for prophylaxis after laparoscopic cholecystectomy. The combination of ondansetron and dexamethasone was more effective in prevention of postoperative nausea and vomiting than when ondansetron was used alone. Also the

combination of granisetron and dexamethasone produced 98% PONV [5] free in patients undergoing laparoscopic cholecystectomy versus 83% PONV free with granisetron alone.

Materials and methods

This is a prospective study on patients undergoing laparoscopic cholecystectomy from October 2014 to February 2015. Institutional review board approval and informed consent forms were obtained from all human subjects. This study consisted of 200 patients. 164 patients completed the study. 82 patients in group 1 and 82 patients in group 2. Exclusion criteria included allergies or hypersensitivity to the study drugs, history of chronic nausea and vomiting, had nausea and vomiting in the past 24 hours prior to anesthesia, had received any anti-emetics or any drug with antiemetic properties during the 24 hours before anaesthesia, age of > 70 years, were pregnant or breast feeding or had a condition requiring chronic opioid use. Patients were randomised in two groups, namely group 1 received granisetron and dexamethasone while group 2 received ondansetron and dexamethasone. The study medications were administered immediately after induction of anaesthesia in both treatment groups. The time of each vomiting episode and the time and intensity of each nausea episode were collected. The intensity of each nausea episode was graded as mild (discomfort noticed but no disruption of anticipated normal activity), moderate

(discomfort sufficient to reduce normal activity) or severe (inability to perform normal activity). Metoclopramide was given if patients vomited, complained of moderate or severe nausea. Nausea and vomiting assessments were made up to 30 minutes following metoclopramide administration and response was defined as improvement of PONV symptoms. Postoperative pain was also followed up at 1, 7, 24 hours postoperatively.

Results

Out of 200 patients who initially signed the informed consent form, 164 patients (82 in group 1 and 82 in group 2) completed the study.

Total response means no moderate, no severe nausea, no rescue antiemetic use. In this study, Granisetron + Dexamethasone was found to be as effective as when compared to ondansetron + Dexamethasone as at 0-1 hour, 100% of patients in group 1 had no vomiting and 97.56% of patients had no vomiting in group 2. Total response was present in 97.56% in group 1 and 95.12% in group 2. The percentage of patients who received metoclopramide was 8.53% in both

the groups. At 1-7 hour, 97.56% of patients in group 1 had no vomiting and 100% of patients had no vomiting in group 2. Total response was present in 96.34% in group 1 and 93.90% in group 2. The percentage of patients who received metoclopramide was 4.87% in group 1 and 2.43% in group 2. At 7-24 hour, 97.56% of patients in group 1 had no vomiting and 100% of patients had no vomiting in group 2. Total response was present in 95.12% in group 1 and 95.12% in group 2. The percentage of patients who received metoclopramide was 2.43% in both the groups. 4 out of 82 patients complained of dizziness in group 1 and 4 out of 82 patients complained of dizziness in group 2. 6 out of 82 patients complained of headache in group 1 and 6 out of 82 patients complained of headache in group 2 in the post anaesthesia care unit. Pain scores in group 1 were at 0-1 hr was 6 ± 2.4 , at 1-7 hour was 5.4 ± 0.7 and at 7-24 hour was 3.5 ± 0.9 . Pain scores in group 2 were at 0-1 hr was 7 ± 2.3 , at 1-7 hour was 5.9 ± 2.7 and at 7-24 hour was 4.5 ± 0.2 . In between the two groups, there was no significant difference in the side effects and pain scores (**Table – 1, Table – 2**).

Table – 1: Demographic data.

	Granisetron + Dexamethasone (n=82)	Ondansetron + Dexamethasone (n=82)
Age (years)	47.5±10.8	48.7±11.2
Gender (Male/Female)	42/40	40/42
Type of surgery		
Lap Cholecystectomy	54	60
Lap Herniorrhaphy	28	22
History of PONV	6	7
History of motion sickness	2	1
Delayed gastric emptying	5	4
History of smoking	15	20

Discussion

Few studies have reported the use of dexamethasone with other anti-emetics as prophylaxis after laparoscopic cholecystectomy. In a prospective randomized double-blind study

done by Alias S Dabbous, et al. [6], compared the effectiveness of dexamethasone 8 mg with either granisetron 1 mg or ondansetron 4 mg in the prevention of postoperative nausea and vomiting in patients undergoing laparoscopic

surgery. Hundred ASA I and II patients scheduled for laparoscopic surgery were enrolled in the study and 84 patients completed it. Following induction of anesthesia, group I (n = 42) received granisetron 1 mg and dexamethasone 8 mg, group II (n = 42) received ondansetron 4 mg and dexamethasone 8 mg. Nausea and vomiting episodes, pain scores as well as side effects were recorded during the first hour and subsequently during the first 6 and 24 hours postoperatively. Satisfaction scores were obtained at discharge. There was no statistically significant difference between the 2 groups during the 1st 24 hours following surgery in regards to pain scores, satisfaction and side effects manifestations. At 0-1 hour interval, 100% of patients in group I and 97.6% in group II had no vomiting. Total response (no moderate or severe nausea and no rescue anti-emetics) was 83.3% in group I and

80.95% in group II, and metoclopramide was used in 7.1% of patients in both groups. At 1-6 hours interval, 97.6% of patients in group I and 100% in group II had no vomiting. Total response was 92.8% in group I and 90.9% in group II, and metoclopramide was used in 4.76% of patients in group I and 2.38% in group II. At 6-24 hours no vomiting occurred in 97.6% of patients in group I and 100% in group II. Total response was 95.2% in both groups, and metoclopramide was used in 2.38% of patients in both groups. This study concluded that the combination of dexamethasone 8 mg with either granisetron 1 mg or ondansetron 4 mg following induction of anesthesia in patients undergoing laparoscopic surgery showed no statistically significant difference in antiemetic efficacy with minimal side effects and excellent patient satisfaction.

Table – 2: Efficacy outcome.

	Granisetron + Dexamethasone (n=82)	Ondansetron + Dexamethasone (n=82)
No vomiting		
0-1 hour	82 (100%)	80 (97.56%)
1-7 hour	80 (97.56%)	82 (100%)
7-24 hour	80 (97.56%)	82 (100%)
Total response		
0-1 hour	80 (97.56%)	78 (95.12%)
1-7 hour	79 (96.34%)	77 (93.90%)
7-24 hour	78 (95.12%)	78 (95.12%)
Metoclopramide		
0-1 hour	7 (8.53%)	7 (8.53%)
1-7 hour	4 (4.87%)	2 (2.43%)
7-24 hour	2 (2.43%)	2 (2.43%)

P Gupta, et al. [7], in this study 200 patients were undergoing laparoscopic cholecystectomy, the patients were divided into two groups. One group received preoperative dexamethasone (Group 1) and other group received ondansetron (Group 2). After surgery, patients were observed for any episode of nausea or vomiting or whether the patient required any antiemetic drug in the preoperative period. The results

were that the two groups were comparable in outcome, in terms of post-operative nausea and vomiting, in patients undergoing laparoscopic cholecystectomy. In group 1, 24% of patients had nausea as compared to 30% in group 2 (P=0.2481). 12% of patients had vomiting in group 1 and 18% of patients had vomiting in group 2 (P=0.3574). This study concluded that preoperative intravenous low dose

dexamethasone reduces the incidence of PONV and is comparable to intravenous ondansetron. In study done by Xiao-Ying Si, et al. [8], it was conducted to identify all relevant randomised clinical trials. The primary outcome was PONV in the early period (0-3 hours, 0-4 hours, or 0-6 hours), late period (>6 hours), and the overall period (0-24 hours). The results were that nine randomised clinical trials with a total of 1089 patients were included in the analysis. Pooled analysis showed that dexamethasone combined with other anti-emetics provided significantly better prophylaxis than single anti-emetics in the early period [odds ratio (OR): 0.34; 95% confidence interval (CI): 0.21-0.55; $p < 0.001$], late period (OR: 0.35; 95% CI: 0.22-0.57; $p < 0.001$), and the overall period (OR: 0.36; 95% CI: 0.27-0.49; $p < 0.001$). Correspondingly, rescue antiemetic usage was significantly less in the combination therapy group (OR: 0.22; 95% CI: 0.12-0.41; $p < 0.001$). The most frequently reported adverse events were headache, dizziness, and itching. The incidence of adverse events did not differ between the two groups. It concluded that dexamethasone combined with other anti-emetics was significantly better than single anti-emetics for prophylaxis of PONV in patients undergoing laparoscopic cholecystectomy without apparent side effects. In a study done by J.J. Wang, et al. [9], they evaluated the antiemetic effect of i.v. dexamethasone compared to saline in the prevention of nausea and vomiting after laparoscopic cholecystectomy. This study consisted of 90 patients requiring general anaesthesia for laparoscopic cholecystectomy, it was a randomised, double blinded, placebo controlled study. The dexamethasone group (n=45) received dexamethasone 8 mg i.v. and the saline group received saline 2 ml i.v. at induction of anaesthesia. Anaesthesia was maintained with isoflurane in oxygen. The results were that 10% of patients in the dexamethasone group compared with 34% in the saline group reported vomiting ($P < 0.05$). The total incidence of nausea and vomiting was 23% in the dexamethasone group and 63% in the saline group ($P < 0.001$). This study

concluded that dexamethasone 8 mg decreased the incidence of nausea and vomiting after laparoscopic cholecystectomy. In a study done by Ali Reza Khalaj, et al. [10], evaluated the prophylactic anti-emetic effect of dexamethasone in comparison with metoclopramide and placebo for the prevention of post-operative nausea and vomiting in patients undergoing elective laparoscopic cholecystectomy. In Mostafa Khomeini hospital, a teaching hospital of Shahed University, Tehran, Iran, a randomized, double-blind and placebo-controlled study on 161 patients undergoing general anesthesia for elective laparoscopic cholecystectomy was run. One hundred sixty one patients (124 females and 37 males) requiring general anesthesia for laparoscopic cholecystectomy were studied. The dexamethasone group (n = 53) received dexamethasone 8 mg IV, the metoclopramide group (n = 55) received metoclopramide 10mg IV and the placebo group (n = 53) received 2ml saline IV at the induction of anesthesia. The results were that in the current study, 26.4%, 32.7% and 52.8% of patients reported vomiting in the dexamethasone, metoclopramide and placebo group ($P \leq 0.001$), respectively. The total incidence of nausea and vomiting also reduced to 30.2% with dexamethasone in comparison with 49.1% in metoclopramide group and 58.5% in placebo group ($P \leq 0.001$). This study concluded that Dexamethasone 8 mg is a better anti-emetic agent than metoclopramide for the prevention of post-operative nausea and vomiting after laparoscopic cholecystectomy.

Conclusion

The combination of dexamethasone with either granisetron or ondansetron after induction of anesthesia in patients undergoing laparoscopic surgery showed no statistically significant difference in antiemetic efficacy with minimal side effects and excellent patient satisfaction.

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