

Ondansetron Versus Combined Dexamethasone and Metoclopramide In Prevention of Nausea and Vomiting After Laparoscopic Cholecystectomy

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ABSTRACT

Objective To compare the efficacy of combined metoclopramide and dexamethasone with ondansetron in preventing nausea and vomiting after laparoscopic cholecystectomy.

Study design Randomized controlled trial.

Place & Duration of study Surgical Unit I Combined Military Hospital Rawalpindi, from 1st June 2010 to 3rd January 2011.

Methodology A total of 120 patients were observed for 24 hours after elective laparoscopic cholecystectomy for nausea and vomiting and divided into two groups of 60 patients each. Nausea and vomiting was rated by the patients according to a three point scale (0=no nausea and vomiting, 1=nausea, 2=retching or vomiting).

Results Early postoperative nausea and vomiting was not present in 31 (51.7%) patients of group I and 40 (66.7%) of group II (score = 0). In 11 (18.3%) patients of group I and 12 (20.0%) of group II only nausea was present (score = 1), while 18 (30.0%) patients in group I and 8 (13.3%) in group II scored 2.

The late postoperative nausea and vomiting was not present in 21 (35.0%) patients in group I and 37 (61.7%) in group II (score = 0). In 28 (46.7%) patients in group I and 22 (36.7%) in group II nausea was present (score = 1) while 11 (18.3%) patients of group I and 1 (1.7%) in group II scored 2.

Conclusion Ondansetron was effective as compared to combined metoclopramide and dexamethasone in prevention of post-laparoscopic cholecystectomy nausea and vomiting.

Key words Postoperative nausea and vomiting, Laparoscopic cholecystectomy, Metoclopramide.

INTRODUCTION:

Nausea and vomiting occur frequently in patients undergoing surgical procedures under general anesthesia.¹ The overall incidence of postoperative nausea and vomiting (PONV) has been difficult to

assess, as its etiology is multifactorial and there is seldom only one trigger stimulus.² The important risk factors for the development of PONV are female sex, young age, a history of postoperative nausea and vomiting, non-smoking and long duration of anesthesia.^{3,4} Incidence of PONV is highest in thyroid surgery and laparoscopy.^{5,6}

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Laparoscopic cholecystectomy for the treatment of cholelithiasis is popular amongst surgeons as well as patients due to its associated advantages, which includes a short hospital stay.⁷ However high

incidences of PONV (53%-72%) have been reported after laparoscopic cholecystectomy.⁶ Prolonged PONV may result in dehydration and electrolyte imbalance, increased risk of pulmonary aspiration of gastric contents and may trigger cardiorespiratory reflexes, opening of the sutures and wound dehiscence.⁸ The etiology of PONV after laparoscopic cholecystectomy is not entirely understood. Therefore, it has been recommended that routine antiemetic prophylaxis should be considered for these high-risk patients.⁹

Currently used antiemetics for prevention of PONV include antiserotonin agents such as ondansetron and granisetron, metoclopramide and dexamethasone.¹⁰ The dexamethasone and metoclopramide combination was used earlier for major gynecological surgery.¹¹ This study compared the efficacy of combined metoclopramide and dexamethasone with ondansetron in prevention of post-laparoscopic cholecystectomy nausea and vomiting.

METHODOLOGY:

This randomized controlled trial was conducted in Surgical Unit I, Combined Military Hospital, Rawalpindi from 1st June 2010 to 3rd January 2011. Patients with American Society of Anesthetists (ASA) physical status I and II scheduled for elective laparoscopic surgery of both genders, aged 18 to 75 year and patients scheduled to be hospitalized for at least 24 hours after the surgery were included. Patients receiving drugs with known antiemetic activity within 24 hours of surgery, experiencing nausea and vomiting 24 hours before surgery, who needed nasogastric tube before, during and after operation, having known allergy to metoclopramide and other dopamine and serotonin receptor antagonists like neuroleptics, with history of motion sickness, who suffered difficult endotracheal intubation at the induction of anesthesia and who received preoperative and postoperative opioid analgesics, were excluded from study.

After fulfilling inclusion criteria and written informed consent, a total of 120 patients were randomly divided into group I and II. Each group comprised of 60 patients. One minute before the induction of anesthesia, Group I received intravenous (I/V) metoclopramide 10 mg and dexamethasone 8 mg. Group II received I/V ondansetron 4 mg. The identity of drugs under study was blinded from the patients and the anesthetists during the surgery and the paramedical staff who gave rescue antiemetics and other medicines to the patients postoperatively.

Variables like technique and duration of anesthesia,

duration of surgery, laparoscopic gases, laparoscopic pressures and intravenous fluid therapy (for 24 hours) were standardized. Same team of surgeons and anesthetists carried out the operations. After operation, patients were transported to postoperative recovery unit (PORU). All postoperative episodes of nausea and vomiting (including retching), occurring within the first 24 hours were recorded 04 hourly except during sleep. This was done by questioning the patients and by spontaneous complaints of the patients.

Nausea and vomiting were rated by the patients according to a three point scale (0 = no nausea and vomiting, 1 = nausea, 2 = vomiting). The minimum as well as maximum (worst) score during each time frame for each symptom was recorded and analyzed. Patients who experienced both nausea and vomiting were included in the vomiting category as about half of the patients with nausea suffer also from vomiting. The proportion of patients with vomiting and without nausea is usually 2% and very small.¹²

Efficacy of study drugs was defined as ability to prevent completely nausea and vomiting associated with laparoscopic cholecystectomy, within first 24 hours of the surgery. Nausea and vomiting during postoperative hours 0-06 was termed early PONV and in hours 7-24 was called late PONV. Nausea and vomiting throughout the 24 hours of observation period was termed overall frequency. Complete response was taken as no nausea and vomiting throughout the 24 hours of observation period and no need for rescue antiemetics. Rescue antiemetics were the drugs used to treat nausea and vomiting occurring from 0 to 24 hours postoperatively.

Data was entered into computer program SPSS version 10 and analyzed. Mean and standard deviation were calculated for age. Frequency and percentage were calculated for sex, frequency of early and late PONV and 24 hours of observation period. Chi Square test was applied on frequency of early and late PONV, 24 hours of observation period and consumption of rescue antiemetics for significance. P value of =0.05 was considered as significant

RESULTS:

Out of 120 patients, three patients were excluded from the study for being converted from laparoscopic cholecystectomy to open cholecystectomy because of severe inflammation, difficult dissection and hazy anatomy of Calot's triangle. Patients had a mean age of 44.58±14.67 year in group I and 44.13±13.39 year in group II. In group I, out of 60 patients 45 (75%) were females and 15 (25%) males.

In group II there were 50 (88.33%) females and 10 (11.66%) males.

Table-I: Comparison of Frequency of Early Post Laparoscopic Cholecystectomy Nausea and Vomiting				
Groups	S c o r e s			P value
	0	1	2	
Group I (n=60)	31 (51.7%)	11 (18.3%)	18 (30.0%)	0.03
Group II (n=60)	40 (66.7%)	12 (20.0%)	8 (13.3%)	

Better prevention of early postoperative vomiting (lower score 2) was achieved in group II. Moreover, majority of group II patients showed no nausea and vomiting in early observational time frame (higher score 0). On the other hand, early anti-nausea effect in group II was marginally better than group I (table I). Observations in the late time frame upheld the superiority of group II for vomiting (lower score 2) and absence of nausea and vomiting altogether (higher score 0). Converse to early time frame observation, group II patients also suffered considerably less nausea than group I patients (table II).

Table-II: Comparison of Frequency of Late Post Laparoscopic Cholecystectomy Nausea and Vomiting				
Groups	S c o r e s			P value
	0	1	2	
Group I	21	28	11	0.03
Group II	37	22	1	

Overall, group II drug was again better in preventing nausea and vomiting than its rival drugs in group I (lower scores 1 and 2 - table III). Use of rescue antiemetics was also noticeably lower in group II as compared to group I (table IV). Majority of group II patients (51.7%) neither suffered from PONV nor needed any rescue antiemetics throughout the 24 hours of observation period (complete response - table V).

Table-III: Comparison of Frequency of Overall Post Laparoscopic Cholecystectomy Nausea and Vomiting				
Groups	S c o r e s			P value
	0	1	2	
Group I	11	26	23	0.01
Group II	29	22	9	

Table-IV: Comparison of Utilization Of Rescue Antiemetics			
Groups	Not given (%)	Given (%)	P value
Group I	34	26	0.04
Group II	51	15	

Table-V: Comparison of Complete Response			
Groups	Yes (%)	No (%)	P value
Group I	11	49	0.001
Group II	31	29	

DISCUSSION:

For measuring nausea and vomiting a visual analogue scale (VAS) (0–10 or 0–100), an 11-point numeric rating scale (NRS) (0–10), or a verbal rating scale (VRS) (none, mild, moderate, severe) may be chosen.¹³ All the rating scales have certain limitations, such as the transversal of sensation into another dimension.¹³ Therefore it was decided to use the VRS based upon three points instead of four, so that it can be more comprehensible for study population.

It was shown that dexamethasone was most effective when administered at the time of induction of anesthesia then at the end.^{14,15} As for ondansetron, it was suggested that in operative procedures lasting more than 2 hours, it might be more relevant to administer the drug towards the end of the surgery as the half-life of ondansetron is approximately 3.5-4 hours in adults.¹⁶⁻¹⁸ Since the mean duration of the procedure in this study was about an hour, the timing of antiemetic administration would not have affected the outcome. Therefore drugs were administered at the time of induction of anesthesia.

This study showed that ondansetron has better anti vomiting effects than antinausea effects in early periods of observation, correlating with a quantitative systemic review done in 2001.¹⁹ Frequency of early nausea for combined metoclopramide and dexamethasone group in this study was 18% which is comparable with an important randomized double-blind multicentre trial.²⁰

Ondansetron was also markedly better in preventing vomiting (2% patients with vomiting versus 18% patients) and marginally better in preventing nausea (37% patients with nausea versus 47% patients) as compared to combined metoclopramide and dexamethasone which is again consistent with other trials.^{19,21} Prominent late antinausea effect of

combined metoclopramide and dexamethasone (47% patients with nausea versus 37% patients) was probably due to presence of dexamethasone which is known for pronounced antiemetic efficacy in late postoperative period.^{16,22} Late vomiting in group I occurred in 18% patients which is quite high to 7.3% of international data. Same increase in the incidence of nausea and vomiting occurred in a study by Wallenborn et al.²⁰

Overall frequency of nausea was significantly more in group I as compared to group II while overall frequency of vomiting was roughly one half in group II as compared to group I. This study showed that ondansetron was better in preventing vomiting than nausea which is again consistent with international literature.^{19-21,23} Utilization of rescue antiemetics was three times more in group I as compared to group II. This was also reported in other studies.²⁴

Degree of complete response was approximately 1.5 times more in group II (50% of group patients showed complete response) than group I (18% of group patients showed complete response) and statistically significant. Complete response rates of 64% were found for ondansetron in one study²⁵ and 50% in another one. The study could not justify the hypothesis that there might be a beneficial effect if dexamethasone is combined with metoclopramide.²¹

CONCLUSIONS:

Ondansetron was more effective as compared to combined metoclopramide and dexamethasone, in the prevention of post-laparoscopic cholecystectomy nausea and vomiting.

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