

Comparative Study between Ondansetron and Dexamethasone for Preventing Postoperative Nausea and Vomiting after laparoscopic Cholecystectomy

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ABSTRACT

BACKGROUND

Postoperative nausea and vomiting (PONV) have been described as the “big little problem”^{1,2} for anaesthesiology for laparoscopic surgery. Commonest cause of morbidity after anesthesia and surgery are pain and postoperative nausea vomiting.^{3,4,5}

METHODS

Institutional ethical committee clearance and written informed consent were obtained from 60 female patients of American Society of Anaesthesiologists physical status I and II, aged between 18 to 65 years, weighing about 50-60 Kg., height 150 to 160 cm, scheduled for laparoscopic cholecystectomy (duration < 90 minutes) under general anaesthesia in this prospective, randomised, double blind controlled study. Patients coming to operation theatre were divided by computer generated randomization in to two groups of 30 each, Group-A (n=30) and Group-B (n=30). A person, who was blind to the randomisation schedule, was administered the study drug 1 minute prior to other I.V. drugs. One of the following regimens, for Group A patients: Ondansetron 4 mg in 2 ml or for Group B patients: Dexamethasone 8 mg in 2 ml were administered. After preoxygenation, general anaesthesia was administered, pneumoperitoneum created, laparoscopic cholecystectomy done, and anaesthesia reversed. For post-operative analgesia Paracetamol (1000 mg) I.V. was administered. All patients were observed post operatively by noting vital signs and complications, if any. All episodes of PONV (nausea, vomiting, retching) were recorded for 12 hrs post operatively. Rescue drug Inj. Metoclopramide 10 mg I.V. was given, if required. All data from each patient was obtained and tabulated.

RESULTS

The age, weight, height, ASA status and duration of surgery of the patients included in study group ($p \leq 0.05$) were comparable and there was no significant statistical difference among the data collected during the study. Incidence of nausea is higher in both groups in the first hour though it is not statistically significant. Within 3-6 hours, patients receiving Dexamethasone had higher incidence of nausea, but it is not statistically significant. Incidence of retching is higher in both groups in the first hour. It is not statistically significant. Vomiting was more in the first 3 hours in both groups. It was not statistically significant. Need for rescue drug (Inj. metoclopramide 10 mg I.V.) was similar in both groups.

CONCLUSIONS

Ondansetron is as effective as Dexamethasone in reducing the incidence of nausea and vomiting in post-operative period of laparoscopic cholecystectomy and has minimal side effects.

KEY WORDS

Postoperative, Nausea, Vomiting, Retching, Emesis, Ondansetron, Dexamethasone, Laparoscopy

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BACKGROUND

Postoperative nausea and vomiting (PONV) have been variously described as the “big little problem,”^{1,2} for anaesthesiology. The commonest cause of morbidity after an anaesthesia and surgery are pain and postoperative nausea vomiting.^{3,4,5} Unrelieved pain is a common cause of PONV^{6,7} and opioids used for pain relief also causes PONV.⁸

In spite of extensive understanding of physiology of nausea and vomiting and abundance of antiemetic medications, certain surgical procedures are associated with unacceptably high incidence of PONV. Laparoscopic surgery is one of them, which is popular for minimal invasiveness but is associated with increased morbidity due to PONV.⁹ Factors believed to contribute are rigorous decompression of abdomen by surgeon,¹⁰ irritation of parasympathetic nerve endings in the abdomen and effect of carbon di oxide on emetic centre.¹¹

Although regarded by medical and nursing staff as minor complication of anaesthesia and surgery, nausea and vomiting are the frequent cause of great distress to the patient. In study by Orkin, approximately three quarter of the patients being questioned, rated freedom from nausea vomiting as their most important postoperative requirement.¹² Patients were willing to accept dysphoria, loss of mental acuity and increased pain, in order to avoid nausea and vomiting. In a questionnaire analysis nausea was second only to failure to wake up, as a reason for fear of general anaesthesia.¹³

Although unpleasant and embarrassing, PONV may occasionally lead to significant morbidity from dehydration, electrolyte imbalance, aspiration of vomitus, wound dehiscence. PONV may lead to prolongation of hospital stay and therefore increased expenses for surgery.

PONV is multifactorial. Several studies have been performed to identify the patients with highest risk factors associated with PONV in postoperative period,¹⁴⁻¹⁷ related to the patients, the surgical procedure or the choice of anaesthesia.

Ondansetron and dexamethasone are two popular drugs used to prevent PONV. Ondansetron is 5-HT₃ receptor antagonist and widely used as antiemetic. Dexamethasone causes better control of late/ delayed PONV¹⁸ by inhibiting prostaglandin synthesis,¹⁹ decreasing 5-HT level in nervous system²⁰ and by its anti-inflammatory action at operative site.²¹

Aims and objective of our study was to compare the effect of Ondansetron and Dexamethasone to prevent postoperative nausea and vomiting after laparoscopic cholecystectomy and to note any adverse reactions of drugs if arises after their use.

METHODS

Institutional ethical committee clearance and written informed consent were obtained in their own language before conducting the prospective, randomised, double blind controlled study. All 60 female patients of the study group belonged to American Society of Anaesthesiologists physical status I or II, between 18 to 65 years of age, 50- 60 Kg. in weight with height between 150 to 160 cm. They were

scheduled for laparoscopic cholecystectomy (Duration < 90 minutes) under general anaesthesia Patients suffering from any systemic or lifestyle diseases, receiving medications for any chronic diseases (Hypertension, diabetes mellitus, cardiac disease, bleeding diathesis, neurological disorder) patients with motion sickness and known allergy to study drugs were excluded from our study. Patients who were sensitive to vomiting, experienced nausea, vomiting or both in 24 hrs., before anaesthesia and had received antiemetic drug in 24 hrs., before anaesthesia and during study were also excluded. In the night (At 8 pm) before the day of operation, oral Midazolam 7.5 mg was given, and patients were advised overnight fasting. In the preoperative area, patient's vital parameters (Pulse rate, blood pressure, respiratory rate, ECG, SpO₂) were recorded as baseline by a non-invasive monitor. Sample size was calculated using the formula $n > 2(Z\alpha + Z1-\beta)^2 \times p^*q/d^2$, where $p = (p1 + p2)/2$, $q = 1-p$, and d is $p1-p2$ Now assuming p value <0.05 to be significant and considering effect to be two sided, we get $Z\alpha = 1.96$; assuming power of study to be 80% we get $Z1-\beta = 0.84$. Taking $p1$ and $p2$ as the percentage of PONV, in the 2 groups as 30% and 5% respectively (based on a pilot study of 10 patients in each group) using the above formula we get $n = 29$ in each group. Hence 30 patients were finally taken in each group. Patients coming to operation theatre were divided by computer generated randomization in two groups of 30 each, Group-A ($n=30$) and Group-B ($n=30$). Monitors were attached and intravenous line was secured. A person, who was blind to the randomisation schedule, prepared the drugs in 2 ml syringes and gave the drug intravenously 1 minute prior to other I.V. drugs. According to the group of the patient, one of the following regimens: Group: A – Ondansetron 4 mg in 2 ml or Group – B – Dexamethasone 8 mg in 2 ml was administered. On the operation table routine monitoring (ECG, Pulse oximetry, NIBP) was started and baseline vital parameters like heart rate, BP (Systolic, diastolic, mean) and arterial O₂ saturation (SpO₂) were recorded. Inj Glycopyrrolate 0.2 mg was given.

After preoxygenation for 3 minutes, Anaesthesia was induced with Thiopentone Sodium (5 mg/Kg.) and Fentanyl (2 microgram/Kg.). Endotracheal intubation was facilitated with Succinylcholine (2 mg/Kg.). Anaesthesia was maintained with N₂O, O₂ @ 60:40, and Isoflurane. Vecuronium bromide, in intermittent doses was used to maintain muscle relaxation. Stomach was evacuated with a nasogastric tube and intra-abdominal pressure was kept <14 mmHg throughout the laparoscopic procedure. After completion of surgery anaesthetic agents were discontinued, intravenous Glycopyrrolate and Neostigmine were used to reverse residual neuromuscular blockade.

Before tracheal extubation nasogastric tube was suctioned and removed. For postoperative analgesia Paracetamol (1000 mg) I.V. was administered. All patients were observed post operatively by noting vital signs and complications, if any. All episodes of PONV (nausea, vomiting, retching) were recorded for 12 hrs., in post operatively. Rescue drug Inj. Metoclopramide 10 mg I.V. was given, if required. All data from each patient was obtained and tabulated.

Nausea is defined as unpleasant sensation associated with awareness of urge to vomit. Retching is defined as laboured, spastic, rhythmic contraction of respiratory muscles without

expulsion of gastric contents. Vomiting is defined as forceful expulsion of gastric contents from mouth. Complete response (Free from emesis) is defined as no PONV and no need for rescue medication.

Statistical Analysis

All recorded data was analysed using Mann-Whitney-Wilcoxon tests or Chi-square test or Students unpaired t test as appropriate and the findings were discussed in detail to draw appropriate conclusion. Categorical variables are expressed as Number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test for Independence of Attributes/ Fisher's Exact Test as appropriate. Continuous variables are expressed as Mean and Standard Deviation and compared across the 2 groups using unpaired t test. The statistical software SPSS version 20 has been used for the analysis. An alpha level of 5% has been taken, i.e. if any p value is less than 0.05 it has been considered as significant.

RESULTS

Patients were comparable regarding age, weight, height and ASA status and there was no significant statistical difference between the age, weight, height, ASA status of the patients included in study group ($p \leq 0.05$). The average age in Group A (Ondansetron) was 41.83 years and in Group B (Dexamethasone) was 41.30 years. The average weight in Group-A (Ondansetron) was 54.5 Kg. and Group-B (Dexamethasone) was 53.47 Kg. The average duration of surgery was 68.67 minutes in Group-A and 67.5 minutes in Group-B. There was no statistically significant difference in duration of surgery among the study groups and groups are comparable to each other in term of duration of surgery.

Incidence of nausea is higher in both groups in the first hour though it is not statistically significant. Within 3-6 hours patients of dexamethasone (Gr B) group had higher incidence of nausea but it was not statistically significant. Incidence of retching was higher in both groups in the first hour. It was not statistically significant. Vomiting was more in the first 3 hours in both groups. It was not statistically significant. Need for rescue drug (Inj. metoclopramide 10 mg I.V.) was similar in both groups.

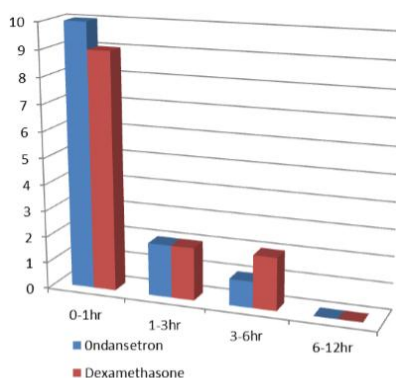


Figure 1. Incidence of Nausea is Higher in both Groups in the First Hour Though it is not Statistically Significant. Within 3-6 Hours Dexamethasone had Higher Incidence of Nausea but it is not Statistically Significant

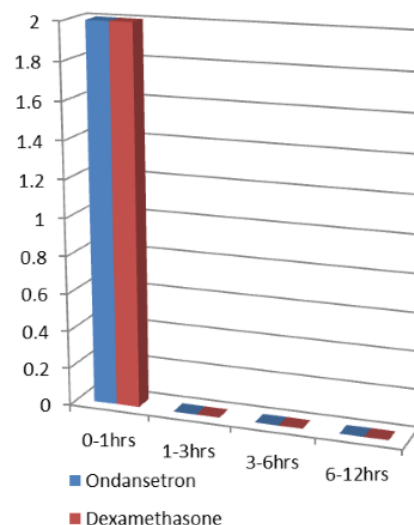


Figure 2. Incidence of Retching is Higher in both Groups in the First Hour. It is not Statistically Significant.

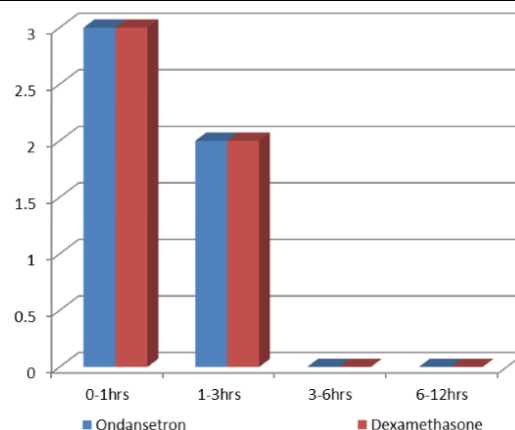


Figure 3. Vomiting was more in the First 3 Hours in Both Groups. It was not Statistically Significant.

Group		Age	Weight	Duration of Surgery (min)
Ondansetron Gr. A	Mean	41.83	54.50	68.67
	Std. Deviation	8.38	3.34	10.58
Dexamethasone Gr. B	Mean	41.30	53.47	67.50
	Std. Deviation	8.61	3.37	10.15
p Value		0.809	0.238	0.665
Significance		Not Significant	Not Significant	Not Significant

Table 1. Showing the Age and Weight Distribution of the Patients included in the Study

		Group		Total	p Value	Significance
		Ondansetron Gr. A	Dexamethasone Gr. B			
Rescue Drug	No	27(90%)	27(90%)	54(90)	1.000	Not Significant
	YES	3(10%)	3(10%)	6(10)		
Complication	Headache	1(3.3%)	0 (0%)	1(1.67%)	0.313	Not Significant
	No	29(96.7%)	30(100%)			

Table 2. Shows the Requirement of Rescue Antiemetic Drug (Inj. Metoclopramide 10 mg I.V. was Similar in Both the Groups) and Incidence of any Adverse Effects Among the Patients

DISCUSSION

Nausea and vomiting in postoperative period are the most distressing and unpleasant experience for a patient. Severe post-operative emesis results in dehydration, electrolyte imbalance, rarely, may lead to a life-threatening complication like aspiration pneumonia and alter the overall outcome of the entire surgical procedure. Incidence of postoperative nausea and vomiting are more with laparoscopic surgery due to manipulation of abdominal viscera, which is a strong emetic stimulus along with pain, anxiety and use of drugs like opioids and NSAID.

The drugs which are used commonly in treatment of PONV are metoclopramide, domperidone, phenothiazines, butyrophenones, anticholinergics and antihistaminic drugs. It was evident from different studies that ondansetron was highly effective in preventing PONV and the incidence of side effects were low with ondansetron. With most of the other drugs the incidence of side effects was high like extrapyramidal symptoms (e.g. metoclopramide, domperidone, Perphenazine, droperidol), haematological abnormalities (e.g.: prochlorperazine), sedation (e.g.: chlorpromazine, droperidol, cyclizine etc.) and adverse cardiovascular effects (e.g.: metoclopramide, chlorpromazine etc.)

Dexamethasone is very much effective antiemetic in patients receiving highly emetogenic cancer chemotherapy. Dexamethasone may antagonize prostaglandin or release endorphins that elevate mood, improve one's sense of well-being, and stimulate appetite. For these reasons, dexamethasone has been studied for preventing PONV.

In this study we compared the efficacy and safety of IV Ondansetron and Dexamethasone as prophylaxis for PONV in laparoscopic cholecystectomy which was chosen because of high incidence of PONV associated with it. In our study the factors that would have contributed to nausea and vomiting may be due to isoflurane and laparoscopic cholecystectomy. Use of face mask, use of nitrous oxide may or may not have contributed to nausea and vomiting. Avoidance of opioids and use of nasogastric tube towards the end of surgery must have helped in preventing PONV.

In a comparative study in 2011, Bhattarai B, Shrestha S et al.²² concluded that combination of ondansetron and dexamethasone is more effective in preventing post-operative nausea vomiting in patients undergoing laparoscopic surgery than ondansetron alone.

In a study in 2008, Gautam B, Shrestha BR et al.²³ proved combination of Ondansetron and Dexamethasone is better than each drug alone in preventing PONV after laparoscopic cholecystectomy. Dexamethasone alone is significantly less effective in preventing early vomiting compared to its combination with Ondansetron; whereas Ondansetron alone is less effective against late PONV as compared with combination therapy.

In another study Gautam B, Shrestha BR, in 2012,²⁴ proved Ondansetron and Dexamethasone were more effective than placebo in controlling PONV after tympanoplasty surgeries. Moreover, dexamethasone was more effective than ondansetron in preventing PONV.

In 2015, Wang X, Zhou Q et al. performed a meta-analysis²⁵ and they proved dexamethasone was as effective and as safe as ondansetron in preventing PONV.

In our study 86% patients in both groups experienced no emesis. The incidence of emesis was higher in first 3 hours in both groups. Retching was observed separately from vomiting. 93% patients in both groups experienced no retching. Incidence of retching was high in the first hour. 33% patients experienced nausea in the ondansetron group and 30% patients experienced nausea in the dexamethasone group. Incidence of PONV was very less at 6 hour and 12 hours in both groups. This study proved that ondansetron and dexamethasone are similarly effective in controlling PONV.

Age Incidence

In a study on some factors affecting the incidence of PONV, Burtles R, Peckett BW et al,²⁶ found a correlation between increase in age and decrease in emesis. Average age in present study was 41.83 in group A (Ondansetron) and 41.30 years in group B (Dexamethasone). In this study the incidence of PONV was more in younger patients in both groups.

Weight Incidence

Obesity is usually seen to be associated with increased incidence of PONV. In a study in 2015, McKenzie R, Kovac A et al.²⁷ found a higher percentage of patients with emetic episodes in heavier group average weight in the study was 47.5 Kg. In our study, the average weight of patients in Group- A (Ondansetron) was 54.5 Kg. and Group-B (Dexamethasone) was 53.47 Kg.

Side Effects

While the purpose of using prophylactic drug is to prevent PONV, we should use drugs with least adverse effect.

In a study in 1995, Dupreyron JP, Conseiller C et al.²⁸ Observed low incidence of side effects with ondansetron, headache and constipation being very little side effects. The side effect in this study was very low with one patient in group A (Ondansetron) developing headache. It was relieved without any treatment. There were no side effects in Group B (Dexamethasone). Thus, both ondansetron and dexamethasone have a low incidence of side effects.

CONCLUSIONS

We observed that Ondansetron is as effective as Dexamethasone in reducing the incidence of post-operative nausea and vomiting in laparoscopic cholecystectomy with minimal side effects. Use of rescue antiemetic is same with Ondansetron as well as Dexamethasone. From this study, we can conclude that Ondansetron, a 5-HT₃ antagonist, in a dose of 4 mg and Dexamethasone, a glucocorticoid, in a dose of 8 mg are both effective prophylactic drugs in the prevention of PONV in laparoscopic cholecystectomy under general anaesthesia.

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