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Original Research Paper

A Prospective Randomized Double-Blinded Clinical Study to Compare the Effect on Post-Operative Nausea and Vomiting (PONV) Following Administration of Ondansetron Alone and Ondansetron and Dexamethasone Combination in Laparoscopic Cholecystectomy

Medical Science

KEYWORDS : Laparoscopic surgery, Ondansetron, Dexamethasone, postoperative nausea and vomiting

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ABSTRACT

Background: *Post operative nausea and vomiting is the second most common complaint and distressing complication of laparoscopic surgery under general anesthesia which would cause unexpected delay in hospital discharge. The incidence of PONV remains unacceptably high (40-75% in the first 24 hrs) following laparoscopic cholecystectomy. This study intends to compare the efficacy on post operative nausea and vomiting (PONV) following administration of ondansetron alone and ondansetron and dexamethasone combination in laparoscopic cholecystectomy under General Anaesthesia.*

Materials and Methods: *228 patients, between 18 to 60 years of age, of ASA class-I and class-II were scheduled which was planned for laparoscopic cholecystectomy under general anaesthesia. Patients were selected and were randomly divided into two groups of 110 patients in one group and 118 patients in another group. Where Group I which received Ondansetron 4 mg alone and the other group assigned as Group II which received Ondansetron 4mg with Dexamethasone 8 mg and administered intravenously to both the groups at the time of peritoneum closure. Postoperatively, the patients were assessed for episodes of nausea, vomiting, retching, need for rescue antiemetic and observed for any adverse effects at intervals of 0-4, 4-8, and 8-24 hours of post-operative period.*

Results: *Results were analyzed statistically. We had found the incidence of PONV and retching was 33% in Group-I and 10.17% in Group-II. The need for rescue antiemetic of total patients was 24.5% in Group-I and 8.5% in Group-II during first 24 hours of post operative period.* ***Conclusions:*** *Combination of ondansetron and dexamethasone was more effective than ondansetron alone in preventing post operative nausea vomiting in patients undergoing laparoscopic surgery.*

INTRODUCTION:

Post operative nausea and vomiting is a common and distressing complication of surgery under general anesthesia. The incidence of PONV remains unacceptably high (40-75% in the first 24 hrs) following laparoscopic cholecystectomy. PONV is the second most common complaint reported (pain is the most common) after surgery. Many patients find PONV more troublesome than the post operative pain itself. It results in significant morbidity and longer stays in hospital especially patients in undergoing laparoscopic cholecystectomy. The incidence of PONV ranges from 25-42% in laparoscopic cholecystectomy when antiemetic treatment is not considered prophylactically. PONV not only causes discomfort to the patient but also leads to complications including electrolyte imbalance, regurgitation and aspiration, increased bleeding and wound dehiscence. Persistant retching and vomiting can cause tension in suture line, venous hypertension, bleeding under skin flaps and increased risk of pulmonary aspiration of vomitus.(1) In addition, PONV may increase perioperative costs, increase perioperative morbidity, increase post anaesthesia care unit stays, delay the time can go back to work, and lead to readmissions.

The etiology of PONV is numerous factors involving individual, anesthetic and surgical risk factors rather than surgery itself. Some risk factors such as patient's characteristic, age, female sex, obesity, smoking status, history of PONV or motion sickness or migraine, use of opoids, duration and type of surgical procedure known so far. But elimination of these factors is not always possible. (2)

There are numerous antiemetic drugs having different mechanism of with varying potencies and pharmacokinetic profiles have been tried for control of PONV. The management of nausea and vomiting has improved greatly in recent years with the introduction of 5-hydroxytryptamine (5-HT3) receptor antagonists and currently recommended as the agent of first choice to control PONV in most instances. (3)

AIMS:

(1) To compare the effect on post operative nausea and vomiting (PONV) following administration of ondansetron alone and ondansetron and dexamethasone combination.

(2) To observe any adverse effects and requirement of rescue antiemetic in the post-operative period of the patients.

MATERIALS AND METHODS:

This prospective randomized double blind clinical study was done after taking approval from the ethics committee. Written informed consent was taken from all the 228 American Society of Anesthesiologists (ASA) physical status 1 and 2 patients undergoing laparoscopic surgery. They were then randomly divided into two groups of 110 patients in one group and 118 patients in another group. One group assigned as Group I which received Ondansetron 4 mg alone and other group assigned as Group II which received Ondansetron 4mg with Dexamethasone 8 mg and administered intravenously to the both groups at the time of peritoneum closure.

INCLUSION CRITERIA:

1) Patients with ASA class I and class II.
2) Aged between 18 to 60 years of both sexes.
3) Patients planned for routine laparoscopic cholecystectomy under general Anaesthesia.

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EXCLUSION CRITERIA:
1) Patients with ASA class III and class IV
2) Patients who had taken antiemetic drugs or any drug which can affect the study.
3) Pregnant women, Lactating mother.
4) Known allergy to any study drug.
5) Those who refused consent were excluded from the study.

Methods:
The patients were visited in the wards for pre-anaesthetic check up in the evening before surgery. Detailed history was taken and clinical examination was done. Each patient received tab Alprazolam 0.5mg and Ranitidine 150mg on the night before surgery. Balanced general anaesthesia was administered to the patient on the day of operation. For premedication Inj. Glycopyrolate 0.2 mg was administered i.v 30 minutes prior to induction to each patient. Inj Tramadol 1mg/kg body weight i.v. was given to patient just before induction. After positioning the patient on the OT table, all the vital parameters were recorded and probes of continuous lead II ECG monitor, non-invasive blood pressure cuff and pulse oximetry probe were attached to the patient and an i.v. line was established with a Ringers Lactate drip. Patients were preoxygenated for 3-5 minutes. All the patients were induced with Inj Propofol 1.5-2 mg/kg and the i.v. lines were flushed followed by Inj succinylcholine 1.5mg/kg administered. All patients were ventilated with 100% oxygen. After achieving effective intubating conditions, intubation was done under direct laryngoscopy. Anaesthesia was maintained with 33% oxygen and 66% nitrous oxide, 1% Isoflurane intermittently with intermittent positive pressure ventilation.Neuromuscular blockage was maintained by Inj. Atracurium Besylate 0.5mg/kg with subsequent top up doses. Monitoring of pulse, BP and ECG tracing were recorded just before induction and intraoperatively. The study drug was administered slowly intravenous at the time of closure of peritoneal cavity. Pulse, BP and ECG were recorded throughout the procedure. Duration of surgery and anaesthesia in minutes was noted. At the end of the operation, antagonism of neuromuscular block was done with Inj Neostigmine 0.05mg/kg and Inj. Glycopyrrolate 0.01mg/kg i.v. Oropharyngeal suctioning was done. Extubation was gently carried out following gentle suction when the airway reflex returned. The incidence of PONV was recorded within the first 24 h of post-operative periods at intervals of 0-4, 4-8, and 8-24 hours. Episodes of PONV were identified by spontaneous complaints by the patients or by direct questioning. Rescue antiemetic was provided with inj. ondansetron 4 mg i.v. in case of patients remained nauseous for more than 15 minutes, or experienced retching or vomiting during the study period (0-24 hours).

RESULTS:
DEMOGRAPHIC PARAMETERS-
Demographic data, duration of surgery in our study patients observed were comparable (table I).

TABLE I: Demographic parameters & surgical time.

Parameters	Group I (N=110)	Group II (N= 118)	p Value
Age (years) Mean ± S.D	37.15 ±11.83	37.06 ±10.69	0.906
Weight (kilograms) Mean ± S.D	50.34 ±7.722	50.24 ±8.97	0.625
Sex (Male/ Female)	31(28.2%)/79(71.8%)	27(22.8%)/91(77.1%)	0.451
Duration of Surgery (minutes) (Mean ± S.D)	68.85 ± 12.13	69.58 ± 13.13	0.659
ASA (I/II)	57(51.81%)/53(48.18%)	59(50%)/59(50%)	0.793

INCIDENCE OF RETCHING-
TABLE II: Incidence of retching.

POST OPERATIVE PERIOD (hours)	GROUP I (%) (N=110)	GROUP II (%) (N=118)	p VALUE
0—4	2 (1.82)	2 (1.69)	1
4—8	1 (0.91)	0	0.48
8—24	1 (0.91)	0	0.48

The total incidence of retching among the patients in group-I was 3.63%, and 1.69% in group-II, during 0-24 hours of post-operative period. It was found to be no statistically significant difference in between the groups.

INCIDENCE OF PONV AMONG FEMALE PATIENTS-
Table III: Incidence of PONV among female patients.

POST OPERATIVE PERIOD (hours)	GROUP I (%) (N=79)	GROUP II (%) (N=91)	p VALUE
0—4	5(6.33)	1(1.10)	0.109
4—8	9(11.39)	1(1.10)	0.008*
8—24	8(10.13)	2(3.30)	0.040*

The incidence of PONV in female patients was 27.85% (22) in Group-I and 4.40% (4) in Group-II during 0-24 hours of post-operative period. There were statistically significant differences in 4-8 hours and 8-24 hours (p values 0.008* and 0.040* respectively). We found no significant difference (p value 0.109) in 0-4 hours of post-operative period.

INCIDENCE OF PONV AMONG MALE PATIENTS-
Table IV: Incidence of PONV among male patients.

POST- OPERATIVE PERIOD (hours)	GROUP–I (%) (N=31)	GROUP–II (%) (N=27)	p VALUE
0—4	1 (3.22)	1 (3.71)	1
4—8	2 (6.45)	2 (7.41)	1
8—24	4 (12.90)	2 (7.41)	0.675

The incidence of PONV in male patients was 22.58% (7) in Group-I and 18.52% (4) in Group-II during 0-24 hours of post-operative period. There were no statistically significant differences in o-24-8 hours of post-operative period (p values 1, 1, & 0.675).

PONV and retching was present in 33 of 110 patients in Group I, whereas 12 of 118 patients had PONV and retching in Group II. This is shown in table II and III.

INCIDENCE OF ADVERSE EVENTS IN PATIENTS IN BOTH THE STUDY GROUPS-

Table V: Incidence of adverse events in patients in both the study groups.

ADVERSE EVENTS	GROUP I (%) (N=110)	GROUP II (%) (N=118)
Headache	2(1.8)	3(2.5)
Dizziness	1(0.9)	1(0.8)
Restlessness	1(0.9)	0
ECG changes	0	0

The overall incidences of adverse event were minimal among both the groups. Headache was the most common complaint and was complained by two patients in the group I (1.8%) and three patients in the group II (2.5%). Dizziness was complained by one patient (0.9%) in the group I and one (0.8%) in Group II. Restlessness was complained by one (0.9) patient in group I and no one had restless in Group II. There was, however no incidence of arrhythmia or QT change in ECG in either of the two groups.

DISTRIBUTION OF THE PATIENTS BY GROUPS AND ADMINISTRATION OF RESCUE ANTIEMETIC:

TABLE VI: Distribution of the patients by groups and administration of rescue antiemetic

Rescue antiemetic in postoperative hours	GROUP–I (%) (N=110)	GROUP–II (%) (N=118)	p VALUE
Yes	27(24.5)	10(8.5)	0.001*
No	83(75.5)	108(91.5)	
Total	110(100)	118(100)	

In Group-I, out of the 33patients who had complained of PONV and retching, 27 patients had received rescue with antiemetic (24.5%), whereas 6 patients who had mild nausea and retching did not need rescue with antiemetic. In Group-II, 10 patients (8.5%) who had complained of PONV and retching received rescue with antiemetic whereas 2 patients who had mild nausea and retching did not need rescue with antiemetic. There was significant difference (p=0.001) in rescue with antiemetic in between the two Groups.

DISCUSSION:

Post operative nausea and vomiting defined as nausea or vomiting occurring within 24 hours after surgery, affects around 20% - 30% of patients but it can even increase upto 80% of patients at high risk. (4) The etiology of PONV is thought to be multifactorial (2) after abdominal surgeries under General Anaesthesia. The age of the patients, type of surgery, anaesthetic procedures, duration of surgery, smoking habit are some of them. In laparoscopic cholecystectomy, PONV may be associated with stretching of peritoneum due to CO2 pneumoperitoneum and the gallbladder surgery itself.

A varied number of interventional methods have been studied for the prevention of nausea and vomiting. Non pharmacological methods include: acupuncture, transcutaneous electrical nerve stimulation, electropuncture and acupressure. Pharmacological methods include: Dopamine receptor antagonist (Phenothiazine, Butrephenone), Histamine receptor antagonist (Dimenhydrinate), Muscarinic receptor antagonists (Scopolamine) and Serotonin receptor antagonist (ondansetron, ramosetron, palanosetron etc). Many drugs like Propofol, Clonidine, Dexamethasone and Ephedrine have also been tried for PONV. Above drugs are effective in reducing PONV with varied efficacy and are associated with unwanted side effects.

In 1990, Introduction of 5-HT3 receptor antagonist was regarded as the major advancement in prophylaxis of PONV, as they lack the major adverse effects, which was seen to occur with traditionally used antiemetic drugs.

In 1980, role of steroids as antiemetic was established and dexamethasone was first introduced in 1981, as an antiemetic agent in patients receiving cancer chemotherapy.

In our study, the incidence of PONV and retching in the Group-I was 30% (33) patients in both sexes, i.e. 21.81% in female and 8.19% in males, in 0-24 hours of post-operative period. In Group-II, the incidence was 10.17% (12) patients in both sexes, i.e. 5.08% in females and 5.08% in males, in 0-24 hours of post-operative period.

We had also found that the incidence of post operative nausea was 4.55% in both sexes in Group-I, i.e. 3.64% in female patients and 0.91% in male patients. In Group-II, the incidence of nausea was 3.39%, i.e. 2.54% in females and 0.85% in males, in 0-24 hours of post operative period. In both the groups, we had found that the incidence of nausea was lesser in males as compared to females, in between 0-24 hours of post-operative period.

Similarly, we had found that the incidence of post operative vomiting was 26.4% in Group-I, i.e. 19.8% in female patients 6.6% in male patients. In Group-II, the incidence of vomiting was 7.08%, i.e. 3.54% in female patients and 3.54% in male patients, in between the 0-24 hours of post-operative period. We have also found that in Group-I, the incidence of vomiting was more than Group-II where the incidence of vomiting was higher in females in compared to the male patients.

There are few studies which were comparable to our study patients undergoing laparoscopic cholecystectomy under general anaesthesia in between 0-24 hours of post-operative period, conducted by Gautam B et (5) al (2008), A.SHORA et al (6) (2007), Basant Bhattarai et al (7) (2011), Nisar Ahmed et al (8) (2012), L. Sanjowal and collegue (9) (2014)

In our study, Ondansetron 4 mg was used as rescue antiemetic in both the groups. If patients remained nauseous for more than 15 minutes, or experienced retching or vomiting during the study period (0-24 hours), then we had given the rescue antiemetic. We found that the incidence of PONV and retching was 30% (33) cases in Group-I, of which (24.5%) 27 cases needed rescue antiemetic. In Group-II, incidence of PONV was 10.1% (12) cases of which 8.5% (10) patients needed rescue antiemetic drug. The need for rescue antiemetic is more in Group I (24.5%) than in Group II (8.5%), which is comparable to a study conducted by Basant Bhattarai et al. (7)

CONCLUSIONS:

In our study, we compared the effect on post operative nausea and vomiting (PONV) following administration of ondansetron (4mg) alone and ondansetron (4mg) with dexamethasone (8mg) combination, in those patients undergone laparoscopic cholecystectomy and concluded as follows: The occurrence of PONV was lower in combination Group II, than Group I. The need for rescue antiemetic was lower in the combination group. We found minimal incidence of adverse events in both the groups. Hence, the efficacy of combination therapy was found to be superior

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to ondansetron alone. The incidence of PONV was higher in female patients compared to male patients in both the groups.

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