

Comparative Study of Single Dose Intravenous Ondansetron and Metoclopramide as a Premedication for Prevention of Post Operative Nausea and Vomiting in Obstetrical Laparoscopic Surgery under General Anaesthesia

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Citation

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Abstract

Post Operative Nausea Vomiting (PONV) is the most unpleasant and distressing consequence in the immediate post-operative period especially after general anesthesia. PONV can delay discharge and may result in unplanned over night hospital admissions.

This is prospective randomized control study of 60 ASA grade I/II patients recruited at Seth G.S. Medical College to find out the efficacy, duration of action, haemodynamic stability, side effects of ondansetron and metoclopramide lower the incidence of PONV in 24 hr of post operative period. The study was undertaken with an aim to investigate 1) The nausea and vomiting in immediate post operative period. 2) Efficacy of single dose I.V. injection of ondansetron (4mg) and metoclopramide on PONV and 3) Side effects of these drugs.

Early antiemetic efficacy abolition of vomiting after 1, 4, 12 hrs was 3.66, 10 and 3.33% respectively from the administration of the study drugs with no further vomiting or nausea episodes after 24 hrs was in the ondansetron group. Similarly, abolition of vomiting after 1, 4, 12 and 24 hrs was 20, 20, 16.66 and 3.33 % respectively in the metoclopramide group compared to the placebo group ($P < 0.001$). This difference was still significant when controlling for age, body weight, history of motion sickness, previous PONV episodes, duration of anesthesia, and intraoperative fentanyl consumption using a logistic model. Therefore the overall results indicated that ondansetron is more effective than metoclopramide for the prevention of PONV.

INTRODUCTION

Pain is not always the patients prime concern in the post operative period, many patients will take nausea and vomiting as the most unpleasant consequence. The number of drugs introduced for the relief of post operative pain have been largely successful but the same cannot be applicable for PONV (Post-operative Nausea and Vomiting).

PONV is associated with general anaesthesia (GA) ever since the ether and chloroform era and the reported incidence were reported to be 75-80%. It still remains a problem, despite an evident clinical perception that its severity has diminished with an estimated incidence of 20-50%. PONV has consequence more far reaching than hitherto appreciated. It affects the patients in more ways than

one and they may be stated as physical, metabolic, psychological and economic.

There are a number of factors influencing the occurrence of PONV which includes Patient factors (Age, gender, obesity, anxiety, history of motion sickness or previous post and vomiting, gastro paresis); Operative procedures; Anesthetic techniques (Drugs for general anesthesia, regional anesthesia and monitored anesthesia care) and Post-operative factors (Pain, dizziness, ambulation, oral in-take, opioids)

Laparoscopic surgery is the one condition, where risk of PONV is particularly pronounced. This technique first gained popularity with its use in gynecologic procedures that began in 1970. The patient group in this study was

predominantly young. Early ambulation and decreased morbidity due to this technique rendered it increasingly popular. This increases the risk of PONV, which is due to pneumo-peritoneum-causing stimulation of mechanoreceptors in the gut. To reduce the incidence of PONV various pharmacological and non-pharmacological methods have been employed since the advent of anaesthesia. Ondansetron is a specific 5 – HT₃ subtype receptor antagonist and represents a major improvement in chemotherapy and radiation therapy induced nausea and vomiting.

Metoclopramide is a dopamine antagonist acting on the CTZ. It is a gastrointestinal tract (GIT) prokinetic drug. It increases lower esophageal sphincter tone and stimulates motility of the upper GIT. This study endeavors to compare the efficacy of ondansetron and metoclopramide in prevention of PONV when given as a single dose of intravenous (i.v.) premedication in obstetrical laparoscopic surgery under GA. The incidence of side-effects was also noted.

MATERIALS AND METHODS

Following approval from Ethics Committee the present study was conducted with ASA physical status I or II total of 60 patients randomized into two groups, in the age group of 18-65 years, during Jan 2007 to June 2007.

TYPE OF STUDY

PROSPECTIVE, RANDOMIZED STUDY

Randomization provides homogenous groups with respect to pretreatment risk factors.

INCLUSION CRITERIA

- Patients in the age group of 18 years to 65 years.
- Patients belonging to ASA grade I or grade II.
- All patients were posted for Laparoscopic surgery

EXCLUSION CRITERIA

- Patients suffering from severe medical illness classifying them as ASA grade III and IV patients.
- Previous history of drug reaction to any of the drugs used in this study.
- History of PONV.

- History of motion sickness.
- Patients who have received anti-emetics in the previous 24 hours

Preoperative assessment was done

Routine investigations were noted

On the day of surgery the patient was examined, vitals noted. Starvation, consent checked premedication given. An IV line was established in all patients.

GROUPS

- Group 1 – Patients Inj. Ondansetron 4mg as a single dose was given by slow i.v. injection without dilution over a period of 5 min, 10min prior to induction of GA.
- Group 2 – Patients Inj. Metoclopramide as a single dose was given 10 mg by slow i.v. injection without dilution over 5 min, 10 min prior to induction of general anaesthesia.

All patients were pre-oxygenated with 100% oxygen for 3 minutes. Injection Midazolam 0.03 mg/kg and pentazocine 0.3 mg/kg injections were used as a premedication. Standard GA was given using thiopentone sodium (4-6 mg/kg) and suxamethonium (2mg/ kg) injection and patients were intubated with Portex cuffed endotracheal tube. Anaesthesia was maintained with N₂O: O₂ in the ratio of 60: 40 and atracurium 0.5mg/kg and patients were reversed with neostigmine 0.05mg/kg Atropine (0.01mg/kg) injections. Intra-operatively vitals were monitored. Fluid was replaced as per requirements. Post-operatively, patients were interviewed for any nausea, retching or vomiting in immediate postoperative period, after 1, 4, 12 and 24 hrs post surgery.

Nausea was assessed subjectively by using intensity score

0 (No nausea); 1 (Mild nausea); 2 (Moderate nausea) and 3 (Severe nausea). Vomiting was assessed subjectively by recording the number of bouts of vomiting and any medication used. Side effects such as giddiness, headache, flushing, sensation of warmth, diarrhea were noted.

EFFICACY ASSESSMENT

The primary efficacy variable in both groups was the

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number of emetic episodes. An emetic episode was defined as a single vomit / or retch or combination of vomiting and / or retch occurring within minute of each other. Complete response of the drug was defined as no emetic episode. Major response was defined as one emetic episode and treatment failure as two or more emetic episode or the receipt of rescue antiemetic. The secondary efficacy variable was nausea, which was graded by intensity score as 0– no nausea to 3– severe nausea. Results were observed and analyzed statistically.

RESULTS

As per demographic data mean age was 38.3 years in ondansetron and 38.5 years in metoclopramide group in our study. Mean weight was 38.8 kgs in ondansetron and 38.5 kgs in metoclopramide group. The maximum cases posted for obstetrical laparoscopic surgery in our study was diagnostic scopy for primary infertility and tubal ligations. The results indicated that both ondansetron and metoclopramide are effective in controlling the incidence of nausea in 1 hours, 4 hours and 12 hours. But ondansetron is more effective than metoclopramide for control of nausea, by applying chi-square test $P < 0.05$, which is statistically significant (Table 1). Our results also further indicated that ondansetron is more effective in controlling the incidence of vomiting by applying chi-square test ($P < 0.005$) which is highly significant (Table 2). Ondansetron significantly reduce the incidence of vomiting in first 24 hours of post-operative period. The chi-square test shows that $P < 0.001$ value is highly significant (Table 3). In the ondansetron group, 2 patients complained of headache, no treatment failures and, no rescue medication was required by any of them. In metoclopramide group, two patients complained of giddiness (6%) and one drowsiness (3%) respectively (Table 4).

Figure 1

Table 1: Comparison of episode of nausea between ondansetron and metoclopramide group

Time	Ondansetron	Metoclopramide
After 1 hr.	4 (13.33%)	7 (23.33%)
After 4 hrs.	4 (13.33%)	8 (26.66%)
After 12 hrs.	2 (6.66%)	4 (13.33%)
After 24 hrs.	0	0

χ^2 test = 5.4; P value < 0.05 (significant).

Figure 2

Table 2: Comparison of episodes of vomiting between ondansetron and metoclopramide groups

Time	Ondansetron	Metoclopramide
After 1 hr.	2 (3.66%)	6 (20%)
After 4 hrs.	3 (10.00%)	6 (20%)
After 12 hrs.	1 (3.33%)	5 (16.66%)
After 24 hrs.	0	1 (3.33%)

χ^2 value = 8.4; P value < 0.005 (highly significant).

Figure 3

Table 3: No of episodes of vomiting in 24 hours

	Ondansetron	Metoclopramide
Number of vomiting episodes	4 (13.33%)	12 (40%)
Absence of vomiting	26 (86.66%)	18 (60%)

χ^2 value = 13.98; P value < 0.001 (highly significant).

Figure 4

Table 4: Side effects with ondansetron and metoclopramide

Side Effects	Ondansetron	Metoclopramide
Headache	2	0
Drowsiness	0	1
Giddiness	0	2

DISCUSSION

The incidence of PONV is vary high in women undergoing general anaesthesia for laparoscopic obstetrical surgeries. In our study, the mean ages were 38.88 and 38.55 years and, mean weights were 38.8 and 38.5 kgs respectively.

Paxton et al have observed in their study that nausea occurred in 25 % of patients who received ondansetron as compared to 59% of patients with metoclopramide. The visual analogue scores were significantly lower ($P < 0.01$) in ondansetron group at 1, 2 and 4 hrs as compared to metoclopramide. The number of patients with no PONV in first 6 hours after operation was 87% in ondansetron group and 60% in metoclopramide ($P < 0.001$) group. In first 24 hrs study patients with no PONV were 82% in ondansetron group and 47% in metoclopramide group ($P < 0.001$). In those patients with previous history of PONV the severity of nausea was less in ondansetron group then metoclopramide ($P < 0.05$). Malins et al have observed 59% nausea in the

ondansetron group and 63% in metoclopramide group₁.

In our study there was 23.33% incidence of nausea in ondansetron group and 53.33% incidence of nausea in metoclopramide group. The visual analogue scores were significantly lower ($P < 0.05$) in ondansetron group at 1, 2 and 4 hrs as compared to metoclopramide.

Paxton et al observed 6 % patients vomited in ondansetron group as compared to 12% in metoclopramide group₄, postoperatively in 24 hrs the percentage of emesis free patients were 65.5% in the ondansetron group than 29.2% in metoclopramide group₃. Naguile et al has observed prophylactic anti-emetic treatment with ondansetron resulted in a lower incidence of PONV than metoclopramide ($P < 0.02$)₃.

In our study 13.33% incidence of vomiting was their in ondansetron group as compared to 40% in the metoclopramide ($P < 0.01$). McRay P and Yip R reported that drugs involved in most randomized controlled trials were ondansetron - 131 than metoclopramide – 67. Although some anti-emetic drugs for PONV have been studied in large numbers of randomized controlled trials many have not been adequately evaluated₂. Raphael et al has observed headache in two patients in ondansetron group, urticaria and flush in one, in metoclopramide group four patients reported headache, two complained of dizziness and 2 were noted to be restless₅. Malins et al observed no significant adverse effects in both groups₁.

In our study two patients complained of headache in the ondansetron group and in metoclopramide group one patient complained of drowsiness and two giddiness respectively.

Paxton et al observed number of patients requiring rescue medication was lowest in the ondansetron group (28%) as compared to 41% in metoclopramide group₃. Naguile et al observed that rescue anti-emetic was first received were longer in the Ondansetron group than metoclopramide group ($P < 0.01$)₄.

Polati et al have recruited one hundred seventy-five patients with PONV during recovery from anesthesia for gynecological laparoscopy were treated intravenously with either ondansetron 4 mg (58 patients), metoclopramide 10

mg (57 patients), or placebo (60 patients). The results indicated that early antiemetic efficacy (abolition of vomiting within 10 min and of nausea within 30 min from the administration of the study drugs with no further vomiting or nausea episodes during the first hour was reported as 93.1% in the ondansetron group, in 66.7% in the metoclopramide group, 35% in the placebo group, suggesting ondansetron 4 mg is more effective than metoclopramide 10 mg and placebo in the treatment of established PONVs₆.

In our study no patients needed rescue medications in both the groups. It is thus clear that ondansetron as compared to metoclopramide is a safe and strong antiemetic drug which can be used effectively in the treatment of PONV.

CONCLUSION

The development of 5-HT₃ antagonist drugs, of which ondansetron is the most widely used, offers a novel and possible more effective approach to control post-operative nausea and vomiting as compared to benzamide metoclopramide.

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