

The Effect of Timing of Ondansetron Administration in Prevention of Postoperative Nausea and Vomiting in Patient Operated Under General Anaesthesia

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ABSTRACT

Introduction: Prevention of postoperative nausea and vomiting (PONV) is always the centre of attention in postoperative patients as it causes unnecessary discomfort to the patient, increases the cost and other consequences. Many antiemetic drugs are used for prevention as well as for treatment. 5 HT₃ receptor antagonist ondansetron is widely used for this purpose but its timing of administration is controversial. So this study was designed to find out whether it is effective when given before or after surgery.

Material and methods: Total 200 patients of both genders who underwent different surgeries under general anaesthesia were included and randomly allotted into two groups. In GROUP I patients were given injections ondansetron 4mg intravenous just before the induction and in GROUP II patients it was given after surgery when anaesthetic gases were turned off.

Results: The incidence of nausea in both the group was 14%. The incidence of vomiting in GROUP I was 2% and in GROUP II was 6%.

Conclusion: There was no significant difference in incidence of PONV between two groups. Injection ondansetron can be given either preoperatively or postoperatively when duration of surgery is less than two hours.

Keywords: Postoperative Nausea and Vomiting, ondansetron, antiemetic

INTRODUCTION

Years have gone by, but postoperative nausea and vomiting (PONV) remains one of the most common post-operative complaints of anaesthesia.¹ Still, the incidence of PONV is 30%.¹⁻⁵ The risk of PONV increases further to 60-70% in the presence of high risk factors.^{2,6,7} There are some consistent predictive risk factors associated with PONV- Female patients, non-smokers, history of PONV and postoperative use of opioids.^{1,8} Studies have shown there are few surgeries that increase the incidence like middle ear surgeries, strabismus correction, gynaecological laparoscopic surgeries but large prospective trials that used multivariable analysis to identify PONV risk factors found no such associations.⁹ PONV demands attention as it leads to unnecessary discomfort to post-operative patients, increases hospital stay, delays discharge from hospital leading to increase cost. Other consequences are suture dehiscence, aspiration pneumonia, dehydration, electrolyte imbalances, and oesophageal rupture.¹⁰ Prevention and treatment of PONV help to decrease psychological distress, and improve recovery time.¹¹⁻¹³ Many authors have stated that avoiding PONV is important to patients more than avoiding postoperative pain. There are many drugs available that have been used to minimise the incidence but no antiemetic can abolish the incidence totally. In fact only 20-30% of patients will respond to any

currently available antiemetic.⁹ Among all the antiemetic, 5HT₃ receptor antagonist have been researched extensively for PONV treatment and confirmed effective with minimal side effects.¹⁴ One of the drugs belonging to this category is ondansetron. It came into clinical practice in 1991.¹⁵ It is highly effective antiemetic and used both for treatment and prophylaxis.¹⁶⁻²² But the timing of administration of this drug is still not well established. As it is known that it has half-life of about 3-4 hours and the controversies remain whether to administer this drug preoperatively or postoperatively to prevent PONV. So this comparative study was designed to know the better time of administration of this drug to prevent PONV and to improve patient satisfaction.

MATERIALS AND METHODS:

This study was conducted in Central Referral Hospital, Gangtok, Sikkim in the department of Anaesthesiology from April 2015 to May 2016. Total 200 patients belonging to ASA physical status grade I and II, aged between 18 to 65 years posted for different surgeries under General Anaesthesia were selected. They were randomly allocated into two groups. Patients belonging to ASA GRADE III and IV, pregnant or menstruating women, patients with history of motion sickness and previous PONV, patients who had received antiemetic drug within 24 hours before surgery, history of smoking and chronic cough were not included in the study. Group I patients received injection ondansetron 4 mg iv during induction and Group II received injection ondansetron 4 mg iv after surgery when anaesthetic gases were switched off. Patient was followed up for PONV for 24 hours. Also numbers of rescue antiemetic used were noted. Results were compiled under each group of drug and analysed finally.

Permission of hospital ethical committee was obtained before proceeding on the study.

The patients were explained the concept and procedure of this study and their consents were taken.

Standardised anaesthetic technique was employed for all the patients after recording vitals like pulse, blood pressure, SPO₂ and a good intravenous access was established. Patient was

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administered injection glycopyrrolate 0.2 mg iv and 1 ug/kg fentanyl as premedication. Patient was induced with sodium thiopentone 4-5 mg/kg followed by 1.0 mg/kg succinylcholine or 0.1mg/kg of vecuronium and was intubated. Anaesthesia was maintained with injection vecuronium 0.01mg /kg, isoflurane 1-2% in combination with 50-60% N₂O with oxygen. Intravenous fluid crystalloids were used. After completion of the surgery, residual neuromuscular blockade was reversed with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01mg/kg). All patients were extubated in the operating room. Duration of anaesthesia and surgery were recorded. Anaesthesia time was noted from induction of anaesthesia to discontinuation of anaesthetic gases, operating time was noted from surgical incision to skin closure. Patients were observed in the recovery room until they were hemodynamically stable, fully conscious and comfortable for an average of two hours. Both nausea and vomiting were assessed by questioning the patient and also observing the need for rescue treatment. Nausea sensation was described by patient not by the doctor. Nausea was defined as a feeling of sickness with an inclination of an impending desire to vomit. Vomiting was defined as the forceful ejection of gastric contents from the mouth.

STATISTICAL ANALYSIS

Data are presented as number and percentages. The statistical analysis was done using SPSS version 20. Analysis of data was done by Chi square test and ANOVA (Analysis of variance). A 'P' value of less than 0.05 was considered statistically significant.

RESULTS

Total number of patients included in the present study was 200 and were divided randomly into two groups. Each group contained 100 patients.

No significant difference was found among two groups regarding age, weight, ASA physical status (Table-1). There were total 64

females in group I out of 100 patients and 76 females in group II out of 100 patients and no significant difference was found (P=0.06).

There was no significant difference between type of surgeries among two groups (P=0.42). There were 59 cases of laparoscopic cholecystectomy in group I and 71 cases in group II. Rest were other surgeries.

Duration of anaesthesia in Group I was 99.50 ±54.97 minutes and in group II was 100.22±62.18minutes and there was no significant difference between two groups (P=0.93). Duration of surgeries in group I was 83.34±52.44minutes and in Group II was 83.34±58.9 minutes with no significant difference.

Incidence of Nausea in Group I was seen in 14 (14%) patients and all of them had only one episode of nausea. In Group II 12 (12%) patients had one episode of nausea and 2 patients had two episodes of nausea. Statistically this difference was not significant (P= 0.253).

Incidence of vomiting in Group I was seen in 2 (2%) patients, of which one patient experienced vomiting once and one patient experienced it twice. Whereas in Group II total 6 (6%) patients suffered from vomiting, among it 5 patients suffered only one episode of vomiting and one patient suffered twice. No significant difference was seen between two groups.

Onset of nausea in group I was seen at 2hours in two patients, at 4 hours in seven patients, at 6 hours in three patients and at 8 hours in one patient and at 14 hours in one patient. In group II nausea seen at 2 hours in six patients, at 4 hours in six patients, at 6 hours in three patients and at 10 hours in one patient.

Onset of vomiting in Group I was seen at 2 hours in one patient, at 4 hours in one patient, at 6 hour in one patient. In Group II onset of vomiting was seen at 2 hour in two patients, at 4 hour in four patients and at 6 hour in one patient.

Rescue antiemetic one time was required by three patients in each group. Two times was required by one patient in Group I only.

DISCUSSION

Postoperative nausea and vomiting (PONV) is defined as "any nausea, retching, or vomiting occurring during the first 24–48 hours after surgery in patients".⁹ This unwanted complaint is always feared and needs to be prevented. The most important step is to use antiemetic drug prophylactically. The question always arise which antiemetic to use among all the available antiemetic drugs. Singhal and colleagues²³ performed a meta-analysis in efforts to compare the efficacy of 5HT₃ antagonists against all non-5HT₃ antagonism for PONV in women undergoing breast surgery. 5HT₃ antagonists were found superior to other

Variables	Group I	Group II	P Value
Age (Years) Mean±SD	39.41±11.39	36.53±11.19	0.073
Sex			
M	36	24	0.064
F	64	76	
Weight (KG) Mean±SD	62.02±11.71	62.60±10.55	0.713
ASA			
I	62	71	0.178
II	38	29	

Table-1: Demographic data of patients

Variables	Group I	Group II	P Value
Duration of surgeries (Minutes) Mean ± SD	83.43±52.24	84.98±57.81	0.842
Duration of anaesthesia (Minutes) Mean± SD	99.50±54.97	100.22±62.18	0.931

Table-2: Duration of surgeries and anaesthesia

	Total incidence of nausea	Incidence of nausea one time	Incidence of nausea two times	P value	Total incidence of vomiting	Incidence of vomiting one time	Incidence of vomiting two times	P value
Group I	14(14%)	14	0	0.341	2(2%)	1	1	0.253
Group II	14(14%)	12	2		6(6%)	5	1	

Table-3: Incidence of nausea and vomiting

	Total anti-emetic rescue	Antiemetic rescue once	Antiemetic rescue more than once
Group I	4	3	1
Group II	3	3	0

Table-4: Antiemetic rescue

pharmacological interventions for the prevention of PONV in patients undergoing breast surgery under general anaesthesia.²³ In the present study, Ondansetron was used as this drug is used in our hospital routinely for prevention of PONV. The dose of 4mg intravenously was used based on the dose used in previous studies and found effective in reducing PONV.^{24,25} After drugs and dosage the most controversial question all anaesthetist deal with is when to administer, whether pre or post operatively. The literatures fail to confirm about the exact timing of its administration which will prove effective in reducing PONV. Four RCTS (randomized control trials) assessed the efficacy and timing of 5-HT₃ antagonist administration in preventing PONV.^{10,25-27} Three trials^{10,25,27} of four RCTs (randomized control trials) assessing 5-HT₃ antagonists demonstrated a significant improvement in PONV in the treatment group compared to placebo. In one trial¹⁰, the 5-HT₃ antagonist was given at the end of surgery, while in the other two trials^{25,27} it was given at induction and no significant differences were found. So this comparative study was chosen to find the time of its administration which will be effective in reducing the incidence of PONV. In the present study in Group I Ondansetron was administered just before the induction drugs were given on the OT table and in group II it was administered when the anaesthetic gases were turned off but before administering the reversal.

In present study the incidence of nausea in Group I and Group II was 14 % and incidence of vomiting in Group I was 2% and in group II 6% which does not show significant difference. The similar study done by Sabah Noori et al²⁸ where they used 4mg ondansetron either preoperatively or post operatively. The incidence of nausea was 12% in pre-operative group and 4% in post-operative group, the incidence of vomiting was 28% in pre-operative group and 32% in post-operative group. They also did not find any significant difference between two groups. It differs from our study in term of the selection of only female patients who underwent laparoscopic cholecystectomy, and use of injection tramadol for pain relief which is considered emetogenic.

The study done by Jun Tang et al²⁹ on 164 female patient who underwent gynaecological laparoscopic surgery to find out the effective timing for administration of ondansetron drug. They found drug was effective in reducing the incidence of PONV when given immediately before the end of surgery.

Another study done by Rui sun et al²⁶ on 75 patients operated for otolaryngologic surgery found no significant differences in incidence of nausea and vomiting when injection 4mg Ondansetron was administered pre and post operatively and was compared with placebo group. The incidence of nausea was 80 %, 68%, 60% in Group I(placebo), II(pre operatively), III (post operatively) respectively and the incidence of vomiting was 12%, 20%, and 4% in Group I,II,III respectively. The important finding was that there was significant reduction in the dose of

rescue antiemetic when injection Ondansetron was administered at the end of surgery. In our study in both the group 3% patient required rescue anti emetic once and only one patient in group I required anti emetic twice.

The study by Norma I. Cruz³⁰ on patients posted for different plastic surgeries concluded that injection Ondansetron 4 mg when given at the end of surgery helps in preventing late PONV. The overall incidence of PONV in control Group which received injection ondansetron just prior to induction was 62% and in the study group which received injection Ondansetron 30 minutes prior to completion of surgery was 38%. The incidence of late nausea and vomiting was 30%, 20% and 17%, 8% in control and study group respectively. In present study no such difference was found. This could be because of the average duration of surgery in present study was less than 2 hours but in the study done by them average duration of surgery was more than two hours.

The study conducted by Wu-Yong –Yu³¹ on 120 patients on laparoscopic cholecystectomy found that late administration of injection Ondansetron was effective in preventing nausea and vomiting. The incidence of PONV in preoperative group which received injection Ondansetron 8 mg, 30 minutes prior to induction was 27.5% and in Post-operative group was 10%. In comparison to above studies, our study included both genders and even the types of surgeries were mixed. However, large prospective trials that used multivariable analysis to identify PONV risk factors found no such associations regarding the type of surgeries. In general, the type of surgery cannot provide reliable, reproducible, and clinically relevant information for assessing the patient's risk of PONV in adult patients.⁹ So, the results could vary from other studies. We avoided the use of propofol, midazolam, dexamethasone, any postoperative opioids, tramadol which could affect the incidence of PONV either by increasing or decreasing the incidence.

Limitations of our study was that the ratio of genders was not equal, which can lead to bias and it's a retrospective study.

CONCLUSION

Our study could not prove any statistical difference in the outcome of incidence of PONV between two groups. Thus it can be concluded that whether injection ondansetron is administered before or after surgery, incidence of PONV does not change significantly when the duration of surgery is less than two hours. Even there was no difference in incidence of rescue antiemetic drug. Also different types of surgeries do not affect the incidence of PONV.

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