A COMPARATIVE STUDY OF ONDANSETRON VERSUS METOCLOPRAMIDE IN THE PREVENTION OF POST-OPERATIVE VOMITING IN ROUTINE MAJOR GYNECOLOGICAL SURGERY UNDER GENERAL ANESTHESIA

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ABSTRACT

This is a comparative study of ondansetron versus metoclopramide in the prevention of post-operative vomiting in routine major gynecological surgery under general anesthesia. The purpose of this study was to perform a comparative study of injection ondansetron 8 mg I.V. with injection metoclopramide 10 mg I.V. in preventing post-operative vomiting. This was a randomized, double blinded study conducted in sixty patients of American Society of Anaesthesiologist (ASA) I and ASA II undergoing routine major gynecological surgery (Transabdominal Hysterectomy, laprotomy and cystectomy, tubal surgery) under general anesthesia. Either of the drug was diluted to 5 ml of normal saline and given intravenously prior to induction of anesthesia. The post-operative period of first 24 hours was divided into two phases, the early (0-6 hrs.) and late (6-24 hrs.). The frequencies of vomiting and requirement of rescue antiemetics in both groups were studied. The general characteristics of the patients in the two groups were similar. In both groups, induction, maintenance, duration of anesthesia as well as the type of surgery and opioids requirement were similar. The data recorded were statistically analyzed using Chi-square test and t-test. The frequency of vomiting was less in ondansetron group compared to metoclopramide group. Rescue antiemetics was given only once in ondansetron group patients, whereas the need of rescue antiemetics was eight times in the metoclopramide group. The difference was statistically significant ($p=0.03$). No unwanted effects were noticed in both groups. Ondansetron seems more effective in preventing Post-Operative Nausea & Vomiting (PONV) than metoclopramide but it has to be evaluated further by more clinical trials and tests in larger series.

Key Words: *Antiemetics, vomiting, general anesthesia, gynaecological surgery.*

INTRODUCTION

Post-operative Nausea and vomiting (PONV) are common and distressing side effects after anesthesia and surgery, more so in gynecological surgery.¹ Severe PONV may be associated with delayed wound healing, pulmonary aspirations of gastric contents, dehydration, electrolyte imbalance and prolong stay in the post anesthesia care unit. This increases use of resources including medical as well as nursing care. Still these days this problem is under treated in our hospitals. The incidence of PONV was about 75% – 80 % during “ether” era and now it has been reported to be 20-30%.^{1,2} The etiology of PONV is

multifactorial. It may have: Patient related factors (age, gender, body weight, history of PONV, motion sickness, gastroparesis), Surgery related factors (type and duration of surgery), Anesthesia related factors (premedication drugs, anesthetic techniques, duration of anesthesia, type and doses of anesthetic drugs) and Post-operative related factors (pain, hypotension, opioids).³ The increased incidence of vomiting with the balanced anesthetic technique has been regarded as due to the use of an opioid-nitrous oxide combination.^{3,6} Residual effect of the relaxant is reversed with acetylcholinesterase inhibiting drugs. The muscarinic effects of these drugs increase gastrointestinal motility, which may cause PONV.^{4,7} The major

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neurotransmitter systems play important roles in mediating the emetic response are Dopaminergic, Histaminic, Cholinergic muscarinic and 5 Hydroxy Tryptamine 3 (5HT3).

Metoclopramide is a popular drug for controlling PONV. Its effect is mediated by antagonism of central dopaminergic receptors.

Ondansetron: Serotonin receptor antagonists (5-HT₃ antagonists) are the newly discovered antiemetics. Ondansetron is the first drug of this class to be used for clinical use in 1991. This drug was first used to prevent nausea and vomiting induced by chemotherapy and radiation therapy. This drug has been found to be much effective in preventing PONV.^{8,9}

AIM OF STUDY

1. To compare incidence of postoperative vomiting in patients undergoing routine major gynaecological surgery under general anaesthesia in two study groups.
2. To compare the need of additional rescue antiemetic in postoperative period in two groups.

METHODOLOGY

Sixty patients of age group 20-65 years of ASA I or ASA II class undergoing major gynecological surgery under general anesthesia were enrolled in the study. . Patients scheduled for the surgery received 5mg of diazepam orally night before surgery and in the morning. Patients were randomly classified to get injection ondansetron 8 mg or injection metoclopramide 10 mg. There were 30 patients in each study group. The anonymous syringe containing either the ondansetron 8 mg or the metoclopramide 10 mg diluted to 5 ml of normal saline, was prepared by the person blinded to the study. The drug was administered intravenously just before the induction of anesthesia by the anesthetist who was blinded to the nature of the drug in the syringe. Patient was induced with inj. Sodium thiopentone (5 mg/kg). Laryngoscopy and intubation was facilitated with inj. Suxamethonium chloride (2 mg/kg) .For analgesia inj. Pethidine (0.8 mg/kg) was used. Anesthesia was maintained with oxygen (33%), nitrous oxide (66%) and halothane. Muscle relaxation was achieved with inj. Pancuronium bromide (0.05mg/kg). At the end of surgery the effect of muscle relaxant was tested using PNS and reversed with injection neostigmine

(0.05 mg/kg) and injection atropine (0.02 mg/kg). For postoperative pain relief patients were given injection Diclofenac I.M. and injection Pethidine (1 mg/kg) IM. Total amounts of Diclofenac and Opioids received by each patient were recorded. The postoperative period was divided into early (1st 6 hours) and late (6-24 hrs.) postoperative period. In post operative ward, if vomiting occurred for more than two times, such patients were treated with rescue antiemetic injection metoclopramide 10 mg I.M. Vomiting episodes and rescue antiemetics were recorded. The data collected were subjected for statistical analysis applying chi – square and t-test.

Exclusion Criteria: Patients who were receiving antiemetics preoperatively i.e. 24 hrs. before the study began, Lactating women, febrile patients and patients of ASA III and IV.

RESULTS

Early postoperative period: $\chi^2=2.78$ and $p=0.10$, late postoperative period: $\chi^2 = 2.09$, $p=0.15$

For the whole post operative period: $\chi^2 =7.50$, $p=0.006$

In the post operative period, the metoclopramide group patients were rescued with antiemetics more frequently than the patients in ondansetron group. With respect to antiemetic requirements in two study groups, the difference was statistically significant ($p = 0.03$).

Fig. 1 : Incidence of vomiting in Ondansetron and metoclopramide group in early and late post-operative periods.

Table I : The incidence of vomiting in two study-groups in early (1-6 hrs.) and late post operative period (6 – 24 hrs.).

		Ondansetron group	Metoclopramide group	Total
Time of first vomiting (hrs)	0-6	3	8	11
	6-24	2	7	9
	Total	5	15	20

Table II : Rescue antiemetic in post-operative period in two study-groups

Rescue antiemetic	Ondansetron group No. of patients	Metoclopramide group No. of patients
Yes	1	8
No	29	22
Total	30	30

$\chi^2=4.71$ (Yates), $p=0.03$

Table III : Average Pethidine received by two study-groups (intra-operative & post-operative)

Ondansetron group, mg	Metoclopramide group, mg
78.57 ± 32.67	79.7 ± 37.5

$t=-0.125$, $p=0.90$

Table IV : Average Diclofenac received by two study-groups post operatively

Ondansetron group, mg	Metoclopramide group, mg
128 ± 36.98	129.31 ± 34.11

$t=-0.105$, $p=0.92$

Table V : Chart showing number of patients having different frequencies of vomiting in two study groups in different types of surgery

Type of surgery	Frequency of vomiting Ondansetron Group						Frequency of Vomiting Metoclopramide Group						P-Value
	0	1	2	3	4	Total	0	1	2	3	4	Total	
TAH	24	4	1	0	0	29	11	5	7	1	0	24	0.0046
Laprotomy and Cystectomy	1	0	0	0	0	1	4	1	0	0	0	5	1.0
Tubal Surgery	0	0	0	0	0	0	0	1	0	0	0	1	Not applicable

The difference in number of patients who had vomiting in the post operative period in two study group undergoing TAH is statistically significant ($p = 0.0046$). Thus the efficacy of metoclopramide in preventing vomiting seems less than Ondansetron in patients undergoing the same type of surgery Transabdominal Hysterectomy (TAH).

DISCUSSION

Postoperative nausea and vomiting is an unpleasant experience which extends the post operative hospital care of operated patients. There are many factors affecting the incidence of PONV including patient characteristics, preanesthetic medications with narcotic analgesics, duration of anesthesia, site of operations, and anesthetic exposure to ether, halothane and nitrous oxide. Beside these anxiety, reflux esophagitis, hypotension, hypoxia, hypocarbia may also cause nausea and vomiting. The first clinical studies on the efficacy of metoclopramide in prevention of PONV were published in 1960.¹¹ Newer drugs like ondansetron, granisetron, tropisetron have been launched to treat and prevent nausea and vomiting.¹² This drug is also effective in preventing PONV and has been proved from many clinical trials.⁹ This drug is not yet being much used in our hospitals to prevent PONV.

The general characteristics of patients in relation to age and body weight were not significantly different in the two study groups. The average age of the sixty patients was 40.65 ± 8.94 yrs and average body weight was 53.58 ± 9.305 Kg. The incidence of PONV is higher when exposure to general anesthesia is prolonged.^{6,7} In this study, the average anesthesia period in metoclopramide group was one hour and thirty-eight minutes, whereas the average time of anesthesia exposure of the patients in Ondansetron group was one hour and twenty-nine minutes. There was no much difference in duration of anesthesia exposure in both groups. In early post operative period there were three incidence of vomiting in Ondansetron group, where as eight patients vomited who received metoclopramide. In late post operative period two patients vomited who received ondansetron where as seven patients vomited who received metoclopramide. Clinically ondansetron seems better than metoclopramide in preventing vomiting in post operative ward, but this could not be proved statistically ($p = 0.1$, $p = 0.15$). In the study conducted by Nagueb and Bakry, ondansetron was found to be better antiemetic than metoclopramide in preventing PONV which was statistically significant ($p = 0.02$).¹⁴ The difference in the requirement of rescue antiemetics in the two groups was statistically significant ($p = 0.03$). From this point of view, ondansetron was found to

be more efficient than metoclopramide in preventing PONV, as less rescue antiemetics was needed in former group. Similarly Lesser and Lip, Moris and Aune found that rescue antiemetics were significantly reduced in patients getting ondansetron in their study.¹⁰

Opioids may cause nausea and vomiting. In our study, total amount of opioids received in ondansetron group was 78.57±32.67 mg, whereas 79.7±37.5 mg of pethidine in metoclopramide group. Thus patients in both groups received opioids almost in similar doses. The amount of opioids in different groups in the study conducted by Lesser and Lip, Polati and Verlato and others were also similar.^{9,10} In this study, a single dose of 8 mg of ondansetron or 10 mg of metoclopramide i.v was used without any side effects in post operative ward. Polati and Verlato used the same dose and they also did not find any side effects in their patients.⁵ The optimal dose of ondansetron was considered to be 4 - 8 mg for preventing PONV. The incidence of PONV is affected by type of surgery performed.¹³ In this study TAH surgery was associated with more frequency of vomiting than in other type of surgery. Even in the same type of surgery vomiting was more frequently encountered in metoclopramide group than in ondansetron group. The difference in incidence of vomiting in two groups undergoing TAH is significant statistically ($p = 0.004$). Prevention of PONV may be particularly important when its occurrence may represent a risk to the patients (depressed level of consciousness, after oral surgery when jaw is wired). Thus patients at high risk of PONV should be considered in using prophylactic antiemetics.

CONCLUSION

From this randomized double blinded comparative study between Ondansetron and Metoclopramide in preventing PONV, it is concluded that there is reduction in vomiting and rescue antiemetics requirement in Ondansetron group than in Metoclopramide group, but it has to be evaluated further by trails in larger groups.

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