7 EFFECT OF TIMING OF ONDANSETRON ADMINISTRATION ON ITS EFFICACY AS A PROPHYLACTIC ANTIEMETIC IN PATIENTS UNDERGOING GYNECOLOGICAL LAPAROSCOPIC PROCEDURES

1st Author: Dr. Shah Vandana., M.D., Assistant professor.
2nd Author: Dr. Gohel Jahnavi ., 1st year anesthesia resident.
3rd Author: Dr. Patel Kirti., M.D., D.A., Professor
Department Of anesthesia, Smt SCL General Hospital, Smt. NHL Municipal Medical College, Ahmedabad.
Corresponding Author: E-mail address: vandanashah78@gmail.com

Abstract:

INTRODUCTION : Although ondansetron (4 mg IV) is effective in the prevention and treatment of postoperative nausea and vomiting (PONV) after gynecological laparoscopic surgery, the optimal timing of its administration, and the effect on the patient's quality of life after discharge have not been established.

METHOD: In this placebo-controlled study, 90 healthy women undergoing gynecological laparoscopic procedures were randomized to receive placebo (Group A), ondansetron 4 mg before induction (Group B), and ondansetron 4 mg at the end of surgery (Group C).

RESULTS: Compared with placebo and ondansetron given before induction of anesthesia, ondansetron administered after surgery was associated with lower nausea, decrease incidence of emesis (more than two episodes), earlier intake of normal fluid and food during first 24 hours post operatively. This prophylactic regimen was also associated with highest patient satisfaction.

CONCLUSION: Compared with placebo and ondansetron given before induction of anesthesia, ondansetron administered after surgery significantly reduced the incidence of PONV in the post anesthesia care unit and during the 24-h follow-up period, it also facilitated the recovery process by reducing the time to oral intake for fluid and a normal diet. It also improves patient's quality of life after surgery.

Key Words: Ondansetron, Antiemetic, Gynecological Laparoscopic Surgery.

"THE EFFECT OF TIMING OF ONDANSETRON ADMINISTRATION ON ITS EFFICACY AS A PROPHYLACTIC ANTIEMETIC IN PATIENTS UNDERGOING GYNECOLOGICAL LAPAROSCOPIC PROCEDURES"

INTRODUCTION: In laparoscopic procedure, the peritoneal cavity is inflated with carbon dioxide, that triggers vagal afferents on the bowel and peritoneum, which induces emesis by activating the vomiting center. This insufflations also leads to abdominal discomfort, if abdominal cavity is not adequately decompressed after the procedure, further adding to general level of unpleasant sensations(1). Pain, Nausea

(subjectively unpleasant sensation associated with awareness of the urge to vomit), vomiting (forceful expulsion of gastric contents from the mouth) and retching (labored, spasmodic, rhythmic contraction of the respiratory muscles without the expulsion of gastric contents) are frequently listed by patients as their most important peri operative concerns(1). Women undergoing gynecological surgery are particularly at risk of experiencing these problems. Obesity appears to increase the risk of PONV because fat soluble anesthetic agents may accumulate in adipose tissue which then release and slowly causing postoperative emesis. Female patients have 3 times greater incidence of emetic symptoms than males, due to increased gonadotropin, estrogen, and plasma progesterone levels during their menstrual cycles(1).

Drugs known to block dopamine, histamine and muscarinic cholinergic receptor have antiemetic effects (2). A wide variety of prophylactic antiemetic, including antihistamines(e.g., hydroxyzine, promethazine), butyrophenones (e.g., droperidol), and gastro kinetic agents (e.g., metoclopramide), have been successfully used to reduce the incidence of postoperative nausea and vomiting (PONV) in the ambulatory setting, but some of these older antiemetic may be associated with undesirable side effects. Ondansetron, a 5-HT, receptor antagonist, is effective for both the prevention and treatment of PONV without producing significant side effects. The most frequently reported side effects of ondansetron include constipation and headache (3). The site of action of ondansetron is thought to be 5-HT_3 receptor located in the visceral afferent vagus and area postrema. Ondansetron administered before induction of anesthesia is based on the hypothesis that blockade of receptors in the chemoreceptor trigger zone before the arrival of emetic stimuli associated with anesthesia and surgery provides greater antiemetic efficacy(4).

AIMS: Ondansetron (4 mg IV) is effective in the prevention and treatment of postoperative nausea and vomiting. The aim of this study is to find out the **effect of timing of ondansetron administration** for (i) Efficacy of drug and (ii) Incidence of PONV (iii) its effect on patient's quality of life after surgery.

MATERIAL AND METHOD: The present study was conducted in 90 patients of ASA I/II, aged 20-60 years, scheduled for elective gynecological laparoscopic surgeries after taking written informed consent. Exclusion criteria: Patients with pregnancy, breastfeeding, renal or liver disease, psychological illness, history of alcoholism or opioid addiction, consumption of antiemetic drug 3 days preceding the intervention, occurrence of nausea or vomiting in the same period and conditions associated with delayed gastric emptying such as gastrointestinal obstruction, pyloric stenosis, chronic

cholecystitis, diabetes mellitus and neuromuscular disorders were excluded from the study. All routine investigations were assessed preoperatively and patients were kept nil by mouth for 8 hours. On arrival in the operating room routine monitoring devices were applied and baseline blood pressure, heart rate, pulse oximetry values were recorded.
Premedication: Inj. Glycopyrrolate 0.2 mg IV and Inj. Fentanyl 1.5-2 microgram/kg IV .
Group A (Placebo): saline,
Group B: Ondansetron 4 mg 2-3 mins before induction,
Group C: Ondansetron 4 mg at the end of surgery
(30 patients in each group).
Induction: inj. Pentothal 3-5 mg/kg IV and inj.succinylcholine 1.5-2 mg/kg IV. Intubation done with appropriate sized cuffed endotracheal tube. Anesthesia was maintained with oxygen, nitrous oxide (N_2O) and sevoflorane (2-3%). Inj. Atracurium 0.5 mg/kg IV given when required. Patients were reversed with inj. Neostigmine 0.05 mg/kg IV and inj. Glycopyrrolate 0.4 mg IV. Tracheal extubation done after proper suctioning. Then patients were transferred to post anesthesia care unit (PACU).
PACU: In the PACU all vitals were monitored. Incidence of PONV noted on admission and 1 hour after that. Metoclopramide 10-20 mg IV was given as the rescue antiemetic if the patient experienced repeated (two or more) episodes of emesis or sustained nausea lasting 15 mins. Assessment of quality of life was done by first fluid intake and resumption of normal food & oral food intake. Level of satisfaction also noted.
Statistical analysis: performed with ANOVA test for continuous variables expressed as mean ± SD (patient's age, weight). Discrete variables, such as the incidence of nausea, vomiting and first oral intake, resumption of normal food and degree of satisfaction, were compared by using chi square, Fisher's exact tests. P value of 0.05 was considered significant.

OBSERVATIONS AND RESULTS

Table 1: Demographic Data

GROUPS	A	B	C
AGE (year)	39 + 7	39 + 9	38 + 9
WEIGHT(kg)	61 + 11	61 + 9	63 + 12
ASA I / II	24 / 6	22 / 8	25 / 5

Table 2: Incidence of PONV

GROUPS	**A**	**B**	**C**	**P Value**	
				A & C	**B & C**
NAUSEA					
On admission to PACU	22(73%)	17(56.66%)	0(0%)	<0.001	<0.001

1 hr later	22(73%)	17(56.66%)	1(3.33%)	<0.001	<0.001
Within 24 hr after surgery	25(83%)	18(60%)	2(6.66%)	<0.001	<0.001
VOMITING					
On admission to PACU	18(60%)	10(33.33%)	0(0%)	<0.001	<0.001
1 hr later	18(33.33%)	11(36.66%)	1(3.33%)	<0.001	<0.005
Within 24 hr after surgery	20(66.66%)	13(43.33%)	1(3.33%)	<0.001	<0.001
RESCUE antiemetic in PACU	25(83%)	22(73%)	3(10%)	<0.001	<0.001

Table 3: Assessment of Quality of Life

GROUPS	**A**	**B**	**C**	**P value**	
				A & C	**B & C**
Resumption of oral fluids : Day of surgery	19(63.33%)	20(66.66%)	27(90%)	<0.025	<0.05
1 day after surgery	9(30%)	7(23.33%)	2(6.66%)	<0.025	**<0.75**
Resumption of normal food : Day of surgery	10(33.33%)	12(40%)	20(67%)	<0.01	<0.05
1 day after surgery	13(43.33%)	8(26.66%)	5(16.6%)	**<0.75**	**<0.25**
Degree of satisfaction : Highly satisfied	10(33.33%)	18(60%)	25(83.33%)	<0.001	<0.05
Satisfied	6(20%)	6(20%)	5(16.6%)	<0.001	<0.01

Chart 1: Incidence of Nausea

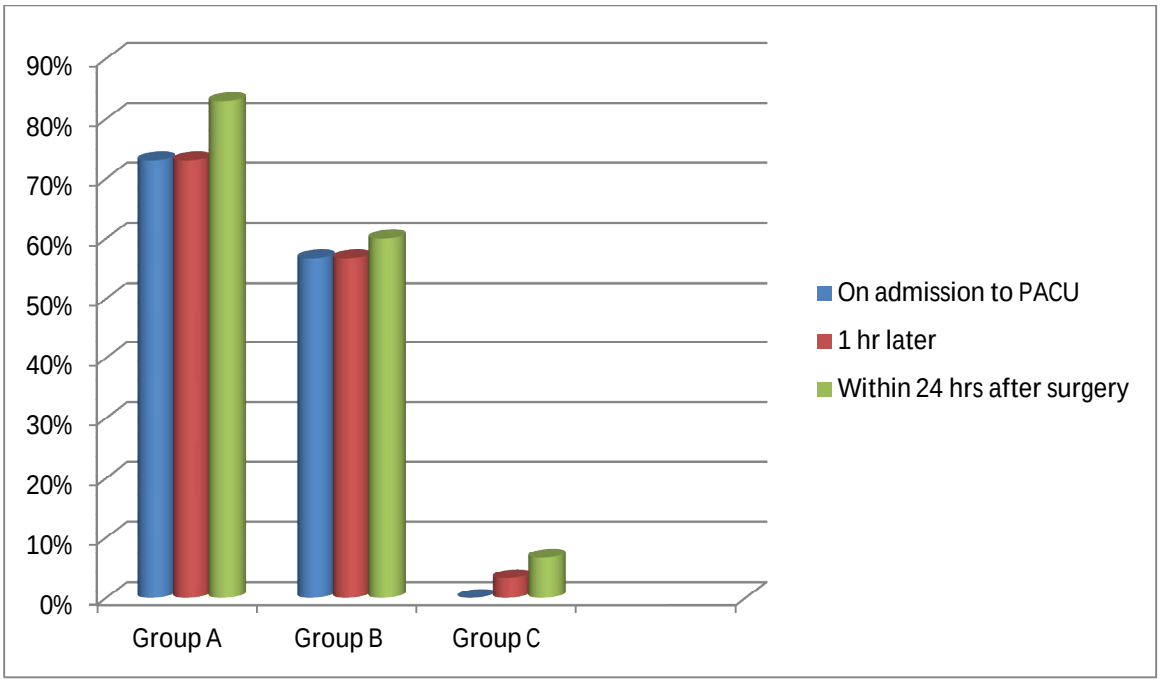
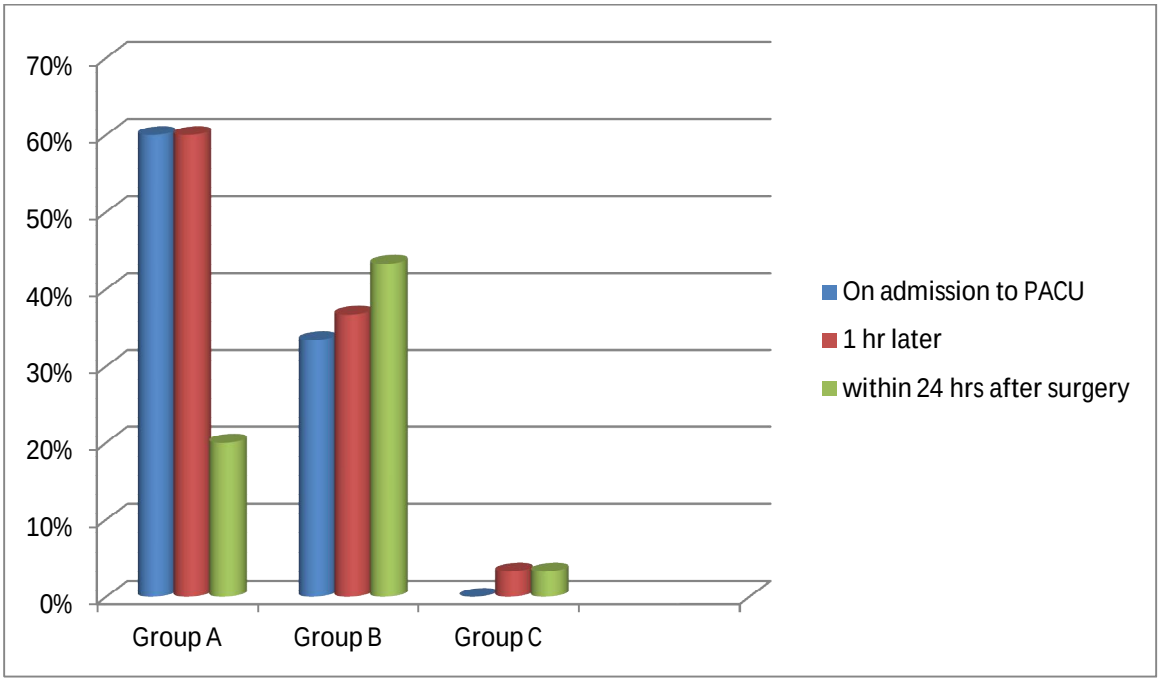


Chart 2: Incidence of vomiting



There was no significant difference in demographic characteristics between all three groups as shown in table 1. In the PACU, patients in Group B & Group C experienced less nausea compared with Group A, whereas the incidence of vomiting was significantly decreased in Group C (Table-2; p values statistically significant). However, the times to resumption of regular fluids and normal food were significantly decreased in Group C (Table 3; p values statistically significant) compared

with other two groups. Patient satisfaction also differed significantly among the three groups, with more patients being highly satisfied in the Group C (Table 3; p values statistically significant). There were no significant differences in the incidence of nonemetic postoperative side effects among all three groups. There were also no significant differences in the times to eye opening, tracheal extubation, response to verbal commands, and orientation among the three groups.

DISCUSSION: Ondansetron, a 5-HT, receptor antagonist, is highly effective in preventing and treating nausea and vomiting. However, in most of the studies evaluating the prophylactic antiemetic efficacy of ondansetron, the drug was administered immediately before the induction of anesthesia. Only one published study has reported that ondansetron was effective in preventing PONV when administered after surgery (5). Ondansetron has a relatively short elimination half-life of 2.8 ± 0.6 hours, it seemed logical that it might be more effective when administered after surgery, thereby producing a more sustained antiemetic effect in the postoperative period (6). The choice of a 4-mg ondansetron dose was based on pooled data from studies that suggested this was the optimal dose for the prophylaxis of PONV. Its lack of side effects has made ondansetron popular in ambulatory surgery (7). The administration of ondansetron at the end of surgery was associated with shorter times to - first oral intake, resumption of the normal meals on the day of surgery, lower PONV. Patient satisfaction was significantly higher in ondansetron treatment groups than in the placebo group. The incidence of nausea was higher than the incidence of vomiting in this study because some patients developed severe nausea without vomiting, whereas all of the patients experiencing emesis were also nauseated.

Jun Tang, Baoguo Wang, Paul F. White,(4) suggested that ondansetron 4 mg IV administered at the end of surgery is more effective in preventing PONV in the PACU, as well as in the post discharge period, than ondansetron administered as a split dose at the induction and the end of surgery. **Philip B, McLeskey C, Chelly J, et al**.(8) noted that dolasetron(another 5-HT_3 antagonist) 12.5 mg IV given 15 min before the end of the anesthetic was as effective in the prophylaxis of PONV as 25-, 50-, and 100-mg doses. There are few direct comparisons of the effect of timing of other antiemetics on their efficacy. **Enrico Polati, Giuseppe Verlato, Gabriele Finco et al.(**2) noted that ondansetron 4 mg IV has a greater efficacy/safety ratio than metoclopramide 10 mg IV when used to treat established PONV. **Klockgether- Radke et al**.(9) suggested that the timing of the administration of droperidol has no influence on postoperative emesis. However, **Kraus et al**.(10) reported that droperidol was more effective for prophylaxis against postoperative emesis when administered preoperatively**. Ferrari and Donlon** (11) determined that metoclopramide 0.15 mg/kg given on arrival in the PACU is an effective antiemetic in children undergoing tonsillectomy procedures.

CONCLUSION: Ondansetron 4 mg IV administered at the end of surgery is more effective in preventing PONV in the PACU, as well as in the post discharge period, than ondansetron administered before the induction of anesthesia. When ondansetron is administered at the end of surgery, it allows early resumption of fluids and normal food and improves the patient's quality of life after surgery.

REFERENCES:

1. Usha Daria, Vinod Kumar; Qualitative Comparison of Of metoclopramide, ondansetron, and granisetron alone and in combination with dexamethasone in the prevention of post operative nausea and vomiting in day care gynecologic laparoscopic surgery under general anesthesia; Asian journal of pharmaceutical and clinical research, vol 5, issue 2, 2012
2. Enrico Polati, Giuseppe Verlato, Gabriele Finco, Walter Mosaner, Salvatore Grosso, Leonardo Gottin, Anna M. Pinaroli, Stefano Ischia; Ondansetron versus metoclopramide in the treatment of post operative nausea and vomiting; Anesth Analg 1997;85:395-9
3. M. Steve Sniadach, and Michael S. Alberts; A Comparison of the Prophylactic Antiemetic Effect of Ondansetron and Droperidol on Patients Undergoing Gynecologic laparoscopy; (Anesth Analg 1997;85:797-800
4. Jun Tang, Baoguo Wang, Paul F. White, Mehernoor F. Watcha, Jinhui Qi, and Ronald H. Wender; The Effect of Timing of Ondansetron Administration on Its Efficacy, Cost-Effectiveness, and Cost-Benefit as a Prophylactic Antiemetic in the Ambulatory Setting; (Anesth Analg 1998;86:274-82
5. Gan TJ, Collis R, Hetreed M. Double-blind comparison of ondansetron, droperidol and saline in the prevention of postoperative nausea and vomiting. Br J Anaesth 1994;72:544-7.11. Milne RJ, Heel RC. Ondansetron: therapeutic use as an antiemetic Drugs 1991;41:574-95
6. Milne RJ, Heel RC. Ondansetron: therapeutic use as an antiemetic Drugs 1991;41:574-95
7. Pearman MH. Single dose intravenous ondansetron in the prevention of postoperative nausea and vomiting. Anaesthesia 1994;49(Suppl):ll-5.
8. Philip B, McLeskey C, Chelly J, et al. Evaluation of dolasetron mesylate dose needed to prevent postoperative nausea and vomiting [abstract]. Anesthesiology 1996;85(Suppl):A37.
9. Klockgether-Radke A, Demmel C, Braun U, Muhlendyck H.Emesis and the oculocardiac reflex: drug prophylaxis with droperidol and atropine in children undergoing strabismus surgery. Anaesthetist 1993;42:356-60.
10. Kraus GB, Giebner M, Palackal R. The prevention of postoperative vomiting following strabismus surgery in children. Anaesthetist 1991;40:92-5.