

POST OPERATIVE NAUSEA AND VOMITING [PONV]: COMPARISON OF TIMING OF ADMINISTRATION OF ANTIEMETICS IN PROLONG SURGERIES

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ABSTRACT

Objective: The objective of this study was to compare the timing of administration of Ondansetron and Dexamethasone in terms of prevention of postoperative nausea and vomiting when given at induction verses thirty minutes before the end of prolong surgeries.

Study Design: Randomized control trial.

Place and Duration of Study: The study was conducted in Main Operation Theatre of Combined Military Hospital Rawalpindi over a period of six months from 17 Apr 2009 to 16 Oct 2009. Cases were selected from OPDs, emergency and also by referral.

Patients and Methods: Total 120 patients were included in this study (60 patients in each group). Group A patients received Ondansetron 4 milligrams and Dexamethasone 8 milligrams intravenous at induction and group B patients received Ondansetron 4 milligrams and Dexamethasone 8 milligrams thirty minutes before reversal of neuromuscular blockade at the end of surgery.

Results: Mean age was observed 41.7 ± 3.7 and 39.9 ± 1.9 in group-A and B, respectively. Comparison of pre-induction and 30 minutes before end of surgery at 0-6 hours reveal nausea and vomiting in 11 (18.3%) in group-A and in 3 (5.0%) patients of group-B. Results were statistically significant ($p=0.022$). At 7-12 hours results were also statistically significant when comparison was made between group-A and B ($p=0.051$), while at 13-24 hours difference between two groups was statistically non-significant ($p=0.314$).

Conclusion: It is therefore established that administering a combination of Inj. Ondansetron 4mg with Inj. Dexamethasone 8mg, was more efficacious in reducing post-operative nausea and vomiting at 0-6 hours when administered 30 minutes before the completion of surgery.

Keywords: Anaesthesia, Dexamethasone, Ondansetron, Post operative nausea and vomiting (PONV).

INTRODUCTION

Nausea and vomiting occurs frequently in patients undergoing surgical procedures under general anaesthesia. Post operative nausea and vomiting is the most common problem which increases the morbidity and creates certain complications regarding management of patients outcome of surgical procedures¹. Important risk factors that predispose a patient to develop post operative nausea and vomiting are female sex, younger age, history of post operative nausea and vomiting, smoking, prolonged anaesthesia, prolonged fasting, rough handling and the use of volatile anesthetics as shown by local and international research. To prevent postoperative nausea and vomiting, different drugs have been used but their relative effects have to be compared².

Currently used antiemetics for prevention of postoperative nausea and vomiting include antiserotonergic agents such as Ondansetron, Granisetron and Dexamethasone. It has been well established that anti-serotonergic agents are effective for the prophylactic control of postoperative vomiting³. For ondansetron and dexamethasone each is estimated to reduce risk of postoperative nausea and/or vomiting (PONV) by approximately 25%⁴. The combination of Ondansetron and Dexamethasone is effective in pre-vention of postoperative nausea and vomiting with minimal side effects⁵.

Traditional anti-emetics used for the control of PONV include anti-cholinergics (e.g. scopolamine), anti-histamine (dimenhydrinate), phenothiazines (e.g. promethazine), butyrophenones (e.g. droperidol) and benzamide (e.g. metoclopramide) in addition to serotonin receptor antagonists (Tropisetron, ondansetron, granisetron, dolasetron and ramosetron)⁶. The rationale of the study was to

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assess the postoperative nausea and vomiting with ondansetron and dexamethasone administration and to compare the timing of administration of Ondansetron and Dexamethasone in terms of prevention of post-operative nausea and vomiting when given at induction versus thirty minutes before the end of prolonged surgeries. The results of this research indicate a clear benefit for patients given general anaesthesia along with administration of Ondansetron and Dexamethasone in terms of better recovery, less hospital stay and better surgical outcome.

PATIENTS AND METHODS

The study was carried out in Main

complaints, pregnant females, patients with history of motion sickness, patients with coexistent cardiovascular and chronic diseases. The study was conducted after approval of the Hospital ethical committee and after the informed consent and explaining the risk and benefits to the patients. These patients were then randomly allocated in two groups by lottery method. In both groups anaesthesia was induced with injection Thiopentone sodium 5 milligram per kilogram body weight. Muscle relaxation was achieved with Injection Atracurium 0.5 mg/kg followed by intubation. Anaesthesia was maintained with Isoflurane 0.6-1%, 60% nitrous oxide with 40% oxygen. Fluids were given according to fluid deficit and

Table-1: Summary of comparison of Group A (pre-induction) and Group B (30 minutes after surgery) in terms of age, gender, and ASA Status.

Group	Group A (Pre Induction)		Group B (30 min before end of surgery)	
Age (Mean ±SD)	41.7±3.7		39.9±1.9	
Sex	Male	Female	Male	Female
	38 (63.3%)	22 (36.7%)	35 (58.3%)	25 (41.7%)
ASA-I No. (%)	32 (53.3%)		34 (56.7%)	
ASA-II No. (%)	28 (46.7%)		26 (43.3%)	

Table-2: Showing comparison of two groups at different time intervals (30 minutes after surgery).

Nausea/vomiting	At 0-6 hours				Nausea/vomiting	At 7-12 hours				Nausea/vomiting	At 13-24 hours			
	Group A		Group B			Group A		Group B			Group A		Group B	
	No.	%	No.	%		No.	%	No.	%		No.	%	No.	%
Yes	11	18.3	3	05.0	Yes	7	11.7	1	01.7	Yes	1	01.7	0	-
No	49	81.7	57	95.0	No	53	88.3	59	98.3	No	59	98.3	60	100.0
Total	60	100	60	100.0	Total	60	100	60	100.0	Total	60	100	60	100.0
<i>p</i> value = 0.022, Chi square=5.18					Chi square=3.78, <i>p</i> value = 0.051					Chi square=1.01, <i>p</i> value=0.314				

Operation Theatre of Combined Military Hospital Rawalpindi over a period of six months from 17 Apr 2009 through 16 Oct 2009. Cases were selected from OPDs, emergency and also by referral. American Society of Anesthesiology (ASA) Physical status I and II, and patients of both gender and ages between 18 and 50 years (because patient's age greater than 50 years might be having coexistent diseases) were included in the study. While exclusion criteria included patients not willing for study, patients on chemotherapy (because of increased incidence of nausea and vomiting), disoriented patients unable to explain their

intraoperative loss.

Group A patients received Ondansetron 4 milligram and Dexamethasone 8 milligram intravenous at induction and group B patients received Ondansetron 4 milligrams and Dexamethasone 8 milligrams thirty minutes before reversal of neuromuscular blockade at the end of surgery.

Postoperative nausea and vomiting were recorded on a time continuum as early, intermediate and late. Early from 0-6 hours, intermediate from 7-12 hours and late from 13-24 hours. Those patients who experienced nausea for more than two hours and patients

having vomiting more than two times were offered rescue antiemetic, injection Metoclopramide 10 milligram intravenously.

All the data collected through the Proforma was entered into the Statistical Package for Social Sciences (SPSS) version 10.0 and analyzed through its statistical package. Mean and standard deviation was used for quantitative data i.e. age, while frequency and percentages were calculated for qualitative data as gender, marital status, education and ASA status. Chi Square was used to compare nausea and vomiting at 0-6 hours, 7-12 hours and 13-24 hours. P value of less than or equal to 0.05 was taken as significant.

RESULTS

Regarding age distribution, most of the patients i.e. 24 (40.0%) in both groups were between 41-50 (8.4%) in group-A and 3.4% were less than 20 years old with mean age 41.7 ± 3.7 and 39.9 ± 1.9 in group-A and B, respectively. In group-A, 38 (63.3%) patients and in group-B, 35 (58.3%) were males while 22 (36.7%) in group-A and 25 (41.7%) were females. In group-A, 32 (53.3%) patients and in group-B, 34 (56.7%) patients had ASA-I status. 28 (46.7%) and 26 (43.3%) in group-A and B had ASA-II status respectively (Table-1/Figure-1). Comparison of pre-induction and 30 minutes before end of surgery at 0-6 hours revealed nausea and vomiting in 11 (18.3%) in group-A and in 3 (5.0%) patients in group-B. The difference was statistically significant ($p=0.022$) at 0-6 hours (Table-2). At 7-12 hours results were also statistically significant when comparison was made between group-A and B with $p=0.051$ (Table-3), while at 13-24 hours difference between two groups was non-significant with $p=0.314$ (Table-4/Figure-2).

DISCUSSION

Nausea is the subjective sensation of an impending urge to vomit, mostly it is perceived in the throat or epigastrium of the patient. Nausea is not an inevitable consequences of vomiting. It is the most troublesome symptom after surgery and anaesthesia. It is thought to be caused by the same stimuli which are responsible for vomiting but the nature of the

higher centers involved is unknown. Nausea is the conscious recognition of the sub-conscious excitation in an area of the medulla closely associated with or part of the vomiting centre and it can be caused by irritative impulses coming from the GIT, impulses originate in the lower brain associated with motion sickness or impulses from cerebral cortex to initiate vomiting.

During nausea gastric tone is reduced and peristalsis in the stomach is diminished or absent. In contrast the tone of duodenum and jejunum is increased and there is frequent reflux of their contents into stomach, however, duodenal and jejunal tones may not be always increased in a nauseated patient. A number of stimuli can produce nausea like viscera medicated pain, labyrinthine disorders and unpleasant memories but the exact higher centers involved are unknown.

Vomiting occurs in two phases. In the prodromal phase or pre-ejection phase, there is increased salivation and feeling of nausea. In this phase muscles of the stomach are relaxed on by increased retrograde peristalsis of the intestine. The later forces small intestinal

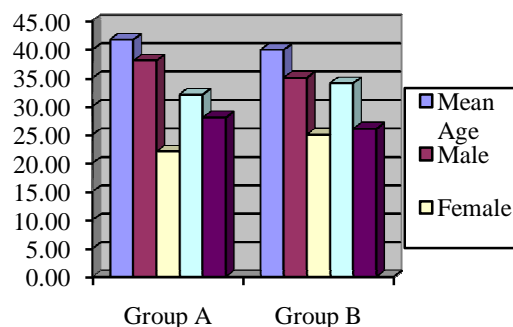


Figure-1: Graphical presentation of group A (pre-induction) and Group B (30 minutes after surgery) in terms of percentages of age, gender, and ASA Status.

contents into the stomach. This first phase is followed by an ejection phase in which anterior abdominal wall muscles and diaphragm contract together, accompanied by retrograde contractions of the striated muscles of the oesophagus with relaxation of the upper

esophageal sphincter. Major and serious consequence of vomiting is loss of both fluid and important electrolytes with the vomitus causing serious metabolic derangements. There are many risk factors which are associated with increased incidence of Nausea and vomiting in patients undergoing laparoscopic cholecystectomy. Pain, fear and anxiety associated with Surgery plays an important role.

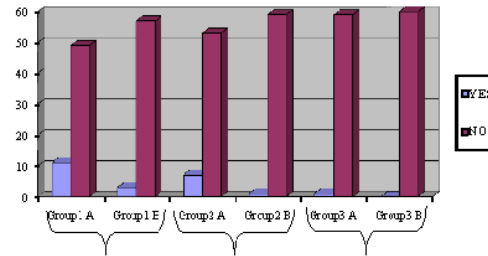
The incidence of post-operative nausea and vomiting (PONV) depends on the type of anaesthesia and surgery, but overall it is estimated to be 20-30%.⁷ The incidence of nausea and vomiting has been shown to be 25-42% with no anti-emetic treatment in patients undergoing laparoscopic cholecystectomy.⁷ Post-operative nausea and vomiting (PONV) affects approximately one-third of patients and can lead to aspiration, dehiscence, esophageal rupture and increased treatment costs if uncontrolled. The causes of PONV are multiple, amongst which pharyngeal stimulation, gastrointestinal distension, abdominal surgery, the anaesthetic agent, pain, opioid use, hypoxia, hypotension, vestibular disturbances and psychological factors are important⁸.

The efficacy of anti-emetic therapy for the prevention and treatment of PONV may be enhanced by combination therapy. This technique allows the use of various drugs which act at different receptor. Presently, there is considerable interest in this and most studies have found combination to be significantly more effective than single drug. The most commonly used drugs and combination therapy are droperidol-ondansetron and ondansetron-dexamethasone combinations of cyclizine and prochlorperazine are also possible⁹.

Many studies have used preoperative Dexamethasone administration just before induction of anaesthesia¹⁰. Glucocorticoids act on the intracellular receptor and the effects are mediated through altered prostaglandin synthesis, via gene transcription. Onset of biologic action of glucocorticoids is 1-2 hours^{11,12}. In our study, Group A patients received Ondansetron 4 milligram and

Dexamethasone 8 milligram intravenous at induction and group B patients received Ondansetron and Dexamethasone thirty minutes before reversal of neuromuscular blockade at the end of surgery. Nausea and vomiting were assessed as early, intermediate and late as it is the standard used in our hospital & all studies before¹³.

In present study, the administration of



p-value		
Figure 1 (0-6 hrs)	Figure 2 (7-12 hrs)	Figure 3 (13-24 hrs)
0.022	0.051	0.314

Figure-2: Comparison of nausea and vomiting in the three groups at 0-6 hours, 7-12 hours and 13-24 hours. p value of less than or equal to 0.05 was taken as significant.

Dexamethasone and Ondansetron in subjects reduced the incidence of PONV, 30 minutes before the end of surgery at 0-6 hours. This finding is in accordance with the findings of researchers Henzi et al. in a recent study¹⁴. However, these authors included inpatients in their analysis and defined late PONV as that occurring from 0 to 24 hours postoperatively (not restricted to the post-discharge period).

Apfel et al in their study have demonstrated by conducting a multicenter, randomized controlled trial that Ondansetron, Droperidol and Dexamethasone used as monotherapies reduced the incidence of PONV by 24-26% in high risk patients after general anesthesia.¹⁵ In addition, the incidence of PONV was further reduced by multimodal therapy from a 52% risk (no prophylaxis) to 37%, 28% and 22% with the use of one, two and three antiemetics, respectively, and it did not matter which combination of antiemetics were used¹⁵. The rationale of conducting this study

was to evaluate and find out if there is a decrease in postoperative nausea and vomiting and this in turn would benefit patients in terms of better recovery, less hospital stay and better surgical outcome. It is generally accepted that outpatient surgical procedures are cost effective and efficient method of patient care. Nausea and vomiting after surgery can negate the benefits of outpatient surgery by increasing recovery time, intensity of nursing care and patient morbidity. Laparoscopic procedures have been known to cause more significant PONV because of the creation of pneumoperitoneum involved in the procedure. This findings of our study endorses the use of antiemetics to reduce PONV.

CONCLUSION

It is the finding of our study that combination of Inj. Ondansetron 4mg with Inj. Dexamethasone 8mg given 30 minutes before the end of surgery is more efficacious in preventing post operative nausea and vomiting. Moreover it is recommended that multimodal combination prophylactic therapy should be considered in patients who are at increased risk of developing post-operative nausea and vomiting.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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