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Study on efficacy of Ondansetron and Dexamethasone combination and Ondansetron alone in prevention or reduction of Post-operative nausea and vomiting after elective surgeries

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Abstract

The postoperative nausea and vomiting (PONV) are well recorded recognized uncomfortable complications of anesthesia and surgery. PONV is considered as minor problem, in spite of them being the leading causes of morbidity in post operative surgical cases. The present study is designed to evaluate the efficacy of intravenous injection of ondansetron and intravenous injection of dexamethasone combination, when compared to intravenous injection of ondansetron alone in prevention or reduction of PONV in elective surgeries under general anesthesia.

Prospective randomized study was carried out in 200 adult patients male and female undergoing elective surgeries under general anesthesia and where grouped into 2 groups Group-A received intravenous injection of ondansetron 4 mg. Group B received intravenous injection of ondansetron 4 mg and intravenous injection of dexamethasone 8 mg. Incidence of early nausea was statistically highly significant ($p < 0.001$) between the groups. 51 patients of Group A had mild nausea compared to 20 patients in Group B. 8 patients in Group A had moderate nausea compared to no patients in Group B. The difference between the groups with respect to the incidence of delayed nausea was statistically significant ($p < 0.01$) between two groups. Early retching was found to be significant while the difference in delayed retching between the groups was highly significant.

Incidence of early vomiting was recorded non-significant, while delayed vomiting between the groups was statistically significant. From the current study we conclude that the combination therapy of intravenous injection of ondansetron 4 mg and intravenous injection of dexamethasone 8 mg before induction is safe and more effective than that of intravenous injection of ondansetron 4 mg alone in reducing the incidence of early nausea and delayed nausea and vomiting and long term prevention of postoperative nausea and vomiting in patients undergoing elective surgeries under general anesthesia. It can also be concluded that this combination therapy is safe with less adverse effects.

Key words: Ondansetron, Dexamethasone, Postoperative nausea and vomiting (PONV)

Introduction

The uses of general anesthetic drugs are well recorded to relive the pain during and after the surgical procedures in patient's health care. Use of these anesthetic agents causes postoperative nausea and vomiting (PONV) as their contraindications. Lot of research has been carried out to reduce the pain in the patients during and after surgery by administering general anesthetic drugs, but its complication of PONV is considered as minor problem and neglected in spite of them being the leading causes of morbidity in post operative surgical patients [1]. It was reported that the incidence of PONV was as high as 75 to 80% followed by opioid premedication and prolonged ether anesthesia [2]. Esophageal tears, gastric herniation, muscular strain and fatigue were recorded in postoperative patients due to persistent PONV [3]. Fluid and electrolyte loss accompanying vomiting may lead to dehydration and life threatening electrolyte imbalance [4]. In addition, it also increases the risk of pulmonary aspiration and an increase in intracranial pressure and intraocular pressure may even cause blindness [3]. Most important of all, PONV may have psychological impact on the patients and it may be so severe as to cause aversion towards surgery. In an earlier survey of 71% of ambulatory patients were dissatisfied with the outcome of their surgeries, noted PONV as the reason [4]. Inspite of the scientific advancement; using less emetic anesthetic agents, improved pre and post-operative medication, refinement of operative technique and identification of patient predictive factors, PONV still occur with unacceptable frequency and is described as the "big little problem" [5]. Antiemetic drugs play an important role in the therapy of PONV, though many drugs have been used in the prophylaxis and treatment of PONV, no drug has been proved significantly effective and a search for a better drug continues. The Current study was designed to study the efficacy of intravenous injection of ondansetron (4 mg) and intravenous injection of dexamethasone (8 mg) combination, when compared to intravenous injection of ondansetron (4 mg) alone in the prevention or reduction of PONV after elective surgeries under general anesthesia.

Material and Methods

Sample size was calculated by using statistical methods by using sample size table and by using available statistical software and enrolled 200 adult patients undergoing elective surgeries under general anesthesia at mamata medical college and general hospital were enrolled for studies. Institutional ethical committee approval and written informed consent were obtained from the patients posted for various surgeries requiring general anesthesia were selected. The study population was divided into 2 groups of 100 patients between the age group of 20-60 years patients allotted to the group by using table of randomization. Group A: received intravenous injection of ondansetron (4 mg). Group B: received intravenous injection of ondansetron (4 mg) and intravenous injection of dexamethasone (8 mg).

Inclusion criteria: Patients in the age group of 20 – 60 years with ASA I and ASA II undergoing elective surgeries under general anesthesia were included in the study.

Exclusion criteria: Patients with previous history of PONV in surgery, renal impairment, hepatic disease, neurological, endocrinal abnormalities, pregnancy and lactation, motion sickness, vomiting were excluded from the study

All the patients were subjected to the routine preoperative evaluation and assessed their basic and vital parameters. Patients were given routine, standard preoperative instructions. On the day of surgery, no premedication was given. Intravenous Injection of ondansetron (4 mg) was given to group A and intravenous injection ondansetron (4 mg) plus intravenous injection of dexamethasone (8 mg) was given to group B patients 10 minutes prior to

induction and preanesthetic medication was followed as per the protocol. After preoxygenation for 3 minutes, general anesthesia was induced with intravenous injection of thiopentone sodium (2.5%) 3-5 mg/kg. Relaxation was obtained by injecting intravenous injection of scoline 1 mg/kg body weight and either nasotracheal intubation or orotracheal intubation with an appropriate sized cuffed portex tube was done. Anesthesia was maintained with nitrous oxide, oxygen, halothane (0.5-1%) and controlled ventilation with non-depolarizing muscle relaxant intravenous injection vecuronium 0.05 mg/kg. The patient's vital parameters were monitored throughout the surgery. On the completion of surgical procedure nitrous oxide and halothane were discontinued. Thorough suctioning of the mouth and throat were carried out, neuromuscular blockade was reversed with intravenous neostigmine 0.05 mg/kg body weight and injection glycopyrolate 0.01 mg/kg body weight. Patients were shifted to the recovery room for further observation once the patients regained laryngeal and pharyngeal reflexes, consciousness, with homeostasis maintained and all the vital parameters were normal patients were shifted to their wards.

Time and duration of the surgery was recorded to follow the incidences of PONV. Patients were kept in observation for 24 hours postoperatively to record the incidences of nausea, retching and vomiting for every hour for 4 hours and then at the end of 24 hours with any other complications. Each episode of emesis producing atleast 5 ml was recorded. Repeated vomiting, nausea, retching within 1- 2 minute period was recorded as a single episode. The assessment was carried out using the following format: 0 – None, 1episode – Mild, 2 episodes – Moderate, 3 episodes – Severe. Preventive measures were adopted to the patients who had more than 2 episodes vomiting by antiemetic agent, by intravenous injection of metoclopramide 0.15 mg/kg body weight.

Statistical analysis

Sample size was calculated by using sample size table and Epi software, statistical analysis was carried out by using Graphpad Prism and Sigmastat latest versions and data presented as Mean±SD and results were analyzed by student's "t" test and categorical data was analyzed by chi-square test. $P< 0.05$ was considered as statistically significant.

Results

Most of the patients in both groups are in the range of 20 to 39 years. The mean age in Group A was 30 years and in Group B was 31 years. Further, male patients were 55 to 57% and female patients were 43 to 45 %. In both the cases the difference was statistically not significant.

Post-operative data of nausea, retching and vomiting:

Early nausea: Incidence of early nausea was statistically highly significant ($p < 0.001$). 51 patients in Group A had mild nausea compared to 20 patients in Group B. 8 patients in Group A had moderate nausea compared to no patients in Group B. None of the patients in both groups had severe nausea. Delayed nausea: In group A, 29 patients had mild episodes compared to 12 patients in Group B. 13 patients in Group A had moderate episodes compared to 8 episodes in Group B. None of the patients had severe nausea. The difference between the groups was found to be statistically significant ($p < 0.01$) (Table 1). Early retching: 30 patients in Group A had mild episodes compared to 15 patients in Group B, while 15 patients in Group A had moderate episodes compared to 9 patients in Group B. None of the patients in both Groups experienced severe episodes. Difference between the Groups was found to be significant. Delayed retching: 20 patients in Group A had mild episodes of retching compared to 1 patient in Group B. Moderate episodes were observed in 6 patients of Group A while no patient experienced in Group B. None of the patients had severe episodes. The difference between the Groups was found statistically to

be highly significant (Table 1).Early vomiting: In Group A, 14 patients experienced mild episodes compared to 10 patients in Group B. 2 patients in Group A had moderate episodes compared to 1 patient in Group B. 4 patients in Group A had severe episodes compared to none in Group B. The difference between the Groups was found to be not significant. Delayed vomiting: 6 patients of Group A experienced mild episodes compared to none in Group B. 30 patients in Group A had moderate episodes compared to 3 patients in Group B. None of the patients in both Groups had severe episodes. The difference was found to be statistically significant (Table 1).

Rescue antiemetic**:** current study demonstrated that there was need of antiemetic drugs to stop the excessive vomiting by the patient and was found to be 32 patients in Group A has given emetic drugs when compared to 4 patients in Group B which is statically have positive correlated and our study supports the previous studies of literature (Table 2).

Table 1 Showing the number and percentage of patients having different episodes of nausea, retching and vomiting in post operative care.

	Early			Delayed		
Nausea	**Group A%**	**Group B%**	**P* Value**	**Group A%**	**Group B%**	**P* Value**
No Episode	41 (41)	80 (80)*	P<0.001	58 (58)	80 (80)*	P<0.01
Mild	51 (51)	20(20)*		29 (29)	12 (12)*	
Moderate	8 (8)	0		13 (13)	8 (8)	
Severe	0	0		0	0	
Retching						
No Episode	55 (55)	76 (76)*	P<0.01	74 (74)	99 (99)*	P<0.001
Mild	30 (30)	15 (15)*		20 (20)	1 (1)*	
Moderate	15 (15)	9 (9)		6 (6)	0	
Severe	0	0		0	0	
Vomiting						
No Episode	80 (80)	89 (89)	P>0.05	64 (64)	97 (97)*	P<0.001
Mild	14 (14)	10 (10)		6 (6)	0*	
Moderate	2 (2)	1 (1)		30 (30)	3 (3)*	
Severe	4 (4)	0		0	0	

Table 2 showing the administration of rescue antiemetic in post operative care

	Group A (%)	Group B (%)	P- Value
Required	32 (32)*	4 (4)	P<0.001
Not Required	68 (68)	96 (96)*	

Student ‘t’ test. * Statistically significant with other group

Discussion

PONV can contribute to the development of medical problems and patients with PONV consume more time and resources than that of whom these complications do not exist. The overall incidence of PONV during the first 24 hours after surgery is approximately 30% with comparable variability. This incidence may be larger depending on preoperative patient characteristics, factors related to operation and anesthesia, the intensity of pain and its management in the postoperative period [6]. Ondansteron is highly selective and potent antagonists of 5-hydroxy tryptamine subtype 3 (5-HT_3) receptors in the brain. The mechanism of antiemetic action of corticosteroids is unknown, but may be related to inhibition of prostaglandin synthesis, decrease in 5 – HT_3 level in the CNS and by an anti-inflammatory action at operative site [7]. Nucleus tractus solitarius in the medulla and area postrema are the main regions in which dexamethasone exert its central antiemetic action by exerting its antiemetic action through activation of glucocorticoid receptors [8]. In our study of Group A, 59% patients experienced early nausea while 42% patients experienced delayed nausea. In Group B, 20% of patients had early as well as delayed nausea. Post-operative nausea was less in combination group which is in agreement with the study of Rajeeva Vet.al; [9] in which nausea score was lower in patients receiving ondansetron and dexamethasone than ondansetron alone at 0 hour, 2 hrs and 24 hrs postoperatively. Fewer patients in combination group had late nausea similar to finding of Lopez et.al; [10] where only 12% of patients in combination group had delayed nausea as compared with 38% in the ondansetron

group. Our study did not correlate with that of Rusch D et.al; [11] whose .study results found that the incidence of postoperative nausea did not differ much in the two high risk groups, 20% in the patients receiving ondansetron and 15% in patients receiving ondansetron and dexamethasone combination. Perhaps the difference in their study was due to inclusion of large number of subjects in their study and variability in surgeries conducted.

Our study regarding incidence of early vomiting in ondansetron group was 20% and delayed vomiting was 36%. This is comparable to Rajeeva Vet.al; [9] concluded that 15% of patients has early emesis and 35% has delayed emesis after ondansetron. In our study combination ondansetron and dexamethzone, the incidence of early vomiting was found to be 11% and delayed vomiting was 3% This is in agreement with the study of Rajeeva V et.al; [9] but does not agree with Lopez et. al; and Rusch D et al [10, 11] which the incidence of postoperative vomiting was similar in both groups 11% in the ondansetron group and 7% in ondansetron plus dexamethasone group. Sanchez –Ledesma et.al; [12] concluded that 70% patients does not has nausea and emetic episode who received ondansetron and dexamethasone which was in agreement to our study where 76% of patients who received the combination showed a complete response. In our study, 4% of patients who received combination of ondansetron and dexamethzone (Group B) required rescue antiemetic support when compared to 32% of patients who received ondansterone (Group A) which was statistically significant and this was in agreement with the study of Lopez-oleando et.al and Rusch et.al; [10,11] combination of ondansetron and dexamethasone required less antiemetic support than ondasterone alone.

The adverse effects, related to the use of combination therapy versus ondansetron alone did not reveal significance in our study. This was in accordance with the study of Rusch D et. al; [11] where it was found that the patients receiving ondansetron and dexamethasone combination had the same degree and number of adverse effects, as did those receiving only ondansetron. It also correlates with the study of Thomas R et. al; [15] whose study reported most frequent adverse events were fatigue, headache, dizziness, but there was no differences between groups. Different studies have been done to control PONV with various combination therapies. The potential advantages of combination therapy using drugs that act on different pathways in the emetic response include improved efficacy, extended duration of the antiemetic effect, the ability to combine drugs with greater antinausea versus greater antiemetic effects and the possibility of using smaller doses of individual drugs compared with monotherapy [17].

Conclusion

From the current study we conclude that the combination therapy of intravenous injection of ondansetron 4 mg and intravenous injection of Dexamethasone 8 mg given 10 min before induction is safe and more effective than intravenous injection ondansetron 4 mg alone in reducing the incidence of early nausea and delayed nausea and vomiting and long term prevention of postoperative nausea and vomiting in patients undergoing elective surgeries under general anesthesia. It can also be concluded that this combination therapy is safe with less adverse effects.

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