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Research Article

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Comparison of the efficacy of ondansetron versus ondansetron and dexamethasone in the prevention/ reduction of post-operative nausea & vomiting after elective surgeries under general anaesthesia

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ABSTRACT

Post Operative Nausea & Vomiting (PONV) has been recognized as one of the major complication after elective surgeries under general anesthesia. The incidence of PONV can be as frequent as 70% to 80% in high risk groups, so prevention or reduction of PONV remains one of the major goals to be achieved. The objective of this study is to compare the efficacy of intravenous ondansetron versus intravenous ondanstetron plus dexamethasone combination in prevention / reduction of PONV after elective surgeries under general anesthesia with respect to early and delayed vomiting and their side effects. Our study was done in 200 patients, randomly divided into 2 groups of 100 patients each. One group received intravenous ondansetron 4mg while the other group received intravenous ondansetron 4mg plus dexamethasone 8mg 30 seconds before induction. Postoperatively patients were assessed hourly for 4 hours and then at 24 hours for degree of nausea, retching and vomiting, requirement of rescue antiemetic and side effects. Vomiting occurring upto 4 hours was considered as early and from 4-24 hours as delayed vomiting. Incidence of early and delayed nausea (20% each) was less in the combination group compared to ondansetron alone (59% and 42% respectively). Delayed vomiting was lower in the combination group (3%) compared to ondansetron alone (36%). We hereby conclude that combination therapy of ondansetron and dexamethasone is superior in controlling post operative nausea and vomiting compared to ondansetron alone.

Keywords: Nausea, Vomiting, Ondansetron, Dexamethasone, General surgery.

INTRODUCTION

Postoperative nausea and vomiting (PONV) are frequent and well recognized unpleasant complications following anaesthesia and surgery. During the past decade, much effort has been placed correctly on ensuring patients adequate pain relief after surgery. However PONV are still viewed as minor problems by some physicians, even though they are leading causes of morbidity in paediatric surgical patients. [1] Inspite of the advances using less emetic anesthetic agents, improved pre and post operative medication, refinement of operative technique and identification of patient predictive factors, nausea and vomiting still occur with unacceptable frequency in association and is described as the “big little problem”. [2]

Early studies reported incidence of postoperative nausea and vomiting as high as 75-80% after opioid premedication and prolonged Ether anesthesia. But in the second half of this century, however these incidences have decreased by almost 50% for various reasons. [3] Persisting PONV is very much distressing and debilitating to the patient and can cause many complications to the patients like esophageal tears, gastric herniation, muscular strain and fatigue. [4] The increase in intracranial pressure and intraocular pressure may even cause blindness. The fluid and electrolyte loss accompanying vomiting may lead to dehydration and life threatening electrolyte imbalance. [5] In addition, it also increases the risk of pulmonary aspiration. [4] Most important of all, PONV may have psychologic impact on

the patient and it may be so severe as to cause aversion towards surgery. In a survey of ambulatory patients who were dissatisfied with the outcome of their operations, 71% cited PONV as the reason. [5]

Antiemetic drugs play an important role in the therapy of PONV. Though many drugs have been tried in the prophylaxis and treatment of PONV, no drug has been proved significantly effective and a search for a better drug continues. The present study was designed to study the efficacy of ondansetron versus ondansetron/dexamethasone combination in the prevention and or reduction of PONV after elective surgeries under general anesthesia.

EXPERIMENTAL SECTION

A prospective study was done after obtaining institutional committee approval and written informed consent of ASA I and ASA II grade adult patients, aged 20-60 years with no history of PONV in previous surgery, motion sickness, Ryle's tube in situ in the past 24 hours undergoing elective surgeries under general anaesthesia in Bapuji Hospital attached to J.J.M. Medical College, Davangere. Patients with renal impairment and hepatic disease, neurological and endocrinal abnormalities, those who were pregnant and lactating, were excluded.

Patients were allocated randomly to receive one of the two treatment regimens (100 each):

Group A: Group which received injection ondansetron 4 mg intravenously

Group B: Group which received injection ondansetron 4 mg and injection dexmethasone 8 mg intravenously

A randomisation list was prepared using a mechanical randomisation device. Injection ondansetron 4 mg intravenously or injection ondansetron 4 mg plus injection dexamethasone 8mg intravenously was given in group A and group B patients respectively 30 seconds prior to induction. This was followed by injection pentazocine 0.5 mg/kg i.v. as an analgesic. No premedication was given. After preoxygenation for 3 minutes, general anaesthesia was induced with injection thiopentone sodium (2.5%) 3-5 mg/kg i.v. along with injection atropine 0.02 mg/kg i.v. Relaxation was obtained by giving injection scoline 2 mg/kg i.v. and either nasotracheal intubation or orotracheal intubation was done. Anesthesia was maintained with nitrous oxide, oxygen, halothane (0.5-1%) and controlled ventilation with muscle relaxant injection vecuronium 0.05 mg/kg i.v. The patient's vital parameters like pulse, blood pressure, oxygen saturation (SpO_2) were monitored throughout the surgery.

Once the surgery was completed, nitrous oxide and halothane were discontinued. Thorough suctioning of the mouth and throat were carried out, neuromuscular blockade was reversed with neostigmine 0.05 mg/kg i.v. and injection atropine 0.02 mg/kg i.v. The patient was laid on the lateral position and extubated. Patients were shifted to the recovery room for further observation. Duration of surgery was noted. Nausea, retching and vomiting were recorded hourly for 4 hours and then at the end of 24 hours. Any other complications were also noted.

The number of episodes of nausea, retching and vomiting were recorded. Each episode of emesis producing atleast 5 ml was recorded. Repeated vomiting within a 1-2 minute period was recorded as a single emesis. The data were taken as follows (0,None ;1episode ,Mild;2 episodes ,Moderate;3 episodes, Severe).Similarly the number of episodes of nausea and retching were also registered and the data recorded as follows (0, None; 1episode, Mild; 2 episodes, Moderate; 3 episodes, Severe).

Nausea was defined as a subjectively unpleasant feeling associated with the awareness of the urge to vomit. Vomiting was defined as an actual physical phenomenon of the forceful expulsion of gastric contents from the mouth. Rescue antiemetic consisted of injection metoclopramide 0.15 mg/kg i.v. and was given for more than 2 episodes of vomiting.

The data are expressed as distribution of cases with corresponding number of episodes of nausea, retching, vomiting and need for rescue antiemetic. Incidence of study results were analyzed by student's "t" test and categorical data was analyzed by chi-square test. The level of significance was taken as $p < 0.05$- Significant, $p > 0.05$- Insignificant.

RESULTS

The study enrolled 100 patients in each group. There were no significant differences between the two groups in patient characteristics & surgical procedures (Table 1 & 2).

Incidence of early and delayed nausea was statistically highly significant (20% vs. 59%, $P < 0.001$) and significant (20% vs. 42%, $P < 0.001$) respectively in ondansetron/dexamethasone combination group compared to ondansetron

group. Incidence of early and delayed vomiting was not significant (11% vs. 20%, P >0.05) and highly significant (3% vs. 36%, P < 0.001) respectively in ondansetron/dexamethasone combination group compared to ondansetron group. The use of rescue medications was statistically highly significant (4% vs. 32%, P < 0.001) in ondansetron/dexamethasone combination group compared to ondansetron group (Table 3, Graph 1 & 2).

There were post operative side effects such as diarrhea, headache and flushing of face, but they did not differ significantly between the two groups (Table 4).

Table 1. Patient Characteristics and Duration of Surgery

Group	Group A	Group B	P value
n	100	100	
Age(yrs)	29.5 (20- 60)	30.9 (20- 60)	0.13
Sex	Male 55 Female 45	Male 57 Female 43	0.88
Duration of Surgery (mins)	50.55±23.4	48.3±21.9	0.48

Table2. Types of surgeries performed

Type Of Surgery	Group A	Group B
Appendicectomy	4	4
Fibroadenoma excision	9	9
Hemithyroidectomy	5	5
Keloid excision	6	6
Lipoma excision	6	5
Lymph node excision	3	2
Mastoidectomy	9	9
ORIF fracture both bone forearm	6	7
Polypectomy	5	5
Sebaceous cyst excision	8	11
Septoplasty	9	10
SMR	6	5
Thyroglossal cyst removal	5	4
Tonsillectomy	19	18

P > 0.05, not significant

Table3. Incidence of Post operative Nausea and Vomiting (PONV) and Need for Rescue Medications

Group	Group A (%)	Group B (%)	P Value
Early			
Nausea			
No Episode	41 (41)	80 (80)	<0.001
Mild	51 (51)	20(20)	
Moderate	8 (8)	0	
Severe	0	0	
Vomiting			
No Episode	80(80)	89(89)	
Mild	14(14)	10(10)	>0.05
Moderate	2(2)	1(1)	
Severe	4(4)	0	
Delayed			
Nausea			
No Episode	58(58)	80(80)	<0.01
Mild	29(29)	12(12)	
Moderate	13(13)	8(8)	
Severe	0	0	
Vomiting			
No Episode	64(64)	97(97)	
Mild	6(6)	0	<0.001
Moderate	30(30)	3(3)	
Severe	0	0	
Rescue Medications			
Required	32	4	<0.001
Not required	68	96	

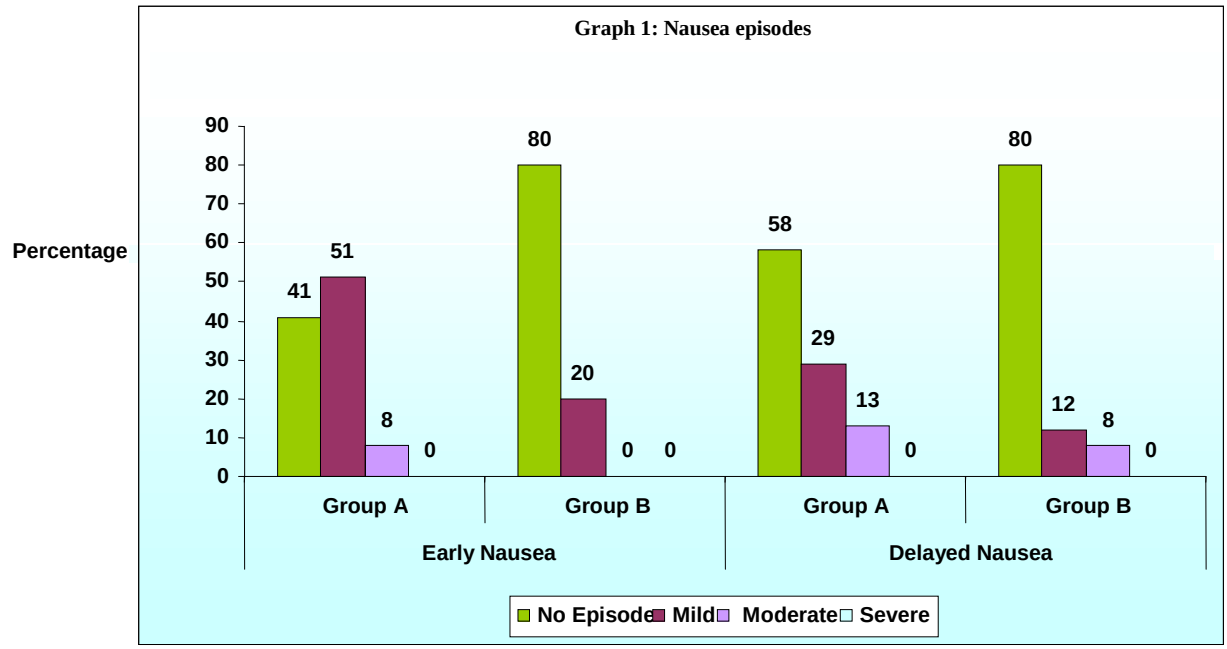
** Chi Square Test; P > 0.05, not significant; P<0.01, Significant; P<0.001, Highly Significant*

Table 4: Side effects

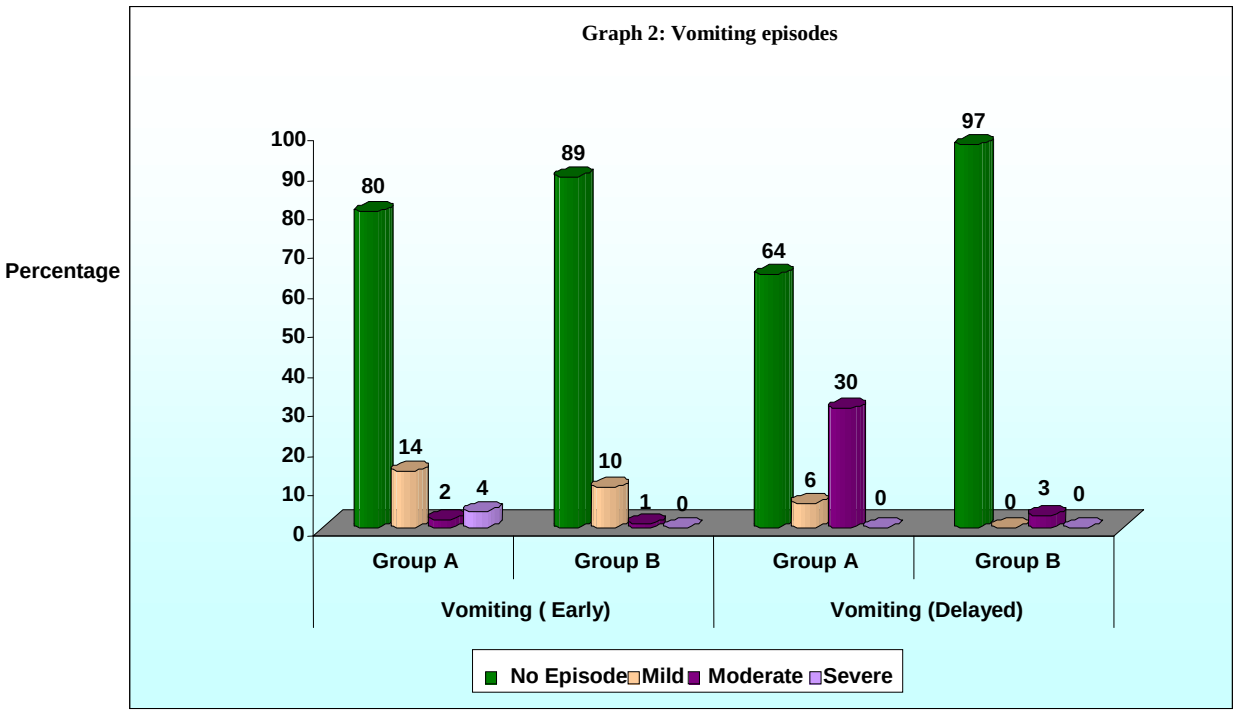
	Group A (%)	Group B (%)	P* Value
Diarrhoea	3 (3)	1 (1)	P>0.05
Headache	8 (8)	5 (5)	
Flushing of face	0	2 (2)	

** Chi Square Test; P > 0.05, not significant*

Graph 1: Nausea episodes



Graph 2: Vomiting episodes



DISCUSSION AND CONCLUSION

PONV is a complication that causes discomfort & dissatisfaction in patients who undergo surgery. It is affected by factors related to surgery, anesthesia & the patient. [6] Our study demonstrated significant difference between the ondansetron/dexamethasone combination and ondansetron alone in both early and delayed nausea. 59% patients experienced early nausea and 42% patients experienced delayed nausea in ondansetron group, while 20% of patients had early as well as delayed nausea in ondansetron/dexamethasone combination group suggesting that a

combination has some benefit over individual drug. Our present study was comparable to the study of Rajeeva et al. [7] Fewer patients in combination group had late nausea similar to finding of Lopez et al, [8] where only 12% of patients in combination group had delayed nausea as compared to 38% in the ondansetron group. Our study did not correlate with that of Rusch D et al, [9] where there was no difference between the two groups. Perhaps the difference in their study was due to inclusion of large number of subjects and variability in surgeries conducted. Patients in our study groups experienced more nausea probably because of usage of pentazocine as premedication.

Our study was comparable to Rajeeva et al [7] which demonstrated 20% and 36% incidence of early and delayed vomiting respectively in ondansetron group. In the combination group of our study, incidence of early and delayed vomiting was found to be 11% and 3% respectively and was also comparable to Rajeeva et al [7] study, but does not agree with Lopez et al, [8] where no patient vomited in early period but only 4% patients had vomiting episodes by 24 hours. In their study patients were undergoing major gynaecological surgery of longer duration than in our study, which may explain their results. It also did not correlate with the study of Rusch D et al [9] in which the incidence of postoperative vomiting was similar in both groups, 11% in the ondansetron group and 7% in ondansetron plus dexamethasone group. This may be because their study was done in only high risk groups and included a large number of patients.

Sanchez –Ledesma et al [10] study stated that a complete response (70%) defined as no nausea and no emetic episode occurred in patients who received ondansetron and dexamethasone and was comparable to our ondansetron/dexamethasone combination group (76%).

A wide dose range study [11] of dexamethasone (2-16 mg) has been used in the management of PONV and emesis related to chemotherapy and after paediatric [12] and gynaecological surgeries.[13] Dexamethasone 8 mg was used most widely and found to be most cost effective and was the reason behind our selection for the present study.

In our present study, 32% of patients in group A required rescue antiemetic compared to 4% of patients in group B and was statistically significant. This was comparable to the study conducted by Rusch et al [9] who showed that patients who were given combination of ondansetron and dexamethasone required less antiemetic. It also correlates with the study of Lopez-oleando et al [8] who showed that fewer patients in the combination group needed antiemetic rescue than patients treated with ondansetron 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. [9] It also correlates with the study of Thomas R et al [13] whose study reported that most frequent adverse events were fatigue, headache, dizziness, but there was no differences between groups. Furthermore, study by Gan TJ et al [14] has found that adverse events have not been noted after a single bolus dose of dexamethasone.

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.

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