ORIGINAL ARTICLE

EFFICACY OF ONDANSETRON ALONE AND ONDANSETRON PLUS DEXAMETHASONE IN PREVENTING NAUSEA AND VOMITING AFTER MIDDLE EAR SURGERY

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Background: Post-operative nausea and vomiting is one of the most frequently occurring side effects affecting one third of the cases. Objective of the study was to compare the efficacy of ondansetron alone and ondansetron plus dexamethasone in preventing postoperative nausea and vomiting after middle ear surgery. **Methods:** This randomized controlled trial was conducted at the Anaesthesia and ENT departments of Ayub Medical College, Abbottabad from January-June 2012. Forty American Society of Anaesthesiologists (ASA) I and 2 physical status patients undergoing middle ear surgery were divided into two groups by blocked randomization. Patients in group-1 (n=20) received ondansetron 4 mg while group-II (n=20) received ondansetron 4 mg with dexamethasone 8 mg just before start of operation. The whole postoperative period of 24 hours was divided into two phases, early 0–6 hours and late phase 6–24 hour. **Results:** Nausea score and its frequency was significantly higher in Group-I ($p<0.05$). Vomiting and its frequency were found more in group-I patients. In Group-II, the nausea score was significantly less ($p<0.01$) at 6 and 24 hours after surgery. The total incidence of vomiting was reduced from 28% in group-1 to 6% in group-II. Rescue antiemetic requirement was significantly less ($p<0.01$) in group-II. **Conclusion:** Prophylaxis with a combination of ondansetron and dexamethasone decreased the incidence of nausea and vomiting after middle ear surgery.

Keywords: Nausea and vomiting, Middle ear surgery, Dexamethasone, Ondansetron

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INTRODUCTION

Postoperative nausea and vomiting (PONV) is defined as nausea and vomiting occurring within 24 hours after surgery. It is one of the most frequently occurring side effects affecting one third of the cases (25–30%) with a relatively high incidence (62–80%) after middle ear surgery.[1–4] Nowadays it is a major concern for the patients and physicians in the postoperative period.[5]

Previous studies found that the incidence of PONV as high as 80% in patients undergoing general anaesthesia for middle ear surgery when no prophylactic antiemetic was given.[1–4] This incidence may justify the use of prophylactic anti-emetics for the prevention of PONV after middle ear surgery. Persistent vomiting is costly in terms of both financial burden and potential medical sequelae.[6–8] The cause of postoperative vomiting in middle ear surgeries is thought to be multifactorial with patients' characteristics, anaesthetic medications, surgical manipulations, and postoperative care all hypothesized to contribute.[7,8] In response to this "Big 'Little' Problem"[9], multiple studies have investigated the effects of newer anaesthetic agents and antiemetic prophylaxis on postoperative vomiting. In general, the results of these studies have been mixed. Marginal improvements, unfavourable adverse effect profiles, and high costs have limited the universal adoption of any single protocol.[10]

Dexamethasone was first reported to be an effective antiemetic drug in patients receiving cancer chemotherapy. Recently, dexamethasone has been found to have a prophylactic effect on postoperative nausea and vomiting in adults undergoing middle ear surgery.[4,11,12] Ondansetron is a carbazalone derivative that is structurally related to serotinin and possess specific 5-HT3 subtype receptor antagonist properties, without altering dopamine, histamine, adrenergic or cholinergic receptor activity. There are numerous studies on the efficacy of ondansetron for prevention of PONV.[4]

Tramer *et al*[13] reported that for every 100 patients at high risk for PONV who receive ondansetron for the prevention of PONV, 20 patients will not vomit who would have vomited without treatment. The optimal prophylactic intravenous dose of ondansetron was likely to be 8 mg for long term efficacy. Its antiemetic efficacy is consistently better than its anti nausea efficacy. Watcha and White re-analyzed data used by Tramer *et al* and found that the absolute success rates for prophylaxis with ondansetron 4 mg and 8 mg did not significantly differ for the separate incidences of nausea and vomiting.[14]

This study aimed at comparing the incidence and frequency of PONV and the need of additional rescue antiemetic in ondansetron group and ondansetron plus dexamethasone group in early and late postoperative period.

MATERIAL AND METHODS

This randomized controlled trial (RCT) was conducted at the Anaesthesia and ENT Departments of Ayub Medical College, Abbottabad, from January–June 2012. Informed consent was obtained from all patients after explaining the merits and demerits of both interventions to the patients. Hospital Ethical Board had accorded approval to the study. The inclusion criteria were ASA-1 ASA-2 physical status of either sex between 20–40 years of age undergoing middle ear surgeries. The exclusion criteria were patients who received anti-emetics within 24 hours before surgery and allergy to any anaesthetic drug, allergy to dexamethasone or ondansetron, pregnant or patients having any medical illness. During preanaesthetic assessment one night before the start of operation all patients were taught about standard four-point ordinal scales for nausea and were requested for their cooperation in accounting nausea and vomiting. Patients were not allowed to have solid/liquid food after midnight before surgery. Patients were pre-medicated with tablet Alprazolam 0.5 mg in the night before surgery.

Patients were randomly assigned to one of the two study groups (20 in each group) through blocked randomization. Patient in Group-I received ondansetron 4mg. Patient in Group-II received ondansetron 4mg with dexamethasone 8 mg intravenously. Personnel not involved in the study prepared identical syringes containing the study drug(s). The drugs were administered intravenously (IV) slowly just before induction of anaesthesia by the anaesthetist who was blinded to the nature of the drug in the syringe. Injection nalbin 10 mg IV was used for analgesia. Anaesthesia was induced with Propofol 2 mg/kg IV, and Succinylcholine 1.5 mg/kg IV was used to facilitate tracheal intubation with cuffed orotracheal tube. Anaesthesia was maintained with isoflurane in oxygen. After operation, patients received diclofenac 75 mg IM if they complained of moderate to severe pain. The postoperative period was divided into early (1st 6 hours) and late (6–24 hours) postoperative period. Patients were monitored for nausea, vomiting and the need for additional rescue antiemetic in postoperative period in the two groups. Mild or severe vomiting was counted as an episode of vomiting, irrespective of the severity. If events of vomiting were separate by >1 min, they were considered separate episodes. Nausea was measured by using standard four-point ordinal scales (4POSS) which is divided from 0–3 scores. Severe nausea (about to vomit) received scores 3, moderate nausea (nauseated without urge to vomit) got scores 2, mild nausea got score 1 and no nausea got 0 score. If two or more episodes of vomiting occurred during the first 24h after anaesthesia, rescue antiemetic injection metoclopramide 10 mg IV was given. Data was analysed using SPSS-16. Chi-square test and t-test were used to determine statistical significance for categorical and quantitative outcome variables respectively at 5% level of significance.

RESULTS

There were 20 patients in both groups each. General characteristics of patients in relation to age, weight and sex, type of surgery, duration of surgery and anaesthesia, total amount of opioid used, intra-operative and postoperative haemo-dynamics which may modify PONV were comparable in the two groups.

In group-I, 9 patients (45%) had nausea and in group-II 4 patients (20%) had nausea. Nausea was found more with the patients in group I, but it was statistically not significant (p>0.05) as shown in Table-1. In groupI total 4POSS was 36 with mean of 1.8±2.4 whereas in group-II it was 10 with mean of 0.5±1.1 with p<0.05 (Table-2)

Total frequency of nausea in group-I was 15 times with mean of 0.75 and in group-II 5 times with mean of 0.25. Frequency of nausea was significantly more in group-I (p<0.05) as shown in Table-3. In group-I frequency of vomiting was 9 times with average of 0.45 and in group-II it was 1 with mean of 0.05. Frequency of vomiting was significantly more in group-I (p<0.05) as shown in Table-2.

Vomiting was found more in patients of group-I with a statistically significant difference with p<0.05 (Table-3).

In both groups nausea scores (4POSS) in early postoperative period and late postoperative period had no statistically significant difference as shown in Table-4 that also gives an account of data of frequency of vomiting in early and late postoperative periods.

In group-I, 3 patients (15%) received rescue antiemetic drug and in group-II, none of the patient received rescue antiemetic drug. Statistically there is no significant difference in between these two groups.

Table-1: Incidence of nausea in two study groups within 6 hours

Study group	No of patients with nausea	Percentage (%)	X^2 value	p-value
Group 1	9	45		
Group II	4	20	2.84	0.09*
Frequency of vomiting				
Group 1	9	45		
Group II	1	5	8.53	0.003*

*Statistically significant

Table-2: Nausea score & Frequency of vomiting in two study groups within 6 hours

Study group	**Number**	Mean(±SD)	***t*-value**	***p***
4 POSS				
Group 1	36	1.8 (±2.41)		
Group II	10	0.5 (±1.1)	2.2	<0.05

*Statistically significant

Table-3: Frequency of nausea and incidence of vomiting in two study groups in 6-24 hours

Group	No of patients	Percentage	$\chi 2$ value	*p*
Nausea				
Group 1	15	75		
Group II	5	25	10.0	0.0018*
Vomiting				
Group 1	6	30		
Group 1I	1	5	4.32	0.037*

*Statistically significant

Table-4: Nausea score in two study groups in early (1-6 hrs.) and late post operative period (6-24 hrs.)

Study group	Post operative period		Mean (±SD)		*t*	*p*
	Early	Late	Early	Late		
4 POSS						
G-I	25	11	1.25(±1.74)	0.55(±1.27)	1.48	>0.1
G-II	8	2	0.4 (± 1.04)	0.1 (± 0.44)	1.26	>0.1

DISCUSSION

Middle-ear surgery (Tympanoplasty or mastoidectomy) is associated with a relatively high incidence of PONV. Previous studies found the incidence of PONV to be between 62% and 80% in patients undergoing general anaesthesia for middle-ear surgery.[2,3] The aetiology of PONV after middle-ear surgery is complex and depends on several factors, which include patient characteristics, types of surgery, anaesthetic drugs and technique and postoperative pain.[11,15]

Middle ear surgery is associated with a high risk for PONV, because the operation may stimulate the vestibular labyrinth, which is innervated by the vestibular portion of cranial nerve VIII (vestibule-cochlear), which in turn activates the chemoreceptor trigger zone (CTZ) in the area postrema.[15] Stimulation of the parasympathetic nerves of pinna during surgical manipulations may induce PONV.[16]

There are different types of drugs, which have been used to prevent PONV. In a recent meta-analysis it was concluded that, it is very likely that the best prophylaxis of postoperative nausea and vomiting (PONV) currently available is by combining dexamethasone with a selective 5-hydroxytryptamine type 3 (5-HT3) receptor antagonist. Such combinations are both safe and efficacious in paediatric, obstetric, breast, middle ear, and other surgery associated with a high risk of PONV.[17]

Results of our study with regard to incidence of nausea and its score are similar to other studies.[1,12,18–20] These studies also found that the nausea score was significantly less in patients receiving combination of ondansetron and dexamethasone than in patients receiving ondansetron alone as an antiemetic drugs.

Vomiting was found significantly more with patients in group-I ($p<0.05$) which is comparable to the studies.[12,19,20] In a study by Panda *et al* (2004)[18], they found that the total incidence of vomiting was reduced from 28% in ondansetron group to 6% in ondansetron and dexamethasone combination group. The result came out to be similar though in their study, antiemetic drugs were administered 30 minutes before the end of surgery whereas in our study the drugs were administered just before the induction of anaesthesia.

In our study, in both the groups there was no significant difference in nausea score and frequency of vomiting in early and late post operative period. The study done by Fujii *et al* (1998)[1] is comparable to our study although they have used granisetron, other generation 5HT3 antagonist. Similarly Eydi M, Hossainzadehi H in 2011 in Iran conducted a study on PONV after middle ear surgery comparing dexamethasone and ondansetron and found both effective when given preoperatively than placebo.[21] Thomas and Jones (2001)[17] found incidence of nausea and vomiting significantly less in the group with the combination of ondansetron and dexamethasone than in ondansetron group in early post-operative period, but in late post-operative period there was no significant difference in the incidence of nausea and vomiting between the groups. In contrast, in our study, there was no significant difference in the incidence of PONV in early and late post operative period. This could be due to the use of nalbin in our study a longer acting drug than fentanyl, which was used in the study of Thomas and Jones.[17] The study of Rajeeva *et al*. (1998)[19], vomiting was found significantly more in the patients in late post operative period in the ondansetron group. This might be because only female gender was enrolled in their study. Incidence of PONV is higher in female gender.[4,11,22] The difference in results may be due to this. Moreover, the menstrual status of the female patients was not described in this study. In our study, in group I, 3 patients (15%) received rescue antiemetic drug and in group-II none of the patient received rescue antiemetic drug with no significant difference. Rajeeva *et al.*[19] also reported similar result in their study. But López-Olaondo *et al.*[12] and Panda *et al.*[18] in their studies, observed that rescue antiemetic requirement was significantly less in patients receiving combination of ondansetron and dexamethasone than in patients receiving ondansetron alone. The total number of patient was 40 in our study and 51 in the study of Rajeeva *et al.*[19] whereas López-Olaondo *et al.*[12] and Panda *et al.*[18] had 100 patients in their studies. So this might have created the difference in the results. In our study, a single dose of 4mg of ondansetron or 4 mg of ondansetron with 8 mg of dexamethasone i.v was used without any side effects in post operative ward. Fujii *et al* (1998)[1] López-Olaondo *et al.* (1996)[12] and Thomas and Jones (2001)[17] in their studies reported adverse events like headache, dizziness and fatigue, but there were no differences between groups.

The limitations of our study are mostly due to small sample size owing to limited resources at the

disposal of researchers. The strengths are that data was rigorously collected and analysed.

CONCLUSION

Although no significant difference is observed between ondansetron alone and ondansetron plus dexamethasone, yet, ondansetron with combination of dexamethasone has better prophylactic antiemetic effect than ondansetron alone to prevent PONV after middle ear surgery under general anaesthesia.

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