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ORIGINAL ARTICLE

Low Dose Dexamethasone versus Ondansetron for Prevention of Post-operative Nausea and Vomiting after Tympanomastoid Surgery A Comparative Study

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ABSTRACT

Background: One of the most common complications after tympanomastoid surgeries are postoperative nausea and vomiting (PONV). PONV may lead to undesirable adverse effects. Many anti-emetics have been studied for prevention of PONV. The aim of this work is to assess the effect of a low dose of dexamethasone on avoidance of PONV after tympanomastoid surgeries and to compare it with ondansetron.

Methods: This comparative prospective randomized double-blind clinical survey was performed on 30 patients scheduled for elective tympanomastoid surgeries. They were classified into two equal groups; one of them received 5 mg of dexamethasone IV (group D) and the other received 4 mg of ondansetron IV (group O) just after giving anesthesia induction. The prevalence and intensity of PONV were assessed in all patients using Bellivelle's scoring system.

Results: Statistically, the incidences and severity of PONV in group O and in group D were comparable.

Conclusions: There was no significant difference between the effects of IV administration of low dose of each of dexamethasone (5 mg) and ondansetron (4 mg), just after induction of general anesthesia on the incidence and severity of nausea and vomiting after tympanomastoid surgeries and the associated side effects.

Key words: Postoperative; Ondansetron; Dexamethasone; Vomiting; Tympanomastoid.

INTRODUCTION

Postoperative nausea and vomiting (PONV) is known as the nausea and vomiting in patients that occurred after any surgical operation. PONV could start from post-anesthesia care unit (PACU) to the initial hours of assigning the patients to the ward. PONV could occur without any distinctive cause like hypotension [1].

The occurrence of PONV has been shown to vary from 20 to 30 % after numerous surgical procedures and in several methods of anesthesia. Indeed, it has been reported that PONV is the second commonest postoperative complaint [2]. It results in several undesirable outcomes such as; administration of numerous treatment modalities, delayed discharge from the hospital, unexpected hospitalization and patient dissatisfaction. Moreover, it has been reported that PONV occurs in an incidence of 50 to 80 % of patients undergoing tympanomastoid surgeries [3].

Dexamethasone is reasonably priced and has no threatening side effects when used in patients experiencing throat, nose and ear surgical operations and ear. However, if it is used over a longer period than few days, the common side-effects to systemic glucocorticoids could occur [1]**.** The antiemetic characteristics of glucocorticoids are well-known. However, the mechanism of dexamethasone and methylprednisolone as an antiemetics is not well known [4]**.**

Ondansetron is known as a serotonin 5-Hydroxytryptamine 3 (5-HT3) receptor antagonist. Its major utilization is the prevention of vomiting following chemotherapy. The influences of ondansetron are assumed to be on both the central and peripheral nerves. Ondanestron diminishes the vagus nerve activity, which inhibits both the serotonin receptors in chemoreceptor trigger zone (CTZ) and vomiting center in medulla oblongata [1]**.**

Since 1990s, the development of 5-HT3 receptor antagonists progressed the antiemetic therapy protocol. The impact of 5-HT3 receptor antagonists to decrease PONV is substantial. Ondansetron is the primary medicine announced

in this group. The clinical dose of the drug is 4-8 mg, which is usually safe and does not have any side effects [1].

The aim of the present study is to estimate the effect of small dose of dexamethasone on avoidance of PONV after tympanomastoid surgeries and to compare it with ondansetron. The primary outcome is complete response to the studied antiemetic drugs, while the secondary outcome is patients' satisfaction.

METHODS

An approval from the scientific committee of anesthesia department and the institutional review board (IRB) was obtained from faculty of medicine, Zagazig University. Written informed consent was attained from all patients. The comparative prospective randomized double-blind clinical study has been carried out in ear, nose and throat department of zagazig university on 30 patients. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

The Sample size measured assuming that percent of nausea and vomiting of group D (low dose dexamethasone) is 10% and of group O (ondansetron) is 60%, so the sample size is 30 divided in 2 groups (15 in each group) using open Epi info by means of power of test 80% and Confidence Interval 95%.

Patients were divided into two groups by means of computer created randomization table: Group D: 15 patients received 5 mg dexamethasone IV, Group O: 15 patients received 4 mg of ondansetron.

The Inclusion criteria for the patients were as follow ; 21-50 years old patients, male or female, American Society of Anesthesiologists (ASA) physical status class I and II undergoing elective unilateral tympanomastoid surgeries under general anesthesia, body weights ranged from 70-95 kg.

The excluded criteria were *Patient refusal, patients with hypersensitivity to one of the used* drugs, patients received antiemetics 48 hours before surgery, diabetes mellitus, hypertension, renal failure and patients with gastrointestinal disorders. As well, patients with preceding history of PONV, duration of surgery more than 4 hours, opioids or steroids within one week before operation and patients on antidepressants.

All patients were visited in anesthesia clinic and were informed in details the anesthetic procedure. Informed consent was signed and full history was taken. All patients were kept nil orally before the operation (8 h for greasy meals, 6 h for light meals and 2 h for fluids). No premedications were administered for the patients.

On entry to the operating room, standard monitoring was applied to all patients. It includes pulse oximeter, arterial non-invasive blood pressure (NIBP) and electrocardiogram (ECG). The baseline reading of heart rate (HR), mean arterial blood pressure (MAP) and arterial oxygen saturation were record.

Anesthesia has been induced by IV propofol (2-2.5 mg/kg), 50- 100 Ug fentanyl citrate and cis-atracurium (0.1-0.2 mg/kg) to facilitate endotracheal intubation. After tracheal intubation, groups D and O have received 5 mg (1 ml) dexamethasone IV and 4 mg (2 ml) ondansetron IV, respectively.

Anesthesia was maintained by 1.2 mean alveolar concentrations (MAC) of isoflurane in oxygen. Ventilation was generally controlled mechanically and adjusted to maintain an end-tidal extent of carbon dioxide between 35 to 45 mm Hg. Muscle relaxation maintenance has been attained by intravenous cis-atracurium (0.03 mg/kg) periodically every half an hour.

During operation, MAP, HR and oxygen saturation have been recorded every 15 min.

At the end of surgery, isoflurane was discontinued. The reversal of muscle relaxant was done using neostigmine methylsulfate and atropine with (0.05 mg/kg) IV and (0.02 mg/kg) IV, respectively, for antagonism of neuromuscular block. The patient was extubated after suction of any secretions in airway.

Paracetamol (15 mg/kg with dose not exceeding 1 gm per day) was given just after the surgery as an analgesia for all patients.

Patients were followed up postoperatively for 4 hours, throughout the follow up period, MAP, respiratory rate (RR) and HR were recorded every half an hour.

Nausea and vomiting were evaluated for 24 hours as stated by the following aspects: incidence of nausea and vomiting, frequency, severity as well as the complete responses for antiemetics.

For the purpose of data collection, retching has been considered vomiting. A vomiting episode can be defined as the vomiting events that occurred at a fast sequence (< 1 min between events). If vomiting events were separated by >1 min, they were considered as separate episodes. The frequency of vomiting episodes has been identified by recording vomiting episodes for 24 h after the operation [3].

The severity of vomiting has been assessed by the Bellville scoring scale. That

includes, the lack of nausea and vomiting = 0, nausea=1, nausea with belching = 2, and vomiting = 3 [1,5].

If vomiting occurs in excess of 4 times throughout 24 hours, it can be considered as severe vomiting. If the severe vomiting has been occurred, rescue antiemetics with 10 mg metoclopramide hydrochloride intravenous must be given. However, the treatment may be repeated if necessary [3].

However, the complete response to antiemetics can be defined as no vomiting, nausea and antiemetics during 24-hour post-operative period. This was also considered as the main effectiveness end point of this study.

Data on nausea and vomiting were recorded every 4 hours. Side effects of both drugs were detected and recorded; The increase in blood sugar more than 200 mg/dl, bradycardia (heart rate was < 20% from patient baseline).

STATISTICAL ANALYSIS

Data collected were coded and entered then it can be analyzed by means of Microsoft Excel software. The collected data were then inserted into Statistical Package of Social Sciences (SPSS version 20.0) software for more analysis. Qualitative data have been exemplified as number and percentage. Quantitative data were presented as mean ± SD. To test the differences for significance, the variance and association of qualitative variable have been clarified by Chi square test (X2). Variances between independent quantitative multiple groups are assessed by (ANOVA) analysis of variances. Lastly, P value has been fixed at < 0.05 for substantial difference and less than 0.001 for high substantial difference.

RESULTS

Statistically, the patients' demographic data (Age, weight, sex ratio, ASA ps classes I&II) and duration of surgery and anesthesia in both tested groups were comparable (Table 1).

The incidences of postoperative vomiting in both tested groups were comparable as seen at (Table 2).

Intensity of postoperative vomiting (postoperative vomiting severity scores) in both tested groups were comparable in (Table 3).

The incidence of complete response to antiemetics and need for rescue antiemetics in both tested groups were comparable (Table 4).Only one case (6.7 %) in group D, while no one in group O needed rescue antiemetics with no significant difference between the studied groups.

Regarding the hemodynamics and respiratory values; Statistically, the mean arterial blood pressure, heart rate, respiratory rate, and SpO2 values at the various times of measurements in both tested groups were comparable (Table 5).

No complications for drugs was recorded in both groups and there was no significant difference regarding the blood glucose levels of the studied groups (table 6).

Table (1) :Patients demographic data, duration of surgery and anesthesia in both tested groups

		Group D n = 15	Group O n = 15	F	P
Age (years)		30.86±6.36	33.46±7.9	0.98	0.33
Sex	Male	8	3	4.2	0.12
		53.3%	20.0%		
	Female	7	12		
		46.7%	80.0%		
Body weight (Kg)		74.34±2.13	75.26±3.52	0.847	0.404
ASA ps classes	ASA ps Class I	9	7	0.54	0.46
		60%	46.7%		
	ASA ps class II	6	8		
		40%	53.3%		
Duration of surgery (min)		152.33±40.31	167.33±31.67	1.1333	0.267
Duration of anesthesia (min)		165±40.88	181±34.24	1.1621	0.255

*Group D: Dexamethasone group.
*Group O: Ondansetron group.
*ASA ps: American Society of Anesthesiologists physical status.
Data of age, body weight, duration of surgery and anesthesia were expressed as mean ± standard deviation (SD).
Data of sex and ASA classes were expressed as numbers and percentages.
With F-test and P-value statistically used.

P value < 0.05 was considered statistically significant otherwise it was insignificant.

Table (2) :The Incidence of postoperative vomiting in both tested groups.

			Group		Total	X2	P
			Group D n = 15	Group O n = 15			
Vomiting	Yes	N	3	1	4	1.302	0.25
		%	20.0%	6.7%	13.3%		
	No	N	12	14	26		
		%	80.0%	93.3%	86.7%		

*Group D: Dexamethasone group.
*Group O: Ondansetron group.
Data were expressed as numbers and percentages.
With chi square and P-value statistically used.
P value < 0.05 was considered statistically significant otherwise it was insignificant.

Table (3): Severity of postoperative nausea and vomiting in the patients of both tested groups.

			Group		X2	P
			Group D n = 15	Group O n = 15		
Vomiting score	No	N	9	11	3.3	0.34
		%	60.0%	73.3%		
	Nausea	N	6	2		
		%	40.0%	13.3%		
	Nausea + bleching	N	1	2		
		%	6.7%	13.3%		
	Vomiting	N	3	1		
		%	20.0%	6.7%		

*Group D: Dexamethasone group.
*Group O: Ondansetron group.
Data were expressed as numbers and percentages.
With chi square and P-value statistically used.
P value < 0.05 was considered statistically significant otherwise it was insignificant.

Table (4) :The incidence of complete response to antiemetics in both tested groups.

			Group		**Total**	**X^2**	**P**
			Group D n = 15	Group O n = 15			
Complete response to antiemetics	Yes	N	9	11	20	0.6	0.44
		%	60%	73.3%	66.7%		
	No	N	6	4	10		
		%	40%	26.7%	33.3%		

*Group D: Dexamethasone group.
*Group O: Ondansetron group.
Data were expressed as number and percentages.
With chi square and P-value statistically used.
P value < 0.05 was considered statistically significant otherwise it was insignificant.

Table (5): Mean arterial pressure, heart rate, respiratory rate and SpO2 values at various times of measurements in both studied groups.

	Group D n = 15	Group O n = 15	F	P
MAP before induction	92.2±6.68	91.93±7.54	0.0105	0.919
MAP during operation	75.58±9.579	74.57±8.446	0.0972	0.939
MAP postoperative	92.33±1.311	92.69±1.567	0.239	0.908
HR before induction	78.67±7.67	77.67±7.04	0.138	0.712
HR during operation	73.85±5.301	71.86±2.655	1.6807	0.205
HR postoperative	80.83±1.359	81.51±0.951	1.323	0.269
SpO_2 during operation	99±0	99±00	.	.
RR postoperative	13.54±0.149	13.612±0.191	0.549	0.471

*Group D: Dexamethasone group. *Group O: Ondansetron group.
*MAP: Mean arterial pressure. *HR: Heart rate.
*SpO_2: Oxygen saturation. *RR: Respiratory rate.
Data were expressed as mean ± standard deviation (SD).
With F-test and P-value statistically used.
P value < 0.05 was considered statistically significant otherwise it was insignificant.

Table (6): Blood glucose (in mg/dl) in both tested groups.

	Group C	Group D	F	P
Bl glucose	136±11.05	139.07±12.19	0.5	0.49

*Group D: Dexamethasone group.
*Group O: Ondansetron group.
Data were expressed as mean ± standard deviation (SD).
With F-test and P-value statistically used.
P value < 0.05 was considered statistically significant otherwise it was insignificant.

DISCUSION

The main finding of this study is that PONV was less in group O. But it is important to note that there is no significant difference has been found between the two groups concerning incidence of PONV.

In the present study, the anti-emetics were given just after induction of anesthesia. There is an existent conflict as to the most suitable time of ondansetron and dexamethasone administration to decrease incidence of PONV. **Wang et al.,** [6] revealed that the given dexamethasone is a more effective antiemetic before induction of anesthesia than that used at the end of surgery. **Isik et al.,** [7] in their study administered ondansetron after the ending of skin surgically, while dexamethasone was given after anesthesia induction.

In the present study, it was observed that, there was no significant difference between the blood glucose levels of the studied groups. **Waldron et al.,** [8] reported a meta-analysis and systematic review on forty-five studies involving 5796 patients receiving dexamethasone 1.25–20 mg. They established that the levels of blood glucose were higher at 24 h.

In the present study, no significant difference was found between the incidence of PONV in both tested groups. In agreement with the present study finding, **Erhan et al.,** [9] reported that, prophylactic IV administration of 8 mg of Dexamethasone before induction of anaesthesia, was as effective as 4 mg of ondansetron and 3 mg of granisetron, in reduction of PONV and it was more effective than placebo. In contrast to the present study finding, **Eidi et al.,** [1] performed a study on 219 patients divided into 3 groups , group D received 8 mg of dexamethasone while group O received 4 mg of ondansetron and group C was control group received distilled water, they reported that the incidence and severity of PONV were significantly lower in group D and O than in group C. They also found that, the incidence of PONV was significantly less in group D than that in group O.

Gupta, [10] established that intravenous dexamethasone and ondansetron showed equal results regarding PONV prevention. Furthermore, **Munoz et al.,** [11] achieved a prospective study on 120 adult patients donating PONV in the PACU. They established that the short-term efficiency of dexamethasone to treat PONV was comparable to ondansetron, but inferior to droperidol. Also, **Bolton et al.,** [12] performed a systematic review and meta-analysis on 92 studies. They confirmed that dexamethasone was

a slightly more effective in avoiding post-tonsillectomy PONV than ondansetron.

Based on previous studies, one could propose that the dissimilarity in the findings of these studies might be caused by the following parameters: the type of surgical operations, the wide range of variances in patient's qualities as well as the sample sizes and anesthetic techniques. Moreover, the way that PONV was studied and defined could affect the results. However, it has been reported that the most imperative parameters affected the findings of all is the dosage of antiemetic drugs as well as the timing of their administration [11,13].

In our study the intensity of vomiting was evaluated by the Bellville scoring scale [1,5]. On the other hand, **Isik et al.,** [7] used another scoring system called NVS score. According to NVS scoring system, 0 for patients with no complaint, 1 for patients with mild degree of nausea whereas 2 for patients with moderate degree of nausea, 3 for patients with frequent vomiting and 4 for patients with continuous vomiting.

We established that nausea occurred in 40 % and 13.3 % of group D and O respectively, nausea was significantly higher in Group D. Nausea with bleching occurred in 6.7 % and 13.3% of group D and O respectively. Vomiting occurred in 20 % and 6.7 % of group D and O respectively, while according to **Eidi et al.,** [1] There were only few cases of nausea during 0-2 hours. These few cases showed none significant difference between the three groups. However, there were few of cases of nausea and nausea with belching during 2-8- and 8-16-hours post-operative, but no vomiting has been found. The incidence of nausea and/or nausea with belching was significantly greater in group O or D than those in control groups. Nonetheless, nausea with belching or vomiting has occurred during 16-24 hours nausea in all groups. The incidence of nausea was noticeably lower in groups O and D than that in control group.

The present study established that complete response had occurred in 60% and 73.3%, respectively, in cases of group D and O. There was no significant difference between studied groups.

Liu et al., [14] reported that complete response for anti-emetics occurred in 85 % of cases in dexamethasone and in 60 % of cases in saline group, so complete response was considerably higher in case of dexamethasone group. While in the study of **Wang et al.,** [3] complete response for anti-emetics occurred in 74%, 45% and 36% of cases in dexamethasone, tropisetron and saline groups respectively. So, dexamethasone significantly increased the incidence of complete response.

Number of cases who needed rescue antiemetics was only one case (6.7 %) in group D, while no one in group O needed rescue antiemetics with no significant difference between the studied groups. **Honkovaara,** [15] reported that the additional antiemetics were demanded in 17% of the cases experiencing middle ear surgery and administered 4 mg ondansetron. However, **Isik et al.,** [7] reported that additional requirement for antiemetic was 10% in Group O, while in Group D it was 36.7%.

Limitations for this study were limited number of cases with this inclusion criteria in zagazig university hospitals, difficulties during data collection, some cases lost during follow up so we had to replace them.

Although both dexamethasone and ondansetron were efficient in decreasing PONV, the incidence of PONV was still remarkably high. As a result, further studies would be helpful using other common drugs.

CONCLUSIONS

There was no significant difference between the effects of IV administration of low dose of each of dexamethasone (5 mg) and ondansetron (4 mg), just after induction of general anesthesia on the incidence and severity of nausea and vomiting after tympanomastoid surgeries and the associated side effects.

Declaration of interest, the authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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