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Comparison of Ramosetron and Dexamethasone for Prophylaxis of Postoperative Nausea and Vomiting in Patients Undergoing Middle Ear Surgeries

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Abstract

Background: Nausea and vomiting are common complications of anesthesia and surgery. Patients undergoing middle ear surgeries are exposed to a higher-risk of Postoperative Nausea Vomiting (PONV). These complications may alter the results of reconstruction and anatomical alignments. Numerous antiemetics have been studied to prevent and treat PONV in patients undergoing middle ear surgeries. The aim of this study is to compare the effect of ramosetron and dexamethasone for prophylaxis of postoperative nausea and vomiting in patients undergoing middle ear surgeries. *Methods:* In a randomized controlled clinical trial, 60 patients were divided into two groups, one receiving ramosetron, one receiving dexamethazone, all patients were subjected to middle ear surgeries. The patients in the Group R received ramosetron (0.3 mg IV) and the patients in Group D received dexamethasone (8 mg IV), Using Bellivelle's scoring system, the incidence of PONV and its severity during the 24-hour period after surgery were measured and compared. *Result:* The incidence rates of PONV in dexamethasone group is 89.9%, and with ramosetron group is 29.9%, which showed statistically significance (p - value < 0.0001). The incidence rate of postoperative nausea and vomiting in dexamethasone group is significantly higher than that of ramosetron group. *Conclusion:* Ramosetron 0.3 mg IV given before induction of anesthesia is an effective means of reducing PONV in middle ear surgeries. Compaed to dexamethasone 8 mg IV ramosetron 0.3 mg IV significantly reduces PONV in the immediate postoperative period. Ramosetron is suitable alternative to dexamethasone in controlling PONV

Keywords: Postoperative nausea and vomiting; Dexamethasone; Ramosetron; Middle ear surgeries.

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Introduction

Patients complain of nausea and vomiting after surgical operations, starting from recovery room to the early hours of transferring the patient to the ward, without hypotension and other complications is defined as Postoperative Nausea and Vomiting (PONV).[1] Tympanoplasty and mastoidectomy are two of the most common procedures performed in the middle ear and accessory structures.[2] In middle ear surgeries due to stimulation of the labarynth, incidence and severity of postoperative nausea and vomiting is very high.[2] Following general anesthesia with

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inhaled anesthetics, the rate of postoperative nausea and vomiting has been reported to vary (20% to 30%) and, is the second most common complaint reported following various surgical operations and in different methods of anesthesia.[3]

Ramosetron is a serotonin 5-HT_3 receptor antagonist used mainly as an antiemetic following chemotherapy.

Its effects are thought to be on both peripheral and central nerves. Ramosetron reduces the activity of the vagus nerve, which deactivates the vomiting center in the medulla oblongata, and blocks serotonin receptors in the chemoreceptor trigger zone. However, it is expensive and has some dangerous side-effects such as headaches and high blood pressure that can lead to serious complications, especially in susceptible and hypertensive patients.[1] Dexamethasone, which is used frequently in the patients undergoing ear, throat and nose surgical operations, is cheap and has no serious side-effects. If dexamethasone is given, orally or parenterally, over a period of more than a few-days, side-effects common to systemic glucocorticoids may occur. PONV has multiple causes and is influenced by a number of factors including anesthetics, surgery and individual risk-factors like smoking, anxiety and age. After the age of 50 years, the incidence of PONV decreases to about 13% in every 10 years.[5]

Ramosetron is a selective serotonin 5-hydroxytryptamine Type 3 (5-HT_3) receptor antagonist, has better inhibitory activities than other available antagonists such as ondansetron, granisetron, tropisetron.[6] Because of higher binding affinity and a slower rate of dissociation from the target receptor ramosetron is more potent and has longer-lasting antiemetic effects than older agents.[7] This class of selective 5-HT_3 receptor antagonists prevents serotonin binding to 5-HT_3 receptors at the ends of the vagal afferent branches, which directly signals the vomiting center in the medulla oblongata and in the chemoreceptor trigger zone of the brain.[7,8]

Dexamethasone has been useful in preventing and treating nausea in the patients undergoing chemotherapy, it is widely used in preventing PONV. It has been shown that given intravenously one dose (8–10 mg) of this drug is effective in preventing PONV.[9] However, postoperative nausea and vomiting remain a significant problem. This problem prompted us to compare the efficacy of ramosetron and dexamethasone in the prevention of postmiddle ear surgery nausea and vomiting.

Materials and Methods

The study is a randomized controlled clinical trial performed at Kempegowda Institute of Medical Science and Hospital, Bangalore, Karnataka, over a period of 8 months. Sixty patients with physical conditions of ASA (American Society of Anesthesiologists) I or II undergoing middle ear surgeries were divided into two groups of 30 patients each to receive ramosetron, dexamethasone, preoperatively. Simple randomized sampling procedure was carried out. Patients with digestive problems, a history of treatment with antiemetics and nausea in the preceding 24 hours, perioperative steroids as anti edema therapy or obesity (BMI > 40) were excluded from the study. A written consent was obtained from all the patients. The study was approved by the Ethics Committee. Before the induction of anesthesia, 0.3 mg of ramosetron or 8 mg of dexamethasone administered intravenously to respective groups.

The volume of the administered drug was 2 ml in the two groups. In each group, premedication was given using Midazolam at 0.15 mg/kg, Glycopyrrolate (.01 mg/kg) and Fentanyl at 1–2 μg/kg. Induction was carried out with Propofol (1–2.5 mg/kg) and Atracurium (0.5 mg/kg). Anesthesia maintained with volatile anesthetic agent with isoflurane 1–1.5% with nitrous oxide 60% in oxygen.

All patient received intravenous paracetamol 1 g infusion during surgery. End tidal CO_2 was maintained between 30 and 35 mm Hg. The patient heart rate, systolic and diastolic blood pressure were noted every 15 min.

At the end of the surgery neuromuscular block was reversed with neostigmine and glycopyrrolate. After the clinical assessment of adequacy of reversal of neuromuscular block, trachea was extubated. After the end of surgery all patient received 75 mg diclofenac infusion for postoperative analgesia.

Patients were randomly allocated to receive ramosetron 0.3 mg (given at the beginning of surgery)) (Group R, n = 30), dexamethasone 8 mg (given at the beginning of surgery) (Group D, n = 30). Using a questionnaire, all instances of nausea and vomiting were recorded carefully every few hours for 24 hours until the patient was discharged to the ward. The intensity of vomiting was evaluated through the Bellville scoring scale (lack of nausea and vomiting = 0, nausea = 1, nausea with belching = 2, and vomiting = 3).

Data were collected on the type of the surgical operation, age, ASA category, duration of anesthesia, duration of the operation, blood pressure before and after the operation, saturation of peripheral oxygen (SpO_2), heart rate during the surgery. Presence and the intensity of nausea or vomiting at 0–2, 2–8, 16–24 hours after the operation were recorded.

Time of usage of rescue antiemetic following surgery were analyzed.

Results

There is no differences in patient demographic amoung treatment group. There is no statistically significant differences between the two groups in terms of systolic and diastolic blood pressure, SpO_2. The average systolic or diastolic blood pressure measured before induction in two group were not significantly different.

Table 1: Baseline parameters

Variables	Group D	Group R	Total	*p* - value
Age in yrs	39.57 ± 14.80	37.87 ± 14.62	38.72 ± 14.61	0.656
ASA				
1	20 (66.7%)	20 (66.7%)	40 (66.7%)	1.000
2	10 (33.3%)	10 (33.3%)	20 (33.3%)	
Gender				
Female	13 (43.3%)	12 (40%)	25 (41.7%)	0.793
Male	17 (56.7%)	18 (60%)	35 (58.3%)	

Student *t*-test/Chi-square test.

Table 2: Blood pressure, saturation of peripheral oxygen, duration of operation, duration of recovery

Variables	Group D	Group R	Total	*p* - value
HR (Per Min)	72.31 ± 2.47	71.83 ± 2.21	72.02 ± 2.34	0.432
SBP (mm Hg)	116.41 ± 20.52	113.73 ± 20.35	115.08 ± 20.31	0.618
DBP (mm Hg)	70.82 ± 4.99	71.40 ± 3.88	71.11 ± 4.44	0.616
SpO_2%	99.99 ± 0.2	99.99 ± 0.02	99.99 ± 0.02	1.000

Student *t*–test.

There was no significant difference among PONV in the first two hours of postoperative period. However, in 2 to 8 hours after surgery the PONV in Group D is significantly higher than that in the Group R.

Table 3: Nausea, vomiting, nausea and belching

	Group D (*n* = 30)	Group R (*n* = 30)	Total (*n* = 60)	*p* - value
Belleville's score 0 to 2 hours postop				
Lack of nausea and vomiting (0)	0 (0%)	0 (0%)	0 (0%)	1.000
Nausea (1)	0 (0%)	0 (0%)	0 (0%)	1.000
Nausea and belching (2)	0 (0%)	0 (0%)	0 (0%)	1.000
Vomiting (3)	4 (13.3%)	0 (0%)	4 (6.7%)	0.112
Belleville's score 2 to 8 hours				
Lack of nausea and vomiting (0)	0 (0%)	0 (0%)	0 (0%)	1.000
Nausea (1)	1 (3.3%)	0 (0%)	1 (1.7%)	1.000
Nausea and belching (2)	9 (30%)	0 (0%)	9 (15%)	0.002**
Vomiting (3)	9 (30%)	0 (0%)	9 (15%)	0.002**
Belleville's score 8 to 16 hours				
Lack of nausea and vomiting (0)	0 (0%)	0 (0%)	0 (0%)	1.000
Nausea (1)	0 (0%)	1 (3.3%)	1 (1.7%)	1.000

	Group D (n = 30)	Group R (n = 30)	Total (n = 60)	p - value
Nausea and belching (2)	4 (13.3%)	4 (13.3%)	8 (26.6%)	1.000
Vomiting (3)	0 (0%)	0 (0%)	0 (0%)	1.000
Belleville's score 16 to 24 hours				
Lack of nausea and vomiting (0)	0 (0%)	0 (0%)	0 (0%)	1.000
Nausea (1)	0 (0%)	0 (0%)	0 (0%)	1.000
Nausea and belching (2)	0 (0%)	4 (13.3%)	4 (6.65%)	1.000
Vomiting (3)	0 (0%)	0 (0%)	0 (0%)	1.000

Chi-square/Fisher Exact Test.

Table 4: Rescue antiemetic distribution in two groups of patients studied

Time for rescue antiemetic (Hours)	Group D	Group R	Total	p - value
NR (not received)	3 (10.0%)	21 (70%)	24 (40%)	0.0000021*
0–2	4 (13.3%)	(0)	4 (6.67%)	0.03842747*
2–8	19 (63.3%)	(0)	19 (31.6%)	< 0.001*
8–16	4 (13.3%)	5 (16.6%)	9 (15%)	0.71739745
16–24	0 (0.0%)	4 (13.3%)	4 (6.67%)	0.03842747*
Total	30 (100%)	30 (100%)	60 (100%)	

- Rescue antiemetic was required significantly in first 2 hours and 2 to 8 hours in Group D with a p - value of < 0.001 where as rescue antiemetic was not required during this time in Group R after surgery.
- 2 to 8 hours postoperatively was the time when maximum patients required antiemetic in Group D compared to Group R.
- The p - value < 0.0001 proves that lesser number of Group R patients required rescue antiemetic in the study period.

Table 5: Comparison of total number of patients requiring rescue antiemetic in both groups

Duration in hours for rescue antiemetic	Group D (n = 30)	Group R (n = 30)	p - value
0 – 24 hours	27	9	0.00001*
Not received	3	21	

The Chi-square test: The p - value is < .00001. The result is significant at p < .05

Discussion

The efficiency of administration of ramosetron (0.3 mg IV) and dexamethasone (8 mg IV) before anesthetic induction on postoperative nausea and vomiting was evaluated in middle ear surgical operations. The postoperative nausea and vomiting incidence rate after middle ear surgical operations has been reported to be significant.[10] The incidence of nausea and vomiting after middle ear surgery is high might be attributed to the complex innervation of this area by the cranial nerves V, VII, VIII and X, and cervical nerves II and III.[11,12] The proximity of cranial surgical field to the semilunar ducts and vestibular system, and heat and vibration transmission at excision of the surgical field through stimulation of the ampulla can lead to postoperative nausea, dizziness, and vomiting. Therefore, postoperative nausea and vomiting are more common in these patients.[9]

Ramosetron is a newer 5-HT_3 receptor antagonist which is more potent and has a longer duration of antiemetic action than the older agents. This has been attributed to the higher binding affinity and slower rate of dissociation from the target receptor of ramosetron compared to ondansetron. The elimination half-life of ramosetron is also longer than that of ondansetron (9 h *vs* 3.5 h). Many of the recent studies have shown that ramosetron is more effective than ondansetron in preventing PONV for the patients undergoing various other surgeries.[13–15] The benefits of administering dexamethasone as

a more costeffective antiemetic and efficacious analgesic drug[35] should be weighed against the potential side-effects.[16]

In the this study, the incidence rates of PONV in dexamethasone group is 89.9%, and with ramosetron group is 29.9%, which showed statistically significance (p value < 0.0001). The incidence rate of postoperative nausea and vomiting in dexamethasone group is significantly higher than that of ramosetron group. Limited studies have compared the effects of dexamethasone and ramosetron on PONV. Further in the immediate period with 0–8 hours, 76.6% in Group D had nausea and vomiting, compared to none in Group R which is statistically significant p (< 0.001). Yoon-Kang Song et al., conducted a study on effects of ramosetron and dexamethasone on postoperative nausea, vomiting, pain, and shivering in female patients undergoing thyroid surgery and conclude that two antiemetic drugs, ramosetron and dexamethasone, significantly reduced the incidence and severity of postoperative nausea and the need for administration of rescue antiemetic drugs.[17] Lopez-Olaondo et al. reported that dexamethasone was as effective as ondansetron in reducing nausea and vomiting induced by chemotherapy.[18] Another study showed that dexamethasone was a little more effective than ondansetron in preventing posttonsillectomy PONV.[19] Also, a study of 60 patients undergoing laparoscopic cholecystectomy showed that the incidence rate of PONV in the dexamethasone group was significantly lower (20% *versus* 43.3%).[20] The difference in the findings of the above studies might be related to wide range of differences in sample sizes, patients qualities, type of surgical operations and anesthetic techniques, the way that PONV was defined and studied.

The present study, showed that ramosetron was more effective than dexamethasone in preventing PONV; therefore, it may be more suitable to be administered in such a situation where we can reduce the amount of recue antiemetic and complications arising out of PONV.

Conclusion

- Ramosetron 0.3 mg IV given before induction of anesthesia is an effective means of reducing PONV in middle ear surgeries;
- Compaed to dexamethasone 8 mg IV ramosetron 0.3 mg IV significantly reduces PONV in the immediate postoperative period;
- Ramosetron is suitable alternative to dexamethasone in controlling PONV.

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