An Observational Study of Intravenous Granisetron Vs Oral Gabapentin in Preventing Postoperative Nausea and Vomiting after Middle Ear Surgery

Malini Mehta[1], Akshata Thakurdesai[2], Sujay Thakkar[3]

[1]Professor, [2]3rd year Resident,[3]Assistant Professor, Department of Anaesthesiology, Dhiraj Hospital, Smt. B.K. Shah Medical Institute and Research Centre, Sumandeep Vidyapeeth, An Institution Deemed to be University, Vadodara, Gujrat, India

Abstract

Background- Postoperative nausea and vomiting (PONV) is one of the most unpleasant complications after middle ear surgery. Several studies have demonstrated use of gabapentin as antiemetic. This study aims at comparison of intravenous granisetron vs oral gabapentin in preventing PONV.

Methods - 64 patients of ASA I or II between the ages of 18 and 65 years were divided equally into two groups. Patients in group I received 3mg granisetron iv 2 minutes and patients in group II received 300 mg gabapentin orally 1 hour prior to surgery. Patients were premedicated with inj. glycopyrrolate and inj. midazolam. Anaesthesia was induced, maintained and reversed in usual manner. Haemodynamic changes and number of episodes of nausea and vomiting were recorded upto 24 hours postoperatively. No statistically significant difference was observed in both the groups at 0 and 1 hour in preventing PONV ($p<0.05$). Next 24 hours postoperatively neither group showed PONV. No significant haemodynamic changes were observed and there were noside effects in either of the groups.

Conclusion- There was no statistically significant difference in prevention of PONV in the patients who had either received inj granisetron 3mg i.v. 2 minutes prior to surgery or oral Gabapentin 300mg 1hour prior to surgery after middle ear surgery without any side effects.

Keywords- *PONV, Granisetron, Gabapentin, Middle ear surgery.*

Introduction

Postoperative nausea and vomiting is one of the most unpleasant complications[1]. The etiology of postoperative nausea and vomiting is multi factorial[1] and its occurrence depends on duration of surgery, the type of drugs used during anaesthesia[2], the technique of anaesthesia, age and sex and smoking habit.[3] Postoperative nausea and vomiting increases intraocular pressure, increase intracranial pressure,[4] causes wound dehiscence, prolongs duration of stay in the recovery room and hospital.[5]

To prevent postoperative nausea and vomiting, different groups of drugs can be used including promethazine, droperidol, ondansetron, dexamethasone and propofol.[6] Each drug used has their own risks and benefits.

5-HT_3 receptor antagonists are routinely used nowadays to prevent postoperative nausea and vomiting in the patients undergoing surgeries under general anaesthesia. These 5-HT_3 receptor antagonists produced no sedation, extrapyramidal reactions, adverse effects

Corresponding author:
Dr. Sujay Thakkar
Address- S.B.K.S. Medical Institute and Research Centre, Piparia, Waghodia, Vadodara.
Email- akshata.thakurdesai@gmail.com
Number- 7204584089

on vital signs or laboratory tests or drug interactions. (7) Currently available 5-HT_3 antagonists include ondansetron, granisetron, dolasetron, topisetron and palonosetron. This may be the clinical site of action of the 5-HT_3 receptor antagonist on serotonin.

Granisetron is a selective 5-HT_3 receptor antagonist and reduces PONV by stimulation of HT_3 receptors which have antiemetic effects(8). Granisetron as compared with ondansetron is more selective and long acting.

Gabapentin is a gamma γ –aminobutyric acid (GABA) analogue. Several studies have demonstrated its use as antiemetic[9]. Gabapentin in past had shown effectiveness in suppression of nausea and vomiting in perioperative period in patients undergoing laparoscopic cholecystectomy. Gabapentin has also shown its effectiveness as an antiemetic to suppress chemotherapy induced nausea and vomiting in patients of breast cancer. (10)

Gabapentin absorption is dose dependent. When gabapentin is orally administered, its bioavailability is inversely related to dose, due to the saturable L-amino acid transport mechanism in the gastrointestinal tract.[11]

Postoperative nausea and vomiting is common after middle ear surgery. Vomiting after middle ear surgery may be due to increased pressure in the middle ear. Middle ear surgeries disturb the vestibular system and are associated with high incidence of PONV.

Hence, it was planned to carry out an observational study of intravenous granisetron vs oral gabapentin in preventing postoperative nausea and vomiting after middle ear surgery.

Material and Methodology

After obtaining approval from the ethics committee and written informed consent from patients, this study was conducted at Dhiraj hospital in Department of Anaesthesiology. 64 patients between the ages of 18 and 65 years of both gender of Grade-I and II of American Society of Anaesthesiologists (ASA) classification, who were admitted for elective middle ear surgeries under general anaesthesia were divided into 2 groups

Group I - received intravenous granisetron 3mg 2 minutes prior to surgery.

Group II - received oral gabapentin 300 mg 1 hour prior to surgery with sips of water.

Site of Study**:** Department of Anaesthesiology S.B.K.S. Medical Institute and research centre, Sumandeep Vidyapeeth University, Piparia, Waghodia, Vadodara, Gujarat**.**

Study population**-** divided into two groups with 32 patients in each group.

Study Duration**-** The study was initiated after obtaining the permission from institutional ethics committee and was conducted over a period of18 months.

Study Design**-** Observational study

SAMPLE SIZE – calculated using this fomula2 Means: 2-Sample, 2-Sided Equality. It is 64, so we will take 32 patients in each group.

http://powerandsamplesize.com/calculators/Compare-2-Means/2-Sample-Equality[74]

$$nA = \kappa nB and nB = \left(1 + \frac{1}{\kappa}\right)$$

$nA=\kappa nB$ and $nB=(1+1/\kappa)(\sigma z1-\alpha/2+z1-\beta/\mu A-\mu B)2$

Selection criteria

Inclusion Criteria:

- Patients willing to sign informed consent.
- Patients undergoing elective middle ear surgeries under general anaesthesia aged between 18 and 65 years.
- Patients belonging to ASA I or II.

Exclusion Criteria:

- Patients refusal.
- All patients below 18 and above 65 years.
- Patients with ASA III or more.
- Patients with known allergy, sensitivity or any

other form of reaction to any drug

· Patients with systemic comorbidities.

· Patients with preoperative involvement of the inner ear or intraoperative gross damage to the inner ear.

Patients fulfilling the above said inclusion criteria were subjected to study.

Detailed pre-anaesthetic check-up and investigations of all the patients posted for planned middle ear surgery was done a day prior to surgery to decide the fitness and eligibility.

Nausea was defined as subjective unpleasant sensation associated with awareness of the urge to vomit and Vomiting was defined as forceful expulsion of gastric contents from the mouth.

Severity of vomiting was classified as:

Mild: 1-2 episodes

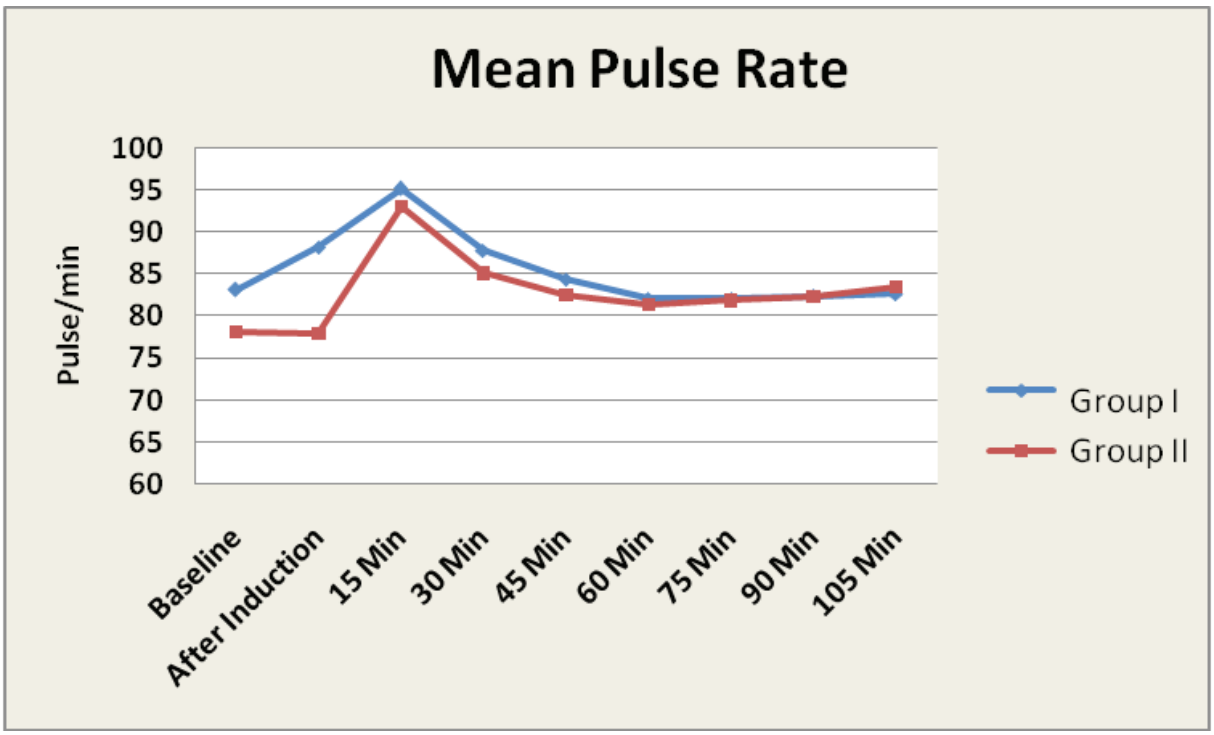
Moderate: 3-4 episodes

Severe: >4 episodes

The rescue antiemetic,i.v.ondansetron 4 mg was administered for severe nausea or two more episode of vomiting and number of doses antiemetics given were recorded.

Results and Discussion

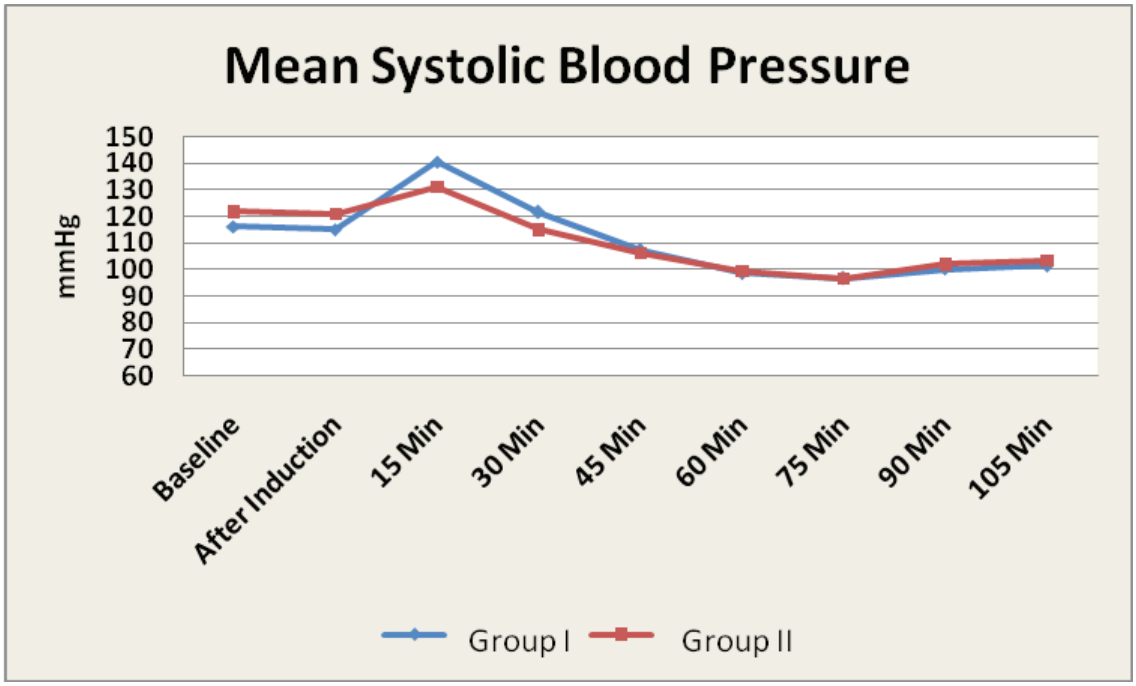
Data was collected, tabulated. Numerical variables were presented as mean & standard deviation (SD) while categorical variables were presented as frequency and percentage. As regard numerical variables; unpaired student –t test was used whenever appropriate, for between-groups comparisons, while for categorical variables; chi–square test was used. A difference with significant level p <0.05 was considered statistically significant.



Graph 1: Graph showing mean pulse rate between the two groups in intraoperative period.

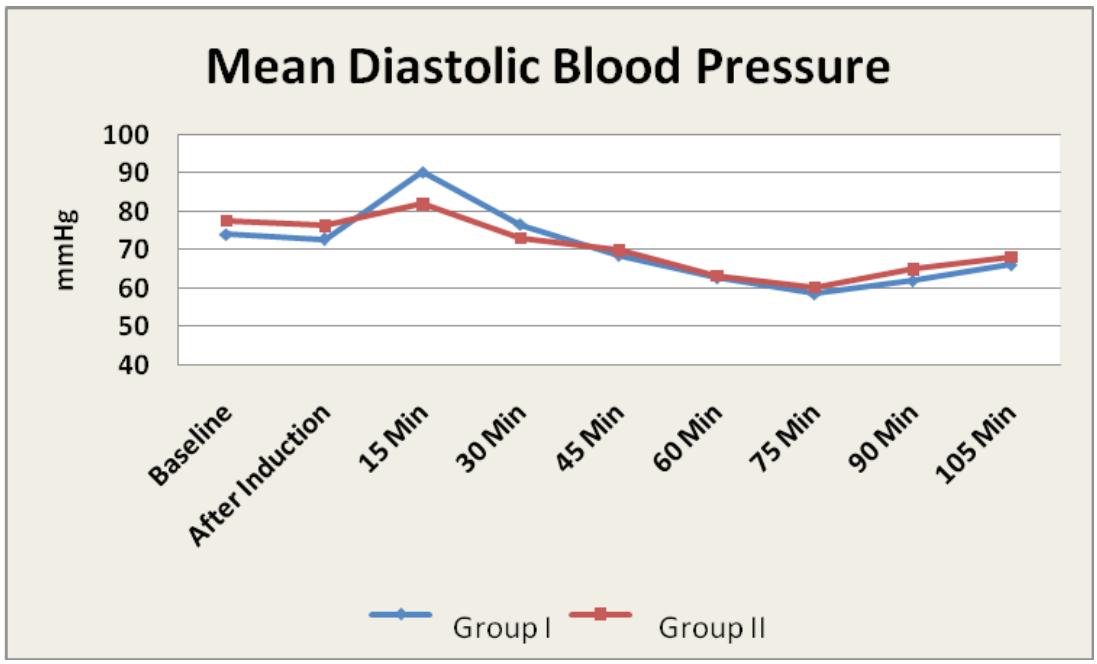
There was statistically significantly lower difference in the mean pulse rate in gabapentin group as compared to granisetron group only immediately after induction ($p<0.0001$). Thereafter no statistically significant difference was observed between the two groups during rest of the study period ($p>0.05$)

GRAPH 2: GRAPH SHOWING MEAN SYSTOLIC BLOOD PRESSURE BETWEEN TWO GROUPS IN INTRAOPERATIVE PERIOD.



The mean systolic blood pressure was stastically highly significantly lower in gabapentin group as compared to granisetron immediately (p=0.033), at 15 minutes (p=0.001) and at 30 minutes (p=0.010) after induction. No significant differences were observed between the groups during rest of the intraoperative study time.

GRAPH 3: GRAPH SHOWING MEAN DIASTOLIC BLOOD PRESSURE BETWEEN TWO GROUPS IN INTRAOPERATIVE PERIOD.

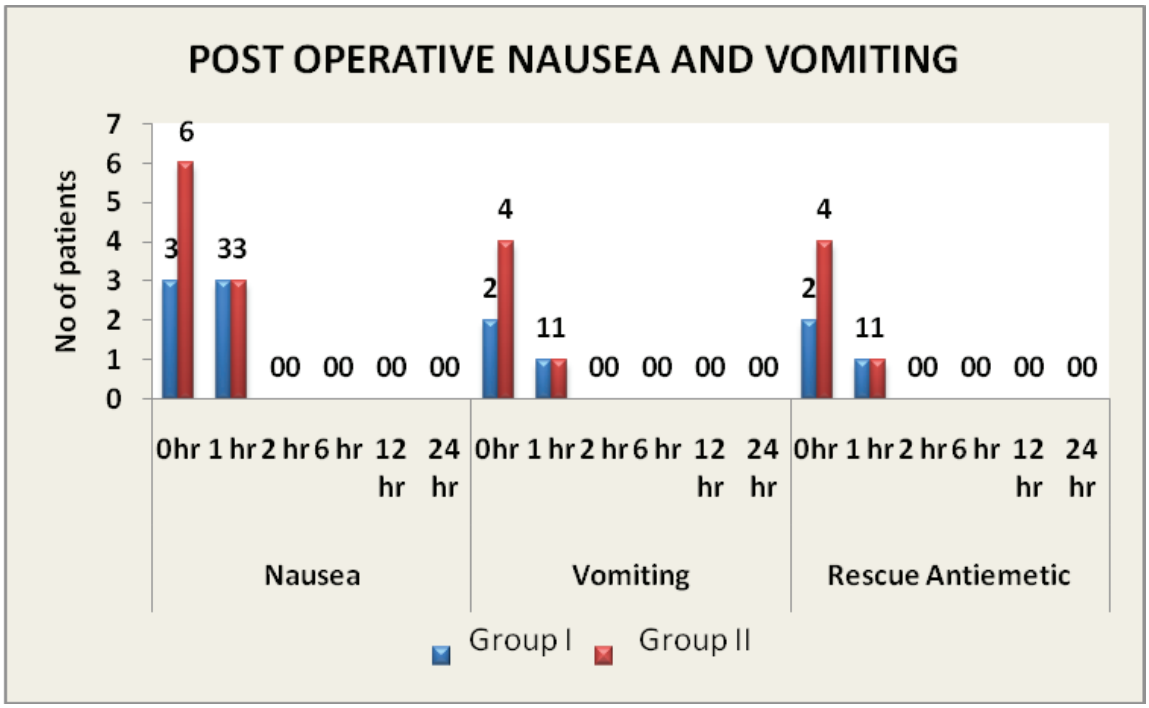


Difference in the mean diastolic blood pressure between the two groups was stastically insignificant at all times except immediately (p=0.042) and at 15 minutes (p<0.0001) after induction which was lower in gabapentin group as compared to granisetron group.

There were no significant differences in the mean pulse rate, mean systolic blood pressure and diastolic blood pressure for 24 hours postoperatively between the groups.

TABLE 1: INCIDENCE OF POST OPERATIVE NAUSEA AND VOMITING AND RESCUE ANTIEMETIC BETWEEN TWO GROUPS

Hours	Group I (Granisetron) (n=32)	Group II (Gabapentin) (n=32)	P value
Nausea			
0	3 (9.37%)	6 (18.75%)	0.280
1	3 (9.37%)	3 (9.37%)	1.000
2	-	-	-
6	-	-	-
12	-	-	-
24	-	-	-
Vomiting			
0	2 (6.25%)	4 (12.5%)	0.391
1	1 (3.12%)	1 (3.12%)	1.000
2	-	-	-
6	-	-	-
12	-	-	-
24	-	-	-
Rescue Antiemetic			
0	2 (6.25%)	4 (12.5%)	0.391
1	1 (3.12%)	1 (3.12%)	1.000
2	-	-	-
6	-	-	-
12	-	-	-
24	-	-	-



GRAPH 4: Graph showing incidence of Postoperative nausea and vomiting and rescue antiemetic between two groups.

9.37% patients in granisetron group had nausea at 0 hour as compared to 18.75% patients in gabapentin group and 9.37% patients had nausea at 1 hour in both the groups. None of the patients had nausea after the 1st hour in either of the groups and no significant difference was observed between the groups in terms of nausea.

6.25% patients of granisetron group had vomiting at 0 hour as compared to 12.5% patients in gabapentin group. 3.12% patients of both the groups had vomiting at first hour which was mild in category. None of the patients had vomiting after the 1st hour in either of the groups. No significant difference was observed between the groups in terms of vomiting.

6.25% patients of granisetron group received rescue antiemetic in the form of injection ondanstron 0.1mg/kg I.V as compared to 12.5 % patients in the gabapentin group at 0 hour and 3.12% patients in both groups received inj ondansetron at 1st hour. None of the patients received rescue antiemetic after the first hour. No significant differences were observed between the two groups in terms of receiving rescue antiemetic.

Postoperative nausea and vomiting (PONV) is a common, unpleasant, and distressing adverse effect that may occur after surgery, dehydration, aspiration pneumonia upto death. It was estimated that one episode of vomiting prolonged postanaesthesia care unit stay by approximately 25 minutes. The incidence of nausea and vomiting was 30% in surgery under general anaesthesia when inhalational anaesthetics were used alone without prophylaxis. It had been reported that 50-80% patients who underwent middle ear surgery experienced PONV. [3,12,13]

In current practise, selective $5HT_3$ receptor antagonists such as granisetron, ondansetron, dolasetron, palonosetron and ramosetron have been widely used as first and second line prophylaxis for preventing PONV because of their efficacy and relatively few side effects.[14] $5HT_3$ receptor antagonists are routinely used nowadays to prevent postoperative nausea and vomiting in the patients undergoing surgeries under general anaesthesia.

Gabapentin was originally used as an anticonvulsant. Various studies suggested its use as antiemetic via multimodal processes.[9]

Postoperative nausea and vomiting after middle ear surgery may be due to increased pressure in the middle ear.Middle ear surgeries disturb the vestibular system and are associated with high incidence of PONV and vertigo, which are further aggravated by use of opioids. A 62-80% incidence of PONV following middle year surgery has been reported.[15,12] Reduction in PONV and opioid-induced emesis was more with use of granisetron, ondansetron and other $5HT_3$ receptor antagonists ($5HT_3$ RA) than other groups of antiemetics, but many patients still experienced PONV and vertigo. [12] Involvement of multiple types of receptors and factors like disturbances in the inner ear from surgical stimulation may be a reason for inadequate control of PONV with a single agent.

We compared granisetron 3 mg IV 2 minutes and oral gabapentin 300 mg orally 1 hour prior to middle ear surgery as gabapentin in a dose of more than 300 mg associated with side effects.

In the study, both groups were comparable with regard to demographic characteristics i.e. age, gender, weight, ASA grade.

In present study no major haemodynamic changes were observed. Heart rate, systolic and diastolic blood pressure between the groups were comparable throughout the study period.(p-value>0.05)

Anuradha swaminathan[16] et al carried a study which also showed no statistically significant difference between the study groups regarding heart rate and mean arterial pressure intraoperatively.

No statistical significant difference was noted in incidence of nausea among both the groups.(p= 0.280 at 0 hour and p= 1.000 at 1st hour) in our study. None of the patients had nausea after 1st hour in either of the group.

Anuradha Swaminathan[16], Heidari M[17] and AzizeBestas[18] et al observed no incidence of nausea after 1st hour postoperatively between the groups.

In our study, the incidence of postoperative vomiting at 0 and 1st hour in group I as compared to 0 and 1st hour in group II. (p value at 0 hour =0.391 and at 1st hour 1.000).

Anuradha Swaminathan[16], Heidari M[17] and Artemisia Papademia[19] et al observed the incidence of postoperative nausea and vomiting between the two groups were statistically insignificant.(p>0.05).

While Sussan Soltani Mohammadi[20] et al observed that none of the patients in gabapentin group had vomiting. (p=0.114)

The incidence of PONV after middle ear surgery is high. It has been reported that 50-80% of the patients who undergo middle ear surgery experience PONV [3,12,13] which is due to the disturbance in vestibular system.

Granisetron is a new $5\text{-}HT_3$ receptor antagonist more selective than ondansetron. It blocks the $5\text{-}HT_3$ receptors at both the central and the peripheral sites. It blocks the $5\text{-}HT_3$ receptors at both the central and the peripheral sites. It acts on the vagal efferent nerves of the gut and produces blockade of $5\text{-}HT_3$ receptors.

The precise mechanism of gabapentin in the prevention of nausea and vomiting is not known but mitigation of tachykinin neurotransmitter activity has been stated to be useful.[21] There is evidence that a selective tachykinins-receptor antagonist improves both acute and delayed nausea and emesis induced by chemotherapy.[22]

Gabapentin is known to have non serious side effect such as dizziness but none of our patients receiving gabapentin experienced dizziness.

Conclusion

There was no statistically significant difference in prevention of nausea and vomiting in the 1st 24 hours postoperatively in the patients who had either received inj granisetron 3mg i.v 2 minutes prior to surgery or oral gabapentin 300mg 1hour prior to surgery after middle ear surgery under general anaesthesia without any side effects.

Source of Fund- Nil

Conflict of Interest- None

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