Original Article

Geranisetron versus gabapentin in preventing postoperative nausea and vomiting after middle ear surgery in adults: A double-blinded randomized clinical trial study

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Abstract

Background: The incidence of postoperative nausea and vomiting (PONV) after middle ear surgery is high. In this study we want to compare the effects of intravenous granisetron and oral gabapentin as a premedication before surgery on the incidence and severity of PONV after middle ear surgery in adult patents.

Materials and Methods: We enrolled 90 patients that were randomly divided into the three groups of 30 in each. Group I received granisetron 3 mg iv 2 minutes before induction of anesthesia; Group II received oral gabapentin 300 mg 1 hour before anesthesia and Group III received placebo. The incidence and severity of PONV were recorded each 15 minutes in the post-anesthesia care unit (PACU) and each 8 hours until 24 hours after discharge from the PACU.

Result: The incidence and severity of nausea and vomiting at different time intervals in Groups I and Group II was significantly lower compared with Group III ($P < 0.05$). There was no significant difference in the incidence of side effects of study drug administration including respiratory depression, apnea, extra pyramidal disorders, drowsiness, dizziness, vertigo and headache in three groups.

Conclusion: The study was shown that using gabapentin and granisetron have equal anti-emetic effects, but significant differences were seen between these two groups compared to the control group. These submit the efficiency of these drugs in preventing PONV.

Key Words: American social anesthesia, 5HT3 receptors, gabapentin, geranisetrone, post operating nausea and vomiting (PONV), visual analogues scale

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INTRODUCTION

Postoperative nausea and vomiting (PONV) is the one of the most unpleasant complications.[1-4] PONV is an unpleasant feeling that are more distressing for patients than pain.[3,5,6] The etiology of PONV is multi-factorial[1,2,7,8] and its occurrence depends on duration of surgery, the type of drugs used during

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anesthesia,[4,9] the technique of anesthesia, age, sex, and smoking habit.[10-12] PONV increases intraocular pressure, increase intracranial pressure,[13] causes wound dehiscence, prolongs duration of stay in the recovery room and hospital.[14-18] Also, PONV is an uncommon cause of aspiration, dehydration, electrolytes disorder and even death[4] especially in children and elderly patients[19] and increase the cost of treatment.[20]

To prevent PONV, different kinds of drugs can be used including promethazine, droperidol, ondansetron, dexamethasone and propofol.[1,2,6,21-23] Despite using different kinds of drugs, PONV is a common side effect yet.[2,3,5,6] Each drug used has their own risks and benefits. For example deroperidol can make dry mouth.[1] Antagonists of 5HT3 receptors can cause prolonged QT interval in ECG or even cardiac arrest.[6]

Khademi *et al*.[24] showed that using oral gabapentin (an anticonvulsant) before surgery significantly reduced the incidence of PONV after open cholecystectomy. Papadima and colleagues[25] reported that intravenous administration of granisetron (a selective serotonin 5-hydroxytryptamine type 3 (5-HT3) receptor antagonists) before surgery reduced significantly the incidence of nausea after total thyroidectomy.

There were no previous studies which compare the efficacy of gabapentin versus granisetron in reducing PONV. So, we design the present study to compare the effect of intravenous granisetron and oral gabapentin as a premedication before surgery on the incidence and severity of nausea and vomiting after the middle ear surgery in adult patients.

MATERIALS AND METHODS

The study is a randomized, double-blinded placebo controlled clinical trial that was done from November 2008 to November 2010 after obtaining institutional approval from Ethic Committee of our University and written informed consent from the patients. The inclusion criteria were patients with ASA I and ASA II, aged between 18 and 60 years, non-pregnant or lactating females, not be in menstruation period, without history of addiction or using anti-vomiting drugs, motion sickness, obesity (body mass index more than 30), central nervous system disorders especially cerebella problems who were candidate for middle ear surgery. If technique of anesthesia was changed or there was uncontrolled bleeding during surgery, the patients were excluded from the study.

If we considered 0.8 power (type II statistical error 20%) to detect a significant difference between three groups with $P = 0.05$ (type I statistical error 0.05), 30 patients per group must be enrolled into our study.

No premedication was given to the patients. Before induction of anesthesia, the patients were informed from using Visual Analogue Score Scale (VAS, 0 = no nausea, 10 = the most severe nausea experienced) for recording of severity of nausea by a nurse. The patients were randomized into three groups by using a computer generated randomization method. Group I received 3 mg iv in a volume of 3 ml 2 minutes before induction of anesthesia; Group II received oral gabapentin 300 mg 1 hour before induction of anesthesia; Group III received placebo. The study drugs were administered by a physician who was not involved in data recording. Data gathering was performed by a nurse who was not informed from the study group allocation.

The standard monitoring included EKG, pulse oximetry and noninvasive blood pressure monitoring. Induction of anesthesia was done by injecting fentanyl 2 μg/kg, sodium thiopenta 5 mg/kg and atracurium 0.6 mg/kg for muscle relaxation. After 3 minutes mask ventilation under oxygen, laryngoscopy and endotracheal intubation was performed. Maintenance of anesthesia was done using isoflurane 1.2% in 50% N_2O in oxygen and morphine for analgesia. At the end of surgery, neuromuscular blockade was reversed by neostigmine 0.04 mg/kg and atropine 0.02 mg/kg iv. Mean arterial blood pressure (MAP), heart rate (HR) and peripheral oxygen saturation (Spo2) were recorded throughout surgery each 15 minutes followed by recording at recovery room every 15 minutes and then after each 8 hours till 24 hours. After operation, the incidence of PONV, severity of PONV and the first time for occurrence of PONV were recorded. The severity of PONV was recorded by using VAS.

The sedation score of patients after surgery was recorded by the following scale:

- Complete consciousness
- Open eyes with sleepy mood
- Closed eyes with good consciousness
- Not having good consciousness
- No consciousness.

Data were presented as mean ± SD or numbers (%). Statistical analysis was performed using the SPSS 16 statistical software package (SPSS Inc., Chicago, IL, USA). Quantitative data were analyzed by using one way ANOVA with Bonferroni correction. Qualitative data were analyzed by using the Chi-square test.

A P value less than 0.05 was considered statistically significant.

RESULTS

The demographic and clinical data including sex, age, BMI, duration of surgery, duration of recovery stay and duration of anesthesia was not significantly different among three groups ($P > 0.05$) [Table 1]. The incidence and severity of nausea was significantly lower in Group I and Group II in comparison with Group III [$P < 0.05$, Tables 2 and 3]. Also, the incidence of vomiting was significantly lower in Group I and Group II in comparison with Group III [$P < 0.05$, Table 4]. There was no significant difference between Group I with Group II with respect to the incidence of nausea and vomiting and severity of nausea ($P > 0.05$). The first time for occurrence of vomiting was significantly longer in Group I and Group II compared with Group III [$P < 0.05$, Table 5]. No significant was noted between Group I and Group II in this regard.

The level of sedation in different time intervals was not significantly different among three groups ($P > 0.05$). There was no significant difference in the incidence of side effects including respiratory depression, apnea, extra pyramidal disorders, drowsiness, dizziness, vertigo and headache among three groups [$P > 0.05$, Table 6].

The study showed that using Gabapentin and Granisetron have equal anti emetic effects, but

Table 1: Demographics and clinical data of patients in three groups

Variable	Granisetron group	Gabapentin group	Control group	*P* value
Male/Female (*n*)	6/24	8/22	13/17	0.127
Age (years)	37.9±14.6	42.3±12.4	36.3±14.9	0.240
Height (cm)	163.2±6.9	165.5±6.3	167.0±9.4	0.162
Weight (kg)	65.6±10.1	68.47±8.6	66.3±13.8	0.582
ASA I/II (*n*)	19/11	17/13	18/12	0.870
Duration of recovery stay (min)	65.1±47.3	64±56.6	66.5±55.9	0.984
Duration of surgery (min)	138.6±40.1	126.8±45.3	120.6±58.2	0.348
Duration of anesthesia (min)	157.5±43.8	151.3±35.0	139.2±46.2	0.237

Data are presented as mean±SD or numbers. ASA: American society of anesthesiologist

Table 2: Incidence of nausea at different time interval in three groups

Timing of measurement	Granisetron group (%)	Gabapentin group (%)	Control group (%)	*P* value
8 hours	5 (5.6)	6 (6.7)	14 (15.6)	0.018
16 hours	4 (4.4)	5 (5.6)	12 (13.3)	0.029
24 hours	3 (3.3)	4 (4.4)	11 (12.2)	0.019

Data are presented as numbers (%)

Table 3: Severity of nausea at different time interval in three groups

Severity of nausea (cm)	Granisetron group	Gabapentin group	Control group	*P* value
Just after arrival to the recovery room	1.3±0.5	1.4±0.4	3.8±0.8	0.008
30 minute	1.1±0.5	1.3±0.4	3.4±4.1	0.011
8 hours	1±0.4	1.1±0.3	3±0.6	0.008
16 hours	0.8±0.3	1.0±0.3	2.5±0.5	0.011
24 hours	0.6±0.3	0.7±0.2	2.1±0.4	0.008

Data are presented as mean±SD

Table 4: Incidence of vomiting at different time interval in three groups

Timing of measurement	Granisetron group (%)	Gabapentin group (%)	Control group (%)	*P* value
8 hours	5 (5.6)	6 (6.7)	14 (15.6)	0.018
16 hours	4 (4.4)	5 (5.6)	13 (14.4)	0.012
24 hours	2 (2.2)	3 (3.3)	10 (11.1)	0.010

Data are presented as numbers (%)

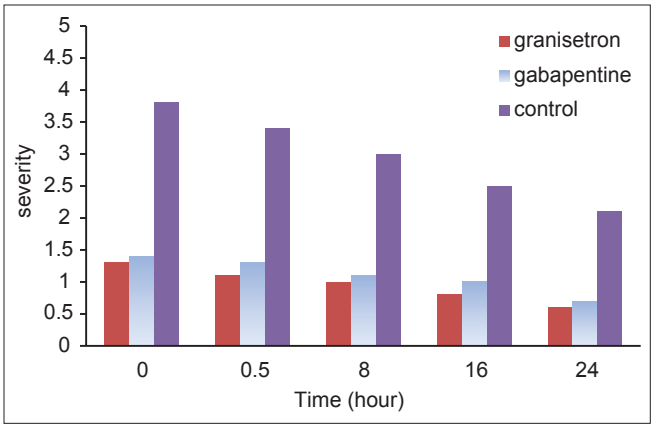

Figure 1: The comparisons anti-emetic effects in three groups gabapentin, granisetron and control up to 24 hours after surgery

Table 5: The first time for occurrence of vomiting in three groups

Variable	Granisetron group	Gabapentin group	Control group	*P* value
First time for vomiting episode (hours)	2.82±0.9	3.4±0.6	0.89±0.4	0.000

Data are presented as numbers (%)

Table 6: The incidence of adverse effects in three groups

Variable (*n*)	Granisetron group	Gabapentin group	Control group	*P* value
Respiratory depression	0	0	0	
Apnea	0	0	0	
Drowsiness	0	0	0	
Dizziness	0	1	0	0.364
Extra-pyramidal symptom	0	1	0	0.364
Vertigo	0	1	1	0.264
Headache	2	0	0	0.184

Data are presented as number

significant differences seen between these two groups compared to the control group. These submit the efficiency of these drugs in preventing PONV [Figure 1].

DISCUSSION

Our study showed that using granisetron 3 mg iv 2 minutes before induction of anesthesia or using oral gabapentin 300 mg 1 hour before beginning of general anesthesia significantly reduced the incidence of nausea and vomiting and severity of nausea in comparison with placebo. No significant difference was noted between granisetron and gabapentin in prevention of PONV.

Nausea and vomiting after surgery are the most unpleasant complications.[1-4] The incidence of PONV is varies from 14% to 82%.[2,3,5,7,26,27] The etiology of PONV is not completely known but from the present data showed that stimulation of four groups of receptors are effective in prevention of PONV. These receptors are: Cholinergic (muscarinic), dopaminergic (D2), histaminergic (H1) and seretoninergic (5HT3).[7] Recently it was shown that antagonists of neurokinin receptors (NK1) were effective in treatment of PONV.[2,5]

Papadima *et al*.[25] in a clinical trial study showed that granisetron 3 mg given before induction of anesthesia significantly reduced the incidence of PONV after total thyroidectomy. In another performed by Ganjare and colleagues[28] it was shown that granisetron 1 mg administered before induction of anesthesia was effective for prevention of PONV. They also showed that granisetron with 1 mg dose was safer than ondansetron 8 mg in this regards because granisetron caused less QT prolongation than ondansetron.

The exact mechanism of granisetron for reducuing PONV has not been explained but it was postulated that it acts by stimulation of 5HT3 receptors which have anti-emetic effects.[28] Khademi *et al*.[24] showed that administration of oral gabapentin 2 hours before surgery significantly reduced the incidence of PONV after open cholecystectomy. Also, the previous studies[29,30] showed that oral gabapentin had significant effect in reducing the incidence and severity of PONV after laparoscopic surgery. It has been postulated that anti-emetic effect of gabapentin is generated by reducing the activity of tachykinin neurotransmitter.[31]

Our study had some limitation; we used only one dosage of gabapentin or granisetron. It was not clear that using different dosage of both drugs have similar effect in reducing PONV. Also, the efficacy of both drugs in reducing PONV was shown only in middle ear surgery. It is suggested that similar studies perform in the other surgeries which were accompanied with significant PONV.

In conclusion our study showed that using oral gabapentin 300 mg 1 hour before surgery had similar and comparable effect to injection of granisetron 3 mg intravenously 2 minutes before induction of anesthesia in reducing the incidence of PONV and severity of nausea after middle ear surgery in adults without causing significant adverse effects.

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