ORIGINAL ARTICLE

Granisetron versus tropisetron in the prevention of postoperative nausea and vomiting after total thyroidectomy

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ABSTRACT

Background: Postoperative nausea and vomiting (PONV) are frequently encountered after thyroidectomy. For PONV prevention, selective serotonin 5-hydroxytryptamine type 3 (5-HT_3) receptor antagonists are considered one of the first-line therapy. We report on the efficiency of granisetron and tropisetron, with that of placebo on the prevention of PONV in patients undergoing total thyroidectomy. **Methods:** One hundred twenty-seven patients were divided into three groups and randomized to receive intravenously, prior to induction of anesthesia, tropisetron 5 mg, or granisetron 3 mg, or normal saline. All patients received additionally 0.625 mg droperidol. All episodes of postoperative PONV during the first 24 h after surgery were evaluated. **Results:** Nausea visual analogue scale (VAS) score was lower in tropisetron and granisetron groups than the control group at all measurements (P<0.01) except for the 8-h measurement for tropisetron (P=0.075). Moreover, granisetron performed better than tropisetron (P<0.011 at 4 h and P<0.01 at all other points of time) apart from the 2-h measurement. Vomiting occurred in 22.2%, 27.5%, and 37.5% in granisetron, tropisetron, and control groups, respectively (P=0.43). **Conclusions:** The combination of the 5-HT_3 antagonists with droperidol given before induction of anesthesia is well tolerated and superior to droperidol alone in preventing nausea but not vomiting after total thyroidectomy.

Key words: *Nausea, vomiting, thyroidectomy, granisetron, tropisetron*

INTRODUCTION

Postoperative nausea and vomiting (PONV) are two of the most common and distressing complications after anesthesia and surgery, and may lead to serious postoperative complications.[1,2] The overall incidence of PONV has been reported to be between 20% and 30%,[3] whereas reported incidence of PONV is between 63% and 84% in patients scheduled for thyroidectomy.[4]

PONV may represent the principal source of discomfort of the entire procedure and the most unpleasant aspect of postoperative recovery.[5,6] Uncontrolled PONV remains the leading cause of delayed discharge or unexpected readmission after ambulatory surgery.[7] Furthermore, it is a risk factor for postoperative bleeding, a complication of particular concern due to the potential for neck hematoma formation and airway obstruction.[5,8] Its incidence varies, according to numerous anesthesia- and non–anesthesia-related factors, yet remaining quite frequent.[9,10] PONV, regardless of clinical severity, is an important issue from the patients' point of view[11]; improvement of the quality of care should therefore include reduction of the incidence and severity of PONV.[12]

Prevention strategies with drugs and nonpharmacologic interventions have been studied extensively.[13-17] Serotonin receptor antagonists, particularly 5-hydroxytryptamine type 3 (5-HT_3) receptor antagonists, are an essential constituent of prophylactic or rescue treatment of PONV in patients at risk, according to respective guidelines.[18] The theoretic basis for these antagonists is sound, since they exert their effects by binding to the 5-HT_3 receptor in the

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chemoreceptor trigger zone and at vagal afferent neurons in the gastrointestinal tract. Moreover, their side effects are minimal and especially their lack of sedation properties makes them particularly suitable for ambulatory surgery.[19]

Preclinical studies have indicated possible differences between tropisetron and granisetron.[20] Unlike granisetron (an indazole), tropisetron is an indole compound. It has high affinity and specificity for 5-HT_3 receptors but appears to have a weak antagonistic effect on 5-HT_4 receptors, whereas granisetron show no affinity for any other than 5-HT_3 receptors. Metabolism of tropisetron occurs predominantly in the liver.

The aim of this prospective, randomized, double-blind, placebo-controlled study was to evaluate and compare the efficiency of tropisetron for preventing PONV compared with that of granisetron or placebo in patients undergoing total thyroidectomy during the first 24 postoperative hours.

METHODS

Patients in this study were prospectively randomized and data were prospectively recorded; then, data were retrospectively collected and analyzed. After obtaining approval from the Ethical Committee of our hospital, and after written informed consent, male or female patients scheduled for total thyroidectomy under general anesthesia from January 2009 until January 2010 were evaluated for study enrollment. Inclusion criteria were age between 18 and 75 years and American Society of Anesthesiologists (ASA) physical status I or II.

Exclusion criteria were known hypersensitivity to 5-HT_3 drugs, body mass index (BMI) ≥35, significant systemic diseases, history of atypical or known gastrointestinal problems and/or previous gastrointestinal operations (not including appendectomy), menstruation on admission, history of tinnitus, and reception of steroids, H_2 antagonists, anticholinergics, antihistamines, butyrophenones, phenothiazines, or metoclopramide 24 h before admission. Patients with an intrathoracic goiter or undergoing a difficult endotracheal intubation (more than two attempts at tracheal intubation) were also excluded. No grants or funds from pharmaceutical companies were acquired.

Study patients were enrolled and randomized with *Bernoulli tables* (which allow "complete" or "unrestricted" randomization, minimizing both selection and accidental biases), to receive prophylactic either intravenous (i.v.) tropisetron 5 mg (1 mg/mL) (T group), i.v. granisetron 3 mg (G group), or i.v. 5 mL normal saline (N/S) 0.9% (control group, C group) in combination with 0.625 mg droperidol, approximately 5 min before induction of anesthesia. All i.v. regimens were diluted with N/S 0.9% to a volume of 5 mL. Upon entrance to the operative room schedule, a code number was assigned to each patient. The anesthesiologist and staff nurses, as well as the operative team, were blinded to the administered agent.

Protocol

The anesthetic technique was identical in all patients. Patients fasted for at least 12 h preoperatively and received oral premedication with 1.5 mg of bromazepam and 40 mg of omeprazol the night before surgery and 3 h before the operation. Ten minutes before induction to anesthesia, all patients received 2.5 mg of midazolam and then parecoxib (40 mg/2 mL i.v.). In all cases, propofol 2 mg/kg and remifentanil 1 μg/kg were the induction drugs and *cis*-atracurium 0.2 mg/kg was administered for muscle relaxation. Meperidine (1 mg/kg) was intramuscularly (i.m.) administered after induction, and maintenance of anesthesia was achieved with sevoflurane minimum alveolar concentration (MAC) 1.0%-1.5% in a mixture of O_2 to air and remifentanil in continuous infusion (0.15-0.2 μg/kg/min).

Nasogastric decompression was not employed, as patients were also included in a clinical audit, evaluating the necessity of nasogastric tube insertion in thyroid surgery. Intraoperative monitoring included electrocardiogram, heart rate, arterial blood pressure (noninvasive method), end expiratory CO_2, O_2 saturation, minute/volume, tidal volume, respiratory rate, airway pressures, and MAC sevoflurane. Pulmonary ventilation was performed under intermittent positive pressure ventilation (IPPV) with a mixture of oxygen and air, maintaining fractional inspired oxygen (FiO_2) at 0.5. Ventilation was adjusted to keep the end-tidal CO_2 between 35 and 40 mmHg. Blood pressure and heart rate variations were maintained within 20% of preoperative values by adjusting anesthetic depth, fluid replacement, and vasoactive drug dosages. Adductor pollicis stimulation over the ulnar nerve at the wrist was the standard method of monitoring neuromuscular function. Train-of-four (TOF) stimulations were used to assess the presence of a residual neuromuscular block. No alternative forms of analgesic were administered to the patients. Atropine 1 mg and neostigmine 2.4 mg were used to reverse residual neuromuscular blockade. All patients were extubated on the operating table and were transported to the postanesthesia care unit (PACU) with supplemental oxygen in consciousness with adequate self-maintained respiratory and cardiovascular function.

Postoperative care

Postoperatively, patients were observed for 24 h. A team of specially trained nurse anesthetists, blinded to the

patient's group, collected postoperative data. Before surgery, all patients were instructed to use a 10-cm visual analogue scale (VAS) (VAS: Endpoints labeled "no pain" and "worst possible pain") in order to describe pain intensity and a verbal rating score with (0-10; 0 being no nausea and 10 being the worst nausea imaginable) for nausea intensity.

The degree of postoperative pain was assessed using the VAS at movement (cough) at 2, 4, 12, and 24 h postoperatively and at the same time the intensity of nausea was graded on a numerical scale 0-10. Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit; retching was defined as the labored, spasmodic, rhythmic contractions of the respiratory muscles; vomiting was defined as the forceful expulsion of gastric contents from the mouth. PONV was evaluated by the following variables: The scores of nausea, episodes of vomiting, and rescue antiemetics (metoclopramide). For the purpose of data collection and analysis, retching (same as vomiting but without expulsion of gastric contents) was considered as vomiting. Vomiting was recorded as either present or absent.

Postoperative care was standardized. Rescue antiemetics (i.v. metoclopramide 10 mg) were administered, in the PACU and in the ward, on demand and if any score of nausea was >6. Analgesia was given to patients complaining of pain. This comprised parecoxib 40 mg i.v. at 12 h postoperatively and meperidine (50 mg i.m.) every 6 h in the ward. Side effects (eg, headache, dizziness, muscle pain) were recorded. The provided scheme of analgesia was proved to be sufficient, with no patient requiring supplementary administration of analgesics. The patients and investigators collecting the data were blinded to the patient's group.

Data analysis

Statistical analysis was performed using parametric tests only for operative time and anesthesia time since the distribution of all other variables was not normal. All tests were double-sided and $P \leq 0.05$ was considered to indicate statistical significance.

An a priori power analysis was used to estimate the required sample size. Review of the current literature revealed an average of 30% reduction or more in the frequency of PONV after thyroidectomy with the use of 5-HT3 receptor antagonist compared to placebo. Based on this effect size estimate, in order to achieve a power ≥0.80 with an alpha level of 0.05 a number of 40 patients in each subgroup was considered adequate. IBM SPSS Sample Power 3 was used for the power analysis.[2,5,21-24]

RESULTS

During the study period, 127 patients were enrolled and randomized into the granisetron (G group, n=45), tropisetron (T group, n=40), or the control group (C group, n=42). The three groups were homogenous in respect to age, gender, weight, height, and operative time as well as to all the usually recognized risk factors for PONV (female sex, history of motion sickness and/or previous PONV, nonsmoking status) [Table 1]. Anesthesia time was significantly lower in the granisetron group [Table 1].

Pain varied significantly among different points of time (*Friedman test* P<0.01, Table 2). VAS pain score was significantly higher in granisetron group 2 h postoperatively in comparison to the controls and significantly lower in the granisetron group 24 h postoperatively in comparison to the tropisetron group [Table 2].

Nausea varied significantly among different points of time [Table 2]. Between groups, analysis revealed statistically significant differences at all points of time. Nausea VAS score was lower in both tropisetron and granisetron groups in comparison to the controls at all points of time, except for the 8-h measurement for tropisetron. Moreover, granisetron performed better than tropisetron apart from the 2-h measurement [Table 2].

Despite significant differences in nausea, significant differences in vomiting were not detected between the three groups at all time measurements [Table 3]. Metoclopramide administration varied significantly between the three groups [Table 4]. These differences were attributed to

Table 1: Patients' clinical and demographic characteristics

	Granisetron (*N*=45)	Tropisetron (*N*=40)	Control (*N*=42)	*P* value
Age				
Mean (±SD)	49 (±14.1)	48 (±13.2)	45 (±14.8)	NS
Weight				
Mean (±SD)	68 (±9.4)	68 (±8.9)	68 (±9.9)	NS
Gender				
Females *N* (%)	36 (80.0)	31 (77.5)	33 (78.5)	NS
Smoking				
Yes *N* (%)	13 (29)	10 (21)	14 (33)	NS
History of PONV				
Yes *N* (%)	4 (8)	7 (18)	6 (14)	NS
Anesthesia time				
Mean (±SD)	113.8*(±18.9)	128.4 (±12.4)	127.1 (±14.4)	*P*<0.01
Operative time				
Mean (±SD)	100.0 (±13.1)	107.2 (±13.6)	103.2 (±15.2)	NS

N – number of patients; PONV – Postoperative nausea and vomiting; SD – Standard deviation, *Granisetron had significantly lower anesthesia time (Bonferroni post hoc testing *P*<0.01)

the significantly lower metoclopramide administration in both granisetron and tropisetron group in comparison to the controls. The percentage of patients actually receiving metoclopramide also varied significantly between the three groups. These differences were attributed to the statistically significant difference between granisetron and the control group [Table 4].

No serious drug-related adverse events were reported and no patient was withdrawn from the study due to adverse events. No clinically significant changes in vital signs were observed during the present study.

DISCUSSION

Pain, nausea, and vomiting are frequently listed by the patients as their most important perioperative concerns, with its incidence reaching up to 30% of surgical patients.[3,6,25-27] PONV can lead to delayed discharge and unanticipated hospital readmission, thereby increasing health care costs.[28]

In the present study, both tropisetron and granisetron groups had lower nausea VAS scores in comparison to the controls at all points of time; these differences were significant in all measurements except that at the 8-h time point where the combination of droperidol and tropisetron was comparable to droperidol alone. Moreover, granisetron performed better than tropisetron at all points of time apart from the 2-h measurement. On the contrary, combination of granisetron or tropisetron with droperidol failed to show significant differences compared with droperidol alone in terms of vomiting probably representing the efficacy of droperidol and rescue antiemetics in preventing vomiting. Moreover, the combination schemes failed to significantly reduce the number of patients that had at least an incident of emesis. This discrepancy compared with previous studies may be due to differences in methodology and terminology regarding PONV among researchers. Still, the combination schemes significantly reduced the percentage of patients who required rescue antiemetics compared with droperidol alone. In addition, the pain VAS score differences among the groups observed at the 2- and 24-h time points are of no clinical significance since all VAS scores were less than 3. All enrolled patients in our study were operated in our ambulatory surgical unit and were discharged during the first postoperative day; for this reason, no cost-effectiveness measurements were included in this study.

Regarding POVN in abdominal surgery, pathogenic mechanisms are obscure, but theoretically any reduction in gastrointestinal ischemia decreases the release of emetogenic substances and therefore the risk of PONV.[15-17] However, abdominal surgery and thyroidectomy are not comparable; thyroidectomy does not involve irritation or distension of gastrointestinal structures that may convey chemoreception or nociception via other afferents than parasympathetic.[5]

Table 2: Pain and nausea visual analogue scale scores

Postoperative pain VAS (h)	Median	*N*>median/*N*≤median)		Control (*N*=42)	*P* value
		Granisetron (*N*=45)	Tropisetron (*N*=40)		
2	1	30/15*	16/24	10/32*	<0.01
4	1	25/20	16/24	21/21	NS
8	2	18/27	15/25	13/29	NS
12	2	19/26	11/29	15/27	NS
24	2	7/38**	14/26	8/34	<0.05

*Granisetron VAS higher than controls 2 h postoperatively; **Granisetron VAS lower than tropisetron 24 h postoperatively; VAS – Visual analogue scale

Postoperative nausea VAS (h)	Median	Granisetron (*N*=45)	Tropisetron (*N*=40)	Control (*N*=42)	*P* value
2	3	14/31	7/33	25/17*	<0.01
4	3	11/34	17/23***	34/8*	<0.01
8	4	6/39**	17/23***	27/15	<0.01
12	4	3/42	16/24***	25/17*	<0.01
24	3	4/41	7/33***	17/25*	<0.01

*Control VAS significantly higher than granisetron and tropisetron groups; ** Granisetron VAS significantly lower than the two other groups; ***Tropisetron VAS significantly higher than granisetron group; VAS – Visual analogue scale

Table 3: Postoperative vomiting

Vomiting (h)	Granisetron (*N*=45)	Tropisetron (*N*=40)	Control (*N*=42)	*P* value
2	0.067 (±0.25)	0.05 (±0.22)	0.095 (±0.29)	NS
4	0.18 (±0.39)	0.22 (±0.48)	0.17 (±0.38)	NS
8	0.09 (±0.29)	0.13 (±0.33)	0.12 (±0.38)	NS
12	0.09 (±0.29)	0.13 (±0.33)	0.17 (±0.38)	NS
24	0.04 (±0.21)	0.03 (±0.16)	0.07 (±0.26)	NS
Number of patients with at least one incident of emesis at 0-24 h *N* (%)	10 (22.2)	11 (27.5)	15 (37.5)	NS
Side effects (headache, dizziness, muscle pain-cramps) (Yes)	3 (7%)	4 (10%)	1 (2%)	NS

Table 4: Metoclopramide administration postoperatively

	Granisetron (*N*=45)	Tropisetron (*N*=40)	Control (*N*=42)	*P* value
Metoclopramide (mg)				
Mean, Median (SD)	4.7, 10 (6.6)	6.8, 10 (7.3)	11.2, 10 (9.9)	<0.01
Metoclopramide (Yes)				
N (%)	17 (38)	21 (53)	29 (70)	0.014

Most probably, the etiology of PONV after thyroidectomy is multifactorial and, unlike chemotherapy-induced nausea and vomiting, one cannot expect the same efficacy of antiemetics.[29] Thyroidectomy is an operation that causes strong vagal stimuli due to the surgical manipulation of the neck structures. Moreover, additional factors both related and unrelated to anesthesia may influence PONV, such as age, gender, body weight, history of motion sickness and/or previous PONV, nonsmoking status, type and duration of operation, type of induction, maintenance neuromuscular blocking drug used, and postoperative pain.[6,26] In this study we standardized many of these factors and there were no differences in these factors among the groups studied.

Prophylactic doses of droperidol (well below 1 mg) are effective for the prevention of PONV.[18] Recently, although, the Food and Drug Administration (FDA) issued a "black-box" warning about droperidol.[30] The warning states that droperidol may cause death or life-threatening events associated with QT prolongation and torsades de pointes. This particular warning was regarded as lacking of solid scientific supporting data, with expert views stated in international fora, suggesting that "if it were not for the "black-box" warning, droperidol would have been the panel's overwhelming first choice for PONV prophylaxis."[18] Nevertheless, under any circumstances, the low-dosage administrated in our study, accompanied by close cardiac monitoring, would not justify any concerns about the possibility of elevated risk for intraoperative QT prolongation, arrhythmias, or cardiac arrest.

In general, combination therapy is superior to monotherapy for PONV prophylaxis,[18] while subsequent interventions to address postoperative nausea and vomiting have limited usefulness compared with the first intervention irrespective of the agent or the combination of drugs chosen.[13] Moreover, rescue treatments are ineffective when the same drug has already been used prophylactically.[13] Gan and colleagues[31] reported that ondansetron (4 mg) was effective in preventing postoperative nausea only in the first 6 h after major breast surgery. Paxton and colleagues[32] also found that ondansetron (4 mg) was effective in reducing nausea only in the first 4 h after laparoscopic gynecologic procedures.

Given the multifactorial nature of postoperative nausea and vomiting, a multimodal approach to reduce or eliminate risk factors will therefore be most successful in its management. 5-HT_3 antagonists are the most common choice for prevention of established PONV for patients undergoing thyroidectomy regardless of the number of prophylactic antiemetics given. Drugs with different mechanisms of action should be used in combination to optimize efficacy. It should, nevertheless, be emphasized that it is important to distinguish between antivomiting and antinausea efficacy since nausea is not a little vomiting.[33] The 5-HT_3 antagonists, which have better antivomiting than antinausea efficacy, are associated with headache and can be used in combination with droperidol, which has greater antinausea efficacy and a protective effect against headache.[34]

Concerning the differences in pain VAS scores between the groups of our study, the proposal of a definitive explanation would be very challenging; nevertheless, only assumptions can be made for this difference in pain scores. The explanation may lie upon the particular differences between granisetron and tropisetron regarding their affinity to the subtypes of 5-HT receptors. Specifically, whereas granisetron shows no affinity for any other than 5-HT_3 receptors, tropisetron binds primarily to 5-HT_3 receptors, but also demonstrates an affinity to 5-HT_4 receptors; however, this particular observation definitely merits further investigation.

The doses of granisetron (3 mg) and tropisetron (5 mg) used in this study were chosen because they have been proved to be optimal for treatment of nausea and vomiting induced by various highly emetic chemotherapy regimens and for the prevention of PONV.[28,35] We have administered tropisetron and granisetron immediately before the induction of anesthesia to maximize its potential preemptive antiemetic effect. However, a study comparing tropisetron 5 mg given with premedication or at the end of surgery did not reveal a significant difference in the incidence of PONV.[13]

Dose-ranging studies comparing intravenous granisetron 0.1, 1 and 3 mg in adults, determined that granisetron 1 or 3 mg was the optimum effective prophylactic dose when administered immediately before the start of anesthesia or for treatment of PONV[36,37]; moreover, a statistically significant linear relationship between vomiting control and granisetron dose for the treatment of PONV was noticed.[37] However, in other studies on PONV prevention, intravenous granisetron 40 μg/kg was determined to be the optimal dose for adults.[38] The exact mechanism of granisetron in preventing PONV is not known, but it has been suggested that it may act on sites containing 5-HT_3 receptors with demonstrated antiemetic effects.

Tropisetron has been studied for prevention and treatment of PONV in adults and has an elimination half-life of 8-12 h.[25] Pharmacokinetic variables also affect antiemetic efficacy. The clinical duration of action would be longer with a larger dose of tropisetron.[39] Tropisetron 5 mg i.v. before the start of anesthesia has been found effective

for prevention of PONV after breast and gynecologic surgery.[39,40]

CONCLUSIONS

We conclude that the combination of i.v. 5-HT_3 antagonists with droperidol given shortly before induction of general anesthesia is well tolerated and superior to droperidol alone in preventing nausea after total thyroidectomy. Although granisetron and tropisetron had a significant impact on nausea VAS scores, a large percentage of the thyroidectomy patients had at least a vomiting incident while these combination schemes failed to show significant differences compared to droperidol alone in terms of vomiting incidences. Studies comparing tropisetron and granisetron with other antiemetics among different patient populations are necessary to further determine the role of 5-HT_3 antagonists in the prophylaxis of PONV.

REFERENCES

1. Sonner JM, Hynson JM, Clark O, Kattz JA. Nausea and vomiting following thyroid and parathyroid surgery. J Clin Anesth 1997;9:398-402.
2. Fujii Y, Tanaka H. Comparison of granisetron and ramosetron for the prevention of nausea and vomiting after thyroidectomy. Clin Ther 2002;24:766-72.
3. Kim SI, Kim SC, Baek YH, Ok SY, Kim SH. Comparison of ramosetron with ondansetron for prevention of postoperative nausea and vomiting in patients undergoing gynaecological surgery. Br J Anaesth 2009;103:549-53.
4. Fujii Y. The benefits and risks of different therapies in preventing postoperative nausea and vomiting in patients undergoing thyroid surgery. Curr Drug Saf 2008;3:27-34.
5. Akin A, Esmaoglu A, Gunes I, Boyaci A. The effects of the prophylactic tropisetron-propofol combination on postoperative nausea and vomiting in patients undergoing thyroidectomy under desflurane anesthesia. Mt Sinai J Med 2006;73:560-3.
6. Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology, treatment, and prevention. Anesthesiology 1992;77:162-84.
7. Wetchler BV. Postoperative nausea and vomiting in day-case surgery. Br J Anaesth 1992;69:33S-9S.
8. Thompson DP, Ashley FL. Face-lift complications: A study of 922 cases performed in a 6-year period. Plast Reconstr Surg 1978;61:40-9.
9. Kenny GN. Risk factors for postoperative nausea and vomiting. Anaesthesia 1994;49:6-10.
10. Koivuranta M, Laara E, Snare L, Alahuhta S. A survey of postoperative nausea and vomiting. Anaesthesia 1997;52:443-9.
11. Macario A, Weinger M, Truong P, Lee M. Which clinical anesthesia outcomes are both common and important to avoid? The perspective of a panel of expert anesthesiologists. Anesth Analg 1999;88:1085-91.
12. Macario A, Claybon L, Pergolizzi JV. Anesthesiologists' practice patterns for treatment of postoperative nausea and vomiting in the ambulatory Post Anesthesia Care Unit. BMC Anesthesiol 2006;6:6.
13. Apfel CC, Korttila K, Abdalla M, Kerger H, Turan A, Vedder I, *et al*. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. N Engl J Med 2004;350:2441-51.
14. White PF, Hamza MA, Recart A, Coleman JE, Macaluso AR, Cox L, *et al*. Optimal timing of acustimulation for antiemetic prophylaxis as an adjunct to ondansetron in patients undergoing plastic surgery. Anesth Analg 2005;100:367-72.
15. Henzi I, Walder B, Tramer MR. Metoclopramide in the prevention of postoperative nausea and vomiting: A quantitative systematic review of randomized, placebo-controlled studies. Br J Anaesth 1999;83:761-71.
16. Habib AS, El-Moalem HE, Gan TJ. The efficacy of the 5-HT3 receptor antagonists combined with droperidol for PONV prophylaxis is similar to their combination with dexamethasone. A meta-analysis of randomized controlled trials. Can J Anaesth 2004;51:311-9.
17. Macario A, Chung A, Weinger MB. Variation in practice patterns of anesthesiologists in California for prophylaxis of postoperative nausea and vomiting. J Clin Anesth 2001;13:353-6.
18. Gan TJ, Meyer T, Apfel CC, Chung F, Davis PJ, Eubanks S, *et al*. Consensus guidelines for managing postoperative nausea and vomiting. Anesth Analg 2003;97:62-71.
19. Habib AS, Gan TJ. Evidence-based management of postoperative nausea and vomiting: A review. Can J Anaesth 2004;51:326-41.
20. Wolf H. Preclinical and clinical pharmacology of the 5-HT3 receptor antagonists. Scand J Rheumatol Suppl 2000;113:37-45.
21. Lee SY, Lee JY, Park SY, Kim JH, Cho OG, Kim JS, *et al*. Prophylactic antiemetic efficacy of granisetron or ramosetron in patients undergoing thyroidectomy. Asian J Surg 2002;25:309-14.
22. Fujii Y, Saitoh Y, Tanaka H, Toyooka H. Prevention of post-operative nausea and vomiting with combined granisetron and droperidol in women undergoing thyroidectomy. Eur J Anaesthesiol 1999;16:688-91.
23. Fujii Y, Tanaka H, Kobayashi N. Granisetron, droperidol, and metoclopramide for preventing postoperative nausea and vomiting after thyroidectomy. Laryngoscope 1999;109:664-7.
24. Fujii Y, Saitoh Y, Tanaka H, Toyooka H. Prophylactic antiemetic therapy with granisetron in women undergoing thyroidectomy. Br J Anaesth 1998;81:526-8.
25. Kovac AL. Prevention and treatment of postoperative nausea and vomiting. Drugs 2000;59:213-43.
26. Kapur PA. The big "little problem". Anesth Analg 1991;73:243-5.
27. Gold BS, Kitz DS, Lecky JH, Neuhaus JM. Unanticipated admission to the hospital following ambulatory surgery. JAMA 1989;262:3008-10.
28. Hill RP, Lubarsky DA, Phillips-Bute B, Fortney JT, Creed MR, Glass PS, *et al*. Cost-effectiveness of prophylactic antiemetic therapy with ondansetron, droperidol, or placebo. Anesthesiology 2000;2:958-67.
29. Joris JL, Poth NJ, Djamadar AM, Sessler DI, Hamoir EE, Defêchereux TR, *et al*. Supplemental oxygen does not reduce postoperative nausea and vomiting after thyroidectomy. Br J Anaesth 2003;91:857-61.
30. FDA strengthens warnings for droperidol [Internet]. Available from: http://www.fda.gov/bbs/topics/ANSWERS/2001/ANS01123.html [Last accessed on 2008 Jan 23].
31. Gan TJ, Ginsberg B, Grant AP, Glass PS. Double-blind, randomized comparison of ondansetron and intraoperative propofol to prevent postoperative nausea and vomiting. Anesthesiology 1996;85:1036-42.
32. Paxton LD, McKay AC, Mirakhur RK. Prevention of nausea and vomiting after day case gynaecological laparoscopy. A comparison of ondansetron, droperidol, metoclopramide and placebo. Anaesthesia 1995;50:403-6.
33. D'Angelo R, Philip B, Gan TJ, Kovac A, Hantler C, Doblar D, *et al*. A randomized, double-blind, close-ranging, pilot study of intravenous granisetron in the prevention of postoperative

nausea and vomiting in patients abdominal hysterectomy. Eur J Anaesthesiol 2005;22:774-9.
34. Tramer MR. A rational approach to the control of postoperative nausea and vomiting: Evidence from systematic reviews. Part II. Recommendations for prevention and treatment, and research agenda. Acta Anaesthesiol Scand 2001;45:14-9.
35. Jordan K, Hinke A, Grothey A, Schmoll HJ. Granisetron versus tropisetron for prophylaxis of acute chemotherapy-induced emesis: A pooled analysis. Support Care Cancer 2005;13:26-31.
36. Fujii Y, Tanaka H, Toyooka H. Reduction of postoperative nausea and vomiting with granisetron. Can J Anaesth 199441:291-4.
37. Wilson AJ, Diemunsch P, Lindeque BG, Scheinin H, Helbo-Hansen HS, Kroeks MV, *et al*. Single-dose i.v. granisetron in the prevention of postoperative nausea and vomiting. Br J Anaesth 1996;76:515-8.
38. Taylor AM, Rosen M, Diemunsch PA, Thorin D, Houweling PL. A double-blind, parallel-group, placebo-controlled, dose-ranging, multicenter study of intravenous granisetron in the treatment of postoperative nausea and vomiting in patients undergoing surgery with general anesthesia. J Clin Anesth 1997;9:658-63.
39. Chan MT, Chui PT, Ho WS, King WW. Single-dose tropisetron for preventing postoperative nausea and vomiting after breast surgery. Anesth Analg 1998;87:931-5.
40. Alon E, Kocian R, Nett PC, Koechli OR, Baettig U, Grimaudo V. Tropisetron for the prevention of postoperative nausea and vomiting in women undergoing gynecologic surgery. Anesth Analg 1996;82:338-41.

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