The Effects of the Prophylactic Tropisetron-Propofol Combination on Postoperative Nausea and Vomiting in Patients Undergoing Thyroidectomy under Desflurane Anesthesia

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Abstract

Purpose: To evaluate the efficacies of tropisetron and tropisetron-propofol combination in the prophylaxis for postoperative nausea and vomiting in patients undergoing thyroidectomy under desflurane anesthesia. (This combination has apparently not been previously investigated for this particular surgery and anesthesia.)

Methods: Prospective, randomized, double-blind study. One hundred five patients aged between 19 and 68 years were included in the study. Group T received 5 mg of tropisetron (tropisetron group, n=35), group TP (tropisetron-propofol group, n=35) received 5 mg of tropisetron and 0.5 mg/kg of propofol, and group P (placebo group, n=35) received saline, immediately after anesthesia induction. The anesthesia induction regimen was applied to all patients, and anesthesia was maintained with 5–7% desflurane and 66% N_2O in O_2.

Results: Group TP reported a lower incidence of postoperative nausea and vomiting (17%) than those in groups T and P (42.8% and 77%, respectively). The postoperative antiemetic requirements were significantly higher in the placebo group compared to the other two groups ($p<0.05$).

Conclusion: The tropisetron-propofol combination is more effective than tropisetron alone in the prevention of postoperative nausea and vomiting after thyroidectomy.

Key Words: Side effects, postoperative, nausea, vomiting, antiemetic, tropisetron, propofol, surgery, thyroidectomy, anesthetics, desflurane.

Introduction

STUDIES REPORT that the frequency of postoperative nausea and vomiting (PONV) after thyroidectomy is approximately 63–84%, for anesthetic agents other than desflurane (1, 2). PONV may represent the principal source of discomfort of the entire procedure, and the most unpleasant aspect of postoperative recovery. Additionally, vomiting may increase the risk of postoperative bleeding (3). Also, increased thoracic and abdominal pressure during retching may produce arterial and venous hypertension. Postoperative bleeding is of particular concern in these patients, as it may produce hematoma in the neck with the potential for airway obstruction.

Desflurane has a low blood/gas solubility that allows rapid induction and recovery. This characteristic has recently made it increasingly popular. However, PONV, the most significant side effect, is frequent (4).

Tropisetron, a highly potent and selective antagonist of serotonin type 3 receptors (5-HT_3), has proven to be effective and well tolerated against nausea and vomiting induced by radiotherapy and chemotherapy (5). It is also effective and well tolerated in the prevention or treatment of PONV in women undergoing gynecologic surgery and laparoscopic cholecystectomy (6, 7).

The numerous studies on the antiemetic effect of propofol at subhypnotic doses have yielded controversial results. Campbell et al. (8) reported that propofol at subhypnotic doses was ineffective against PONV after laparoscopic cholecystectomy, whereas Fujii et al. (9) achieved adequate prophy-

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laxis in patients undergoing thyroidectomy under sevoflurane anesthesia. However, propofol at subhypnotic doses was reportedly ineffective after procedures under desflurane anesthesia (10).

Therefore we investigated the efficacies of the tropisetron and tropisetron-propofol combination in PONV prophylaxis, in patients undergoing thyroidectomy under desflurane anesthesia. (This combination has apparently not been previously investigated for this particular surgery and anesthesia.)

Materials and Methods

After the study protocol was approved by the ethics committee of the University Hospital, 105 patients between 19 and 68 years of age were enrolled. Patients who had gastrointestinal problems, had used a central-acting drug or an antiemetic in the previous 24 hours, were having menstruation or had a history of nausea and vomiting were excluded. The patients were randomized to 3 groups. Group T received 5 mg of tropisetron (n=35), group TP (n=35) received 5 mg of tropisetron and 0.5 mg/kg of propofol, and group P (n=35) received saline, immediately after anesthesia induction. The same anesthesia regimen was administered to all patients. After the patients had been taken to the surgery room, mean arterial pressure (MAP), heart rate (HR), and peripheral oxygen saturation (SpO_2) were monitored. Patients were assigned to one of the three study groups using a computer-generated random number table. Induction was performed with fentanyl (1 μg/kg) and thiopental (6–7 mg/kg); vecuronium (0.1 mg/kg IV) was given to facilitate tracheal intubation. Maintenance was conducted with 5–7% desflurane and 66% N_2O in oxygen. The patients were ventilated to maintain the end-tidal CO_2 level between 30 and 35 mm Hg (Datex Engstrom AS/3 Anesthesia monitor, Helsinki, Finland). Muscle relaxation was maintained with IV vecuronium. The thyroidectomy was performed with patients in the supine position, with the head slightly hyperextended. At the end of the operation, atropine (0.02 mg/kg IV) and neostigmine (0.05 mg/kg) were used to reverse the neuromuscular block. The extubation time (the interval between the cessation of anesthetic gas and extubation), emergency time (the interval between the cessation of anesthetic gas and eye opening) and orientation time (the interval between the cessation of anesthetic gas and the time when the patients could state the current date and their birth date) were recorded.

Postoperatively, the patients were taken to the recovery room. Pain was assessed by means of a visual analog scale (VAS 0: no pain; 10: the most severe pain). Patients with VAS scores higher than 3 were given 75 mg of diclofenac intramuscularly. We evaluated nausea and vomiting by direct questioning or by spontaneous complaint of patients and recorded for the 0–2, 2–6, 6–12 and 12–24 hour intervals. The nurses asked the patients if retching or vomiting had occurred and if they felt nauseated, with only two possible answers (yes or no). Nausea was defined as the unpleasant sensation associated with awareness of urge to vomit; retching was defined as labored, spasmodic, rhythmic contraction of the respiratory muscles without expulsion of gastric contents, and vomiting was defined as the forceful expulsion of the gastric contents from the mouth. No distinction was made between vomiting and retching (i.e., a retching event was considered as a vomiting event). A complete response was defined as no PONV and no need for rescue antiemetic medication. Patients with two or more episodes of vomiting were given metoclopramide (10 mg) intravenously. The intraoperative and postoperative complications were recorded.

Categorical variables were analyzed by using a series of 3×2 Chi-squared tests to determine the differences among the three groups, followed by 2×2 Chi-squared test for intergroup differences. All follow-up analyses were corrected for the number of simultaneous contrasts using the Bonferroni adjustments. A p value <0.05 was considered statistically significant.

Results

The groups did not differ significantly with respect to demographic characteristics, operation and anesthesia durations ($p>0.05$) and there were no significant differences in their extubation, emergency and orientation times ($p>0.05$) (Table 1). The patients' number of PONV and rescue antiemetic requirements are presented in Table 2. Group TP reported a lower incidence of postoperative nausea and vomiting (17%) than those in Group T and Group P (42.8% and 77%, respectively). The postoperative antiemetic requirements were significantly higher in the placebo group compared to the other two groups ($p<0.05$)

Discussion

In this study of thyroidectomy under desflurane anesthesia, the tropisetron-propofol combination was more effective than tropisetron alone or placebo in antiemetic prophylaxis.

The etiology of PONV after thyroidectomy is unclear, but it does occur frequently. This high inci-

TABLE 1
Demographic Data and Anesthesia Duration, Surgery Duration, Extubation, Emergency, and Orientation Time of the Research Groups

	Group T (n=35)	Group TP (n=35)	Group P (n=35)
Age (years)	42.0 ± 11.6	46.2 ± 13.5	43.1 ± 11
Height (cm)	163.3 ± 8.3	162.5 ± 5.7	164.3 ± 9.1
Weight (kg)	70.9 ± 11.9	66.8 ± 9.1	72.0 ± 13.5
Sex M/F	7/28	5/30	6/29
Anesthesia duration (min)	122.0 ± 38.5	116.0 ± 34.7	120.5 ± 33.9
Surgery duration (min)	111.8 ± 37.7	105.2 ± 32.8	109.0 ± 31.0
Extubation time (min)	2.4 ± 1.0	2.6 ± 1.4	2.8 ± 2.0
Emergency time (min)	4.3 ± 1.4	4.7 ± 2.5	4.5 ± 2.5
Orientation time (min)	6.8 ± 1.8	6.9 ± 2.6	6.4 ± 3.0

Values are mean ± SD.

TABLE 2
Number of PONV and Rescue Antiemetic Requirements for the Research Groups

	Group T (n=35)	Group TP (n=35)	Group P (n=35)
Complete response (no PONV, no rescue)	20 (57.2)*	29 (83)*+	8 (23)
Nausea	15 (42.8)*	6 (17)*+	27 (77)
Retching or vomiting	8 (22.8)*	2 (5.7)*	25 (71.4)
Total	15 (42.8)*	6 (17)*+	27 (77)
Rescue antiemetics	8 (22.8)*	2 (5.7)*	25 (71.4)

Values are number of patients n (%)
* p value (χ^2 test) for comparison with placebo group, + p value (χ^2 test) for comparison with tropisetron group
PONV: Postoperative nausea and vomiting

dence is probably related to the age range and sex of the patients (mostly middle-aged woman) and the intense preoperative vagal stimulation (surgical handling of the neck structures) (1). Obesity, anesthesia technique and postoperative pain are also known to increase the frequency of PONV (11). We tried to minimize the effects of these factors by standardizing patient characteristics, surgical procedure, anesthesia technique and postoperative pain control.

The frequency of PONV after desflurane anesthesia is reportedly higher than the frequencies after sevoflurane and isoflurane anesthesia, but rapid recovery is an important advantage (12). Gupta et al. (12), in a meta-analysis of 58 articles published between 1966 and 2002, concluded that desflurane allows rapid recovery, but the frequency of PONV is high. Raeder et al. (13) reported that in laparoscopic cholecystectomy, desflurane cost less and allowed rapid recovery in comparison with propofol, but that prophylaxis for PONV was required. Van Hemelijck et al. (14) reported that use of propofol during induction in desflurane anesthesia was ineffective in preventing PONV. Therefore, we chose to investigate the effects of tropisetron and tropisetron-propofol combination.

Tropisetron is a potent selective 5-HT_3 receptor antagonist that has been successfully used to treat nausea and vomiting after chemotherapy and radiotherapy (15). Its efficacy against PONV has been confirmed (6, 16). Its elimination half-life (8–12 hours) is longer than that of the other 5-HT_3 antagonists (e.g., ondansetron 3.2–3.7 h, granisetron 3–4 h), and a single dose of tropisetron may provide prolonged antiemetic effects (16). In a series of 1513 patients undergoing general anesthesia, Alon et al. (17) found that tropisetron reduced the frequency of PONV and the rescue antiemetic requirement.

The mechanism by which propofol acts as an antiemetic is unclear. Propofol is not thought to have vagolytic properties. Borgeat et al. (18) suggested that propofol may have failed as an antiemetic in patients who had undergone laparoscopic gynecological procedures because of uninhibited vagal stimulation. In our study on patients undergoing thyroidectomy, an operation that causes strong vagal stimuli, the frequency of PONV decreased to as low as 17% with the tropisetron-propofol combination. However, the location and nature of this stimulation in laparoscopy and thyroidectomy are not comparable; in thyroidectomy they do not involve irritation or distension of gastrointestinal structures that may convey chemoreception or nociception via other afferents than parasympathetic. A dopamine D_2 receptor antagonist effect of propofol has also been suggested, but not proved (19). Propofol has also been shown to possess weak 5-HT_3 properties, suggesting a possible effect on the chemoreceptor trigger zone, but not enough to fully explain the efficacy of the drug in emetic syndromes refractory to 5-HT_3 antagonist therapy (20, 21).

Ewalenko et al. (22), in a study of patients undergoing thyroidectomy under isoflurane anesthesia, reported that postoperative propofol infusion (0.1 mL/kg/h) reduced the frequency of PONV to 44% compared to 84% in the placebo group. In a study by Fujii et al. (9) 0.5 mg/kg of propofol was more effective than droperidol and metoclopramide after thyroid surgery under sevoflurane anesthesia. However, in a study comparing sevoflurane and desflurane in patients undergoing

laparoscopic cholecystectomy, Song et al. (10) found that 0.5 mg/kg of propofol decreased the frequency of PONV after sevoflurane but not after desflurane. Eriksson et al. (4) used desflurane, desflurane-ondansetron and propofol-based anesthesia in patients undergoing gynecologic operations and found PONV frequencies of 80% in the single-agent desflurane group, 40% in the desflurane-ondansetron group and 20% in the propofol-based anesthesia group. In our study, addition of tropisetron to propofol was effective in reducing the PONV frequency further.

In conclusion, the tropisetron-propofol combination is more effective than tropisetron alone for the prevention of PONV after thyroidectomy.

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