COMPARISON OF ONDANSETRON, GRANISETRON AND DEXAMETHASONE FOR PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN THYROIDECTOMY PATIENTS IN OUR RURAL TERTIARY CARE CENTRE

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ABSTRACT

BACKGROUND
Postoperative nausea and vomiting is a distressing side effect of anaesthesia and surgery. Thyroidectomy is a surgery with a relatively higher incidence of PONV (60% - 84%). Numerous antiemetics have been studied for the prevention of PONV including traditional agents (Metoclopramide, perphenazine, prochlorperazine, cyclizine and droperidol) corticosteroids and the 5-HT3 receptor antagonists (ondansetron, dolasetron, granisetron and tropisetron).

In this prospective observational study, we compared the efficacy of ondansetron, granisetron and dexamethasone for prevention of PONV following elective total thyroidectomy in female patients in our rural tertiary care centre.

MATERIALS AND METHODS
We studied a total of 100 female patients of age group 21 - 45. Patients who received ondansetron, granisetron, dexamethasone and normal saline were included in four groups of 25 each and were observed for incidence of nausea and vomiting, efficacy and side effects of the drugs. All episodes of PONV in the first 24 hrs., at different time intervals were studied. The association between the type of drug used and the incidence of nausea and vomiting was tested statistically by using chi-square test.

RESULTS
The incidence of nausea and vomiting was 52% in the control group, 44% in dexamethasone group, 28% in the ondansetron group and 12% in granisetron group within 24 hrs.

CONCLUSION
This study clearly demonstrates the superiority of single intravenous dose of Granisetron for the prevention of nausea and vomiting in female patients undergoing thyroidectomy.

KEYWORDS
Dexamethasone; Ondansetron; Granisetron; Thyroidectomy; Female Patients; PONV.


BACKGROUND
Postoperative nausea and vomiting is a common complication after surgery under general anaesthesia,(1) with female patients being more susceptible.(2,3) Persistent nausea and vomiting may result in dehydration, electrolyte imbalance and delayed discharge after outpatient surgery.(4) It can also cause tension on suture line, venous hypertension and increased bleeding under skin flap, pulmonary aspiration of vomitus if airway reflexes are depressed due to anaesthetic drugs.(5)

The incidence of emesis after general anaesthesia is influenced by the type of surgical procedure irrespective of anaesthetic technique.(6) A high incidence of postoperative emesis is seen after head and neck surgery in particular; thyroidectomy is a surgery with a relatively higher PONV incidence of 60 - 84%.(7) Antiemetics are the mainstay of prophylaxis against PONV.(8) Among them 5HT3 antagonists such as ondansetron and granisetron are considered first-line agents due to their high efficacy and fewer side-effects.(9,10) Granisetron as compared with ondansetron is a more selective and longer acting 5HT3 receptor antagonist; efficacy of which for PONV prophylaxis has been demonstrated after different surgical procedures.(11,12,13,14,15) In this study the antiemetic efficacy of the drugs ondansetron, granisetron and dexamethasone were compared with control in female patients who underwent thyroidectomy under general anaesthesia.

MATERIALS AND METHODS
This was a prospective, observational study involving 100 euthyroid female patients of ASA I and II in the age group 21 – 45 undergoing elective thyroidectomy under general anaesthesia. This study was conducted in Govt. T. D. Medical College Hospital, Alappuzha, a rural tertiary care centre. This study was approved by the Ethical Committee, Medical College, Alappuzha. We conveniently chose a sample size of 25 in each group.

Patients with history of migraine, ischaemic heart disease diabetes mellitus, hypertension, history of allergy to antiemetics were excluded from the study.

A thorough pre-anesthetic checkup was done including a detailed history, general and systemic examination and routine and relevant investigations. Informed written consent...
obtained. All patients were advised to fast for 8 hours prior to surgery. All patients received Tab. Alprazolam 0.25 mg and Tab. Ranitidine 150 mg the night before surgery and at 6 am on the day of surgery and Inj. Pethidine 0.5 mg per kilogram body weight + Promethazine 0.25 mg per kilogram body weight IV 10 minutes before surgery.

An intravenous line was secured and ringer lactate was started. Patients were shifted to the operating room. Monitors- NIBP, Pulse oximeter, 3 lead ECG and capnograph were attached. Baseline vital signs were recorded. On the operating table, patients received Midazolam 1 mg and Glycopyrrolate 0.2 mg.

Patients were pre-oxygenated with 100% O2 for 3 minutes. Precurarisation was done with 1/5th of the intubating dose of vecuronium. Patients were induced with Inj. Thiopentone sodium 5 mg/kilogram body weight. To attenuate the stress response to laryngoscopy and intubation, Inj. Lidocaine (preservative free) 1.5 mg/kg body weight was given IV 90 seconds before intubation. After giving Inj. Succinylcholine 1.5 mg/kg body weight, patients were intubated with cuffed endotracheal tube 7 or 7.5 mm (LD) 60 seconds after succinylcholine administration. Anaesthesia was maintained with N:O + O2 2:1 ratio and 0.5% isoflurane. Vecuronium bromide was used for muscle relaxation in a dose of 0.08 mg/kg body weight.

After the removal of the thyroid gland i.e. approximately 30 minutes before the end of surgery, patients received one of the following drugs 2 mL of normal saline, dexamethasone 0.2 mg/kg body weight, ondansetron 0.1 mg/kg body weight slowly and granisetron 0.04 mg/kg body weight slowly IV. All the 4 drugs are routinely given in patients for prevention of PONV in this clinical setting. Patients were included in one of the 4 groups according to the drugs they received till the required sample size was reached. On completion of surgery, the residual neuromuscular blockade was reversed. Patients were extubated, vitals checked and was shifted to the postoperative recovery room. Supplemental Oxygen was administered and patients were observed in the recovery room for 1 hour for any postoperative nausea and vomiting. The patients were asked for any headache. During this time, the blood pressure and pulse rate were recorded. For postoperative analgesia, patients were given Inj. Pethidine 0.75 mg/kg body weight + Promethazine 0.25 mg/kg body weight intramuscularly 8th hourly for 24 hours. Patients were asked to take oral fluids 8 hours after surgery. Patients complaining of headache were treated with intravenous infusion paracetamol 1 gm slowly.

The patients were observed in the postoperative ward at 2 hours, 4 hours, 6 hours, 12 hours and 24 hours after the administration of the drug. An episode of PONV was defined as nausea (subjective feeling of the need to vomit), vomiting (expulsion of stomach contents) or retching (an involuntary attempt to vomit, but not productive of stomach contents).

The incidence of nausea and vomiting in each group was expressed in percentages and proportions and the association between the type of drugs used and the incidence of nausea and vomiting was tested statistically using chi-square test.

RESULTS

Statistical analysis was done using SPSS version 16. All four groups were comparable with respect to age, weight and ASA status. The incidence of nausea and vomiting in the control group is 52%, dexamethasone group is 44%, ondansetron group is 28%, and granisetron group is 12% within 24 hrs.

Incidence of PONV at different time intervals is shown in Table 1.

The association between the type of drug used and the incidence of nausea and vomiting was tested statistically by using chi-square test and the drug granisetron was found to be associated with decreased incidence of nausea and vomiting (Chi square value is 9.19, p value less than 0.05) and was found to be statistically significant as shown in Table 2.

The incidence of nausea and vomiting was assessed at different time intervals. During the time 0 - 6 hours nausea and vomiting was 16% in control group, 28% in dexamethasone group, 0% in ondansetron group and 4% in granisetron group. In the time interval of 6 - 12 hours the incidence was 32% in control group, 12% in dexamethasone group, 24% in ondansetron group and 8% in granisetron group.

During the time interval of 6 - 12 hours the drug granisetron was found to be a more effective anti-emetic and this is found to be statistically significant (Chi-square value 4.5, p value < 0.05) as shown in Table 3.

<table>
<thead>
<tr>
<th>Category</th>
<th>1 Hour n (%)</th>
<th>1 - 2 Hour's n (%)</th>
<th>2 - 4 Hour's n (%)</th>
<th>4 - 6 Hour's n (%)</th>
<th>6 - 12 Hour's n (%)</th>
<th>12 - 24 Hour's n (%)</th>
<th>Within 24 Hour's n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>3 (12)</td>
<td>1 (4)</td>
<td>0</td>
<td>0</td>
<td>8 (32)</td>
<td>1 (4)</td>
<td>13 (52)</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>3 (12)</td>
<td>0</td>
<td>4 (16)</td>
<td>0</td>
<td>3 (12)</td>
<td>1 (4)</td>
<td>11 (44)</td>
</tr>
<tr>
<td>Ondansetron</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6 (24)</td>
<td>1 (4)</td>
<td>7 (28)</td>
</tr>
<tr>
<td>Granisetron</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (4)</td>
<td>2 (8)</td>
<td>0</td>
<td>3 (12)</td>
</tr>
</tbody>
</table>

Table 1. Incidence of Nausea and Vomiting at different Time Intervals

<table>
<thead>
<tr>
<th>Groups</th>
<th>Control n (%)</th>
<th>Dexamethasone n (%)</th>
<th>Ondansetron n (%)</th>
<th>Granisetron n (%)</th>
<th>Chi-square Value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of patients with nausea and vomiting</td>
<td>13 (52)</td>
<td>11 (44)</td>
<td>7 (28)</td>
<td>3 (12)</td>
<td>9.19</td>
<td>&lt; 0.05</td>
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</tbody>
</table>

Table 2. Nausea and Vomiting in 24 Hrs.
The incidence of headache with drugs was assessed for 24 hours and 5 (20%) patients in ondansetron group and 6 (24%) patients in granisetron group had complaints of headache.

Bhattacharya and Banerjee(59) found granisetron 2 mg to be more effective than ondansetron 4 mg in preventing PONV following gynaecological laparoscopy. In our study, we used 0.04 mg/kg body weight of granisetron.

A study on Dexamethasone to prevent postoperative nausea and vomiting, an updated meta-analysis of randomised controlled trials done by De Oliveira GS Jr,1 Castro-Alves LJ, Ahmad S, Kendall MC and McCarthy RJ[20] showed that a 4 mg to 5 mg dose of dexamethasone seems to have similar clinical effects in the reduction of PONV as the 8- to 10-mg dose when dexamethasone was used as a single drug or as a combination therapy. These findings support the current recommendation of the SAMBA guidelines[21] for PONV, which favours the 4-mg to 5-mg dose regimen of systemic dexamethasone. In our study, we used 0.2 mg/kg.

The incidence of nausea and vomiting was compared in the 4 groups at different time intervals. The incidence of nausea and vomiting was 52% in the control group within 24 hours. Of this 32% patients were symptomatic during 6 - 12 hour period.

Incidence of PONV was 54.4% in a 24 hr. period in a prospective, randomised study comparing totally intravenous versus inhalational anaesthetics done on PONV after thyroid surgery by Varimal; Gazzaneli; Cavallaro; De Toma; Tarquini; Guerra; C; Stramaccioni E; and Pietropaoli P.[22] This is comparable to our results.

In our Dexamethasone group, the incidence was 44% at the end of 24 hours with 16% of the patients symptomatic during 2 - 4 hours.

A randomised, double-blind, placebo-controlled clinical trial on efficacy of a single preoperative dexamethasone 8 mg to prevent nausea and vomiting after Thyroidectomy by Tarantino I; Warschkow R; Beutner U; Kolb W; Lüthi A; Lüthi C; Schmied BM and Clerici T found an incidence of 29% in the treatment arm.[23]

Antiemetic prophylaxis in thyroid surgery: a randomised, double-blind comparison of three 5-HT3 agents done by[24] Metaxari M,1 Papaioannou A, Petrou A, Chatzimichali A, Pharmacalidou E and Askitopoulou H. The administration of granisetron reduced significantly the incidence of nausea at 6, 12 and 18 h (26, 18 and 2%, respectively) and vomiting at 6 and 12 h (10 and 6%, respectively).

Our incidence PONV in granisetron group in 4 - 6 hrs, 6 - 12 hrs., within 24 hrs. were 4%, 8% and 12% respectively. In their study, the ondansetron reduced significantly the incidence of nausea and vomiting only at 6 h postoperatively (28 and 12%, respectively). In our study incidence of PONV in ondansetron group was 24%, 4%, 28% in 6 - 12 hrs. 12 - 24 hrs. and within 24 hrs. respectively which was comparable.

### Table 3. Incidence of Nausea and Vomiting with different Time Intervals

<table>
<thead>
<tr>
<th>Time Interval (Hrs.)</th>
<th>Control n (%)</th>
<th>Dexamethasone n (%)</th>
<th>Ondansetron n (%)</th>
<th>Granisetron n (%)</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>0 - 6</td>
<td>4 (16)</td>
<td>7 (28)</td>
<td>0</td>
<td>1 (4)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>6 - 12</td>
<td>8 (32)</td>
<td>3 (12)</td>
<td>6 (24)</td>
<td>2 (8)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>12 - 24</td>
<td>1 (4)</td>
<td>1 (4)</td>
<td>0</td>
<td>0</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

### Table 4. Incidence of Headache with Drugs

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Control</th>
<th>Dexamethasone</th>
<th>Ondansetron</th>
<th>Granisetron</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Headache</td>
<td></td>
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<tr>
<td>5</td>
<td>20</td>
<td>6</td>
<td>24</td>
<td></td>
</tr>
</tbody>
</table>

### Figure 1. Nausea and Vomiting within 24 hrs.

**DISCUSSION**

Postoperative nausea and vomiting is a distressing side effect of anaesthesia and surgery. The main cause of PONV after thyroidectomy is not entirely clear, but it is thought to result from the age range, gender of patients (mostly middle-aged women)[23] and strong vagal stimulation (Surgical handling of neck structures)[7] PONV could adversely affect patients who have undergone thyroidectomy, because vomiting could cause or exacerbate postoperative bleeding inside the surgery site. Such haemorrhage might compress the trachea and lead to acute airway obstruction, which could necessitate tracheal intubation or re-operation to control the bleeding.[10] Therefore, it is reasonable that appropriate PONV prophylaxis should be considered first rather than managing it after PONV is established.

In the present study, 100 euthyroid female patients in the age group of 21 - 45 undergoing elective total thyroidectomy were evaluated for PONV. This is because patients undergoing thyroid surgery are particularly susceptible to PONV.[7-17] In our study, patients received 5HT3 receptor antagonists and dexamethasone as prophylaxis for PONV.

5HT3 antagonists such as ondansetron and granisetron are considered first-line agents due to their high efficacy and fewer side-effects.[6,10] In a study on efficacy, dose-response, and safety of ondansetron in prevention of postoperative nausea and vomiting: a quantitative systematic review of randomised placebo-controlled trials done by Tramer MR,1 Reynolds DJ, Moore RA and McQuay HJ found that the optimal dose range of Ondansetron to prevent PONV is 4 - 8 mg IV with duration of antiemetic effect being dose related.[18] We also used 0.1 mg /kg body weight.
Post-operatively, 20% patients in the ondansetron group and 24% patients in the granisetron group had headache.

Regarding the incidence of PONV, this study clearly demonstrates the superiority of single intravenous dose of granisetron for the prevention of nausea and vomiting in female patients undergoing thyroidectomy.

In a meta-analysis of RCT on 5HT3 antagonists for prophylaxis of postoperative nausea and vomiting in breast surgery conducted by Singhal AK, Kannan S, Gota VS found that 5HT3 antagonists are superior to other pharmacological interventions for the prevention of PONV in patients undergoing breast surgery under general anaesthesia. In our study also, 5 HT3 receptor antagonists were superior to dexamethasone for preventing PONV.

Study on Ondansetron and Granisetron for prevention of post-operative nausea and vomiting following laparoscopic cholecystectomy done by Gauchan S, Thapa C, Shakya P, Bhattachari R, Shakya S in JNMA evaluated nausea and vomiting scores in the first 3 hours period revealed that each of the drugs had a similar antiemetic effect (P > 0.05). This result is similar to our study. In the last 12 hours episodes of nausea, retching and vomiting were significantly higher in ondansetron group. This finding is also similar in our study.

A comparative study on PONV using ondansetron, granisetron and dexamethasone combination after modified radical mastectomy was published by Gupta P and Jain S. The incidence of complete response (no PONV, no rescue medication) was 96% with G + D as compared with 86% with granisetron and 4% with ondansetron during 0 - 3 h after surgery, which was clinically significant (P < 0.05). Similarly, clinically significant response was seen during 3 - 6, 6 - 9, 9 - 12 and 12 - 24 h of surgery. This is similar to our study, which showed superiority of granisetron over ondansetron.

A study conducted by Brij Bihari, Joytsaa Agarwal and Anita Malick in the Institute of Medical Sciences, Banaras Hindu University, Varanasi showed that granisetron (0.04 mg/kg Bw) was superior to Ondansetron (0.1 mg/kg Bw) in middle ear surgery. The incidence of PONV in the different groups were Control group- 76%, Ondansetron group (0.1 mg/Kg Bw)- 28%, Granisetron group (0.04 mg/kg Bw)- 16%. The incidence of nausea and vomiting in the Ondansetron and Granisetron groups were comparable to the present study.

B Subramaniam, R. Madan, S. Sadhasivam (in the Dept. of Anaesthesiology and Dr. Rajendra Prasad Centre for Ophthalmic Sciences, AIIMS, New Delhi) evaluated the antiemetic efficacy of prophylactic Ondansetron (0.1 mg/kg Bw) and Dexamethasone (1 mg/kg Bw) in the prevention of PONV in children undergoing strabismus repair. The incidences in the Dexamethasone (24.4%) and Ondansetron groups (33.3%) were comparable (p=0.49).

CONCLUSION
1. The present study shows that the drug Granisetron is more effective than Ondansetron and Dexamethasone in the prevention of postoperative nausea and vomiting in thyroidectomy patients.
2. During the early postoperative period, Ondansetron and Granisetron were found to be equally effective, but in the late postoperative hours, Granisetron proved to be superior to Ondansetron in the prevention of PONV.
3. The drug Dexamethasone is less effective in the prevention of PONV.
4. Both the drugs, Ondansetron and Granisetron have headache as a side effect.

REFERENCES


