Study of efficacy of Propofol, Ondansetron and Dexamethasone in prevention of post operative nausea & vomiting (PONV) following thyroidectomy

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ABSTRACT

Introduction: Post operative nausea and vomiting is one of the most common and annoying problem after general anesthesia resulting in patient discomfort, delaying discharge from recovery unit and may be at time dangerous resulting in pulmonary aspiration syndrome. Patients undergoing thyroid surgeries are at high risk for development of PONV with reporting incidence of 63% to 84%. We compare the efficacy of propofol, Ondansetron and dexamethasone to prevent PONV. **Material and Methods:** 60 adult patients undergoing elective partial or total thyroidectomy were placed in 3 groups (20 patients in each group)

- Group 1 : Propofol 0.5 mg/kg (15 minutes before reversal)
- Group 2 : Ondansetron 8 mg (15 minutes before induction)
- Group 3 : Dexamethasone 10 mg (15 minutes after induction)

Postoperatively all patients were assessed for the incidence of nausea, vomiting, vital parameters, pain and sedation score, occurrence of sore throat, requirement of rescue antiemetic and other complications for every 4 hours for 24 hours except during sleep. **Results:** Occurrence of PONV was high in group 3 (10%) during first 4 hours postoperatively as compared to other two groups. The entire three groups had similar efficacy in preventing PONV during 4-8 hours postoperatively. Between 8 to 20 hours the incidence is high in group 1 and 2 as compared to group 3.Complete response to PONV in group 3 was found during 12-24 hours while in group 1 and 2 in 20-24 hours postoperatively. Group 3 found to be the most effective in our study. **Conclusion:** Overall incidence of PONV in the first 24 hour period was 35% in group 1, 25% in group 2 and 20% in group 3. Stastically significant difference in the incidence of PONV was noted between group 3 and group 1 & 2. Group 3 found to be the most effective in our study. Delayed emesis is better controlled with Dexamethasone compared with other groups. All three groups found to be effective in preventing PONV as a complete response in later part of post operative period.

Keywords: Post operative nausea and vomiting, General Anesthesia, Dexamethasone, Propofol, Ondansetron, Thyroidectomy

Introduction

PONV is one of the most common and annoying problem after general anesthesia and occurs in about 20-30% of patient's inspite of the newer antiemetic being used. PONV after thyroidectomy is especially frequent with reported rate of 63-84%. PONV results in patient discomfort, delays discharge from recovery unit and may be dangerous and lead to one of the pulmonary aspiration syndrome. PONV is multifactorial in nature and depends on the patient factors, anesthesia techniques used, surgical procedure and certain post operative events. A large number of drugs in the form of antihistaminics, $5HT_3$ receptor antagonists, dexamethasone & propofol are being used currently as an antiemetic to prevent PONV.

Aim: The study was designed to compare the effect of propofol, Ondansetron & Dexamethasone to prevent PONV particularly in thyroid surgery.

- To find out the efficacy of the three groups in preventing PONV and requirement of rescue antiemetics
- To study the effect of antiemetics used on vital parameters, pain & sedation score and analgesic consumption in post-operative period.

Material & Methods

60 adult patients ranging from 20 to 65 years of both sexes undergoing total/subtotal thyroidectomy were

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selected for the study. Patients were assessed adequately in the pre-operative period. Through history and clinical examination, investigations were conducted and analyzed. Only patients belonging to ASA I & II were selected for the study.

Exclusion Criteria

- Intra thoracic goiter
- Gastrointestinal disorder
- H/O motion sickness
- Patients who had received an antiemetic within 48 hours before surgery
- Patients who have suffered difficult endotracheal intubation at the time of induction

After obtaining institutional review board approval, written informed consent was obtained from 60 adult patients undergoing elective partial or total thyroidectomy and were placed in three different groups (20 patients in each group)

Group 1 : received Propofol 0.5 mg/kg (15 minutes before reversal)

Group 2 : received Ondensetron 8 mg (15 minutes before induction)

Group 3: received Dexamethasone 10 mg (15 minutes after induction).Patients were instructed not to receive anything by mouth for at least 8 hours before surgery. Patients were premedicated with Tab. Lorazepam night before surgery and Tab. Diazepam in the morning on the day of surgery. Anaesthetic technique was identical in all patients. Induction of anaesthesia was done with Inj. Glycopyrrolate 0.01 mg/kg IV, Inj. Fentanyl 1.5-2 mcg/kg IV, Inj. Thiopentone Sodium 5 mg/kg and Inj. Succinylcholine 1.5 mg/kg. Anaesthesia was maintained with O2 + N2O and volatile inhalational anaesthetics like sevoflurane or isoflurane. Intermittent positive pressure ventilation was used for ventilation and Inj. Vecuronium bromide as a muscle relaxant intraoperatively. Intra operatively patients were monitored with pulse oximetry, ECG and non invasive blood pressure. After completion of surgery reversal of anesthesia was done with Inj. Glycopyrrolate 0.02 mg/kg and Inj. Neostigmine 0.05 mg/kg and after full muscle tone and power, trachea was extubated. Postoperatively, all patients were assessed for nausea, vomiting, Heart Rate, Blood Pressure, Respiratory Rate and SPO_2 for every 4 hrs post operatively for 24 hrs except during sleep. PONV was evaluated on 4 point ordinal scale (0-No Symptom, 1-Nausea, 2-Retching,3-Vomiting).The primary clinical endpoint was "complete response", defined as no vomiting and no anti emetic drugs needed in the first 24 hrs post operative period. **Nausea** was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit. **Retching** refers to spasmodic respiratory movements conducted with a closed glottis. **Vomiting** was the forceful expulsion of gastric contents from the mouth. Rescue antiemetic Inj. Ondensetron 8 mg i.v was given on patient demand or nausea, vomiting or retching was recorded. If both nausea and vomiting were present in a particular period it was recorded as vomiting only by the virtue of being higher on the ordinal scale. Postoperative pain at the surgical site was assessed by using VAS scale (0-No Pain to 10-Most Severe Pain) and recorded every 4 hr post operatively for 24 hr except during sleep. All the patients were given Inj. Diclofenac Sodium 1.5 mg/kg i.m (max. 75 mg) as analgesic at 8 hr intervals after surgery or earlier if they demanded pain relief. Occurrence of sore throat was recorded and treated with 7% povidone-iodine gargle solution. Sedation score was assessed by using following scale (0 - Completely Awake, 1 – Awake but drowsy, 2 - Asleep but responds to verbal commands, 3 - Asleep but responds to physical stimulation, 4 - Unarousable). Chi-Square test with Yates correction and Student's T test were used as the tests of significance to evaluate efficacy of anti emetics to prevent PONV and other quantitative data obtained in the postoperative period. $P<0.05$ was considered statistically significant.

Results

60 adult patients undergoing thyroidectomy procedure that were selected for the study and divided amongst the three groups (20 patients in each group) had the following parameters.

Table 1: Demographic Data

	Group-1	Group-2	Group-3
Age (yrs)	43.65(19-68)	46.8(20-70)	42.75(25-64)
Sex(F/M)(n)	16/4	15/5	15/5
Weight (kg)	50.4±9.96	53.4±7.31	51.1±6.59
Height(cms)	160±6.8	159.4±7.4	149.6±6.8
History of previous surgery	3	1	2
Duration of anaesthesia(hrs)	2.06±0.46	2.0±0.57	1.98±0.42

Values are given as mean (±SD) or mean (range) or number of patients.

There was no significant difference in the parameters mentioned above in between the three groups.

Table 2:No. of pts (%) with Nausea, Vomiting and Retching requiring rescue anti emetic at 4 hrs interval post operatively

	Group – 1	Group – 2	Group - 3
0 – 4 hr			
Total(Nausea, Vomiting, Retching)	1(5%)	1(5%)	2(10%)
Rescue antiemetic	1(5%)	1(5%)	2(10%)
4-8 hrs			
Total(Nausea, Vomiting, Retching)	1(5%)	1(5%)	1(5%)
Rescue antiemetic	1(5%)	1(5%)	1(5%)
8-12 hrs			
Total(Nausea, Vomiting, Retching)	2(10%)	2(10%)	1(5%)
Rescue antiemetic	2(10%)	2(10%)	1(5%)
12-16 hrs			
Total(Nausea, Vomiting, Retching)	2(10%)	0(0%)	0(0%)
Rescue antiemetic	2(10%)	0(0%)	0(0%)
16-20 hrs			
Total(Nausea, Vomiting, Retching)	1(5%)	1(5%)	0(0%)
Rescue antiemetic	1(5%)	1(5%)	0(0%)
20-24 hrs			
Total(Nausea, Vomiting, Retching)	0(0%)	0(0%)	0(0%)
Rescue antiemetic	0(0%)	0(0%).	0(0%)

In first 4 hrs interval occurrence of PONV is 5% - group 1, 5% - group 2,, and 10% - group 3.
In 4-8 hrs interval the incidence of PONV is 5% -group 1, 5%- group 2, 5%- group 3.
In 8-12 hrs interval the incidence of PONV is comparable between group 1, 2 and 3 (10%, 10% and 5% respectively).
In 12-16 hrs interval the incidence of PONV is comparable between group 2 and 3 (0% and 0%), while it is significantly high in group 1 (10%).
In 16-20 hrs interval the incidence of PONV is 5% in group 1 and 2, while there is complete response (no PONV) in group 3.Complete response (no PONV) in the 20-24 hrs interval occurred in 100% of patients in all the three groups.
There was no significant difference between the requirements of rescue anti emetic between the three groups at any period of interval.

Table 3: Nausea, Vomiting and Retching in our Patients

Grading	Group 1	Group 2	Group 3
Nausea	3	1	2
Vomiting	4	4	1
Retching	0	0	1
P value	0.3574	0.2481	0.4257

P value result shows that there were no significant occurrence of Post Operative Nausea and Vomiting.

Table 4: Mean pulse rate and mean arterial pressure at various time intervals after the completion of surgery

Time	Group – 1	Group - 2	Group – 3
0-4 hr			
Pulse rate	77.7±6.53	77±7.21	76.6±6.12
MAP	90.95±7.02	90.15±7.77	87.65±7.80
4-8 hrs			
Pulse rate	80.2±6.48	79.8±5.9	77.3±5.81

MAP	94.55±6.37	92.4±6.69	88.7±7.80
8-12 hrs			
Pulse rate	79.7±9.45	81.5±8.6	76.4±7.52
MAP	95.25±7.01	94.45±5.67	88.6±8.22
12-16 hrs			
Pulse rate	80.9±10.31	82.7±6.5	77.6±8.64
MAP	96.15±6.04	93.2±5.37	91.35±7.07
16-20 hrs			
Pulse rate	82.1±7.8	83.8±5.57	79±7.24
MAP	97.4±5.93	93.65±6.72	91.5±7.03
20-24 hrs			
Pulse rate	80.5±6.41	83.7±6.49	79.6±7.44
MAP	96.65±5.34	93±7.8	91.3±6.86

The difference in blood pressure (MAP) and pulse rate was not statistically significant between the three groups at any measured time interval after surgery.

Table 5:No. of pt (%) with Sore Throat Using VAS Score

Time	Group-1	Group-2	Group-3
0-4 hrs	0(0%)	1(5%)	0(0%)
4-8 hrs	2(10%)	1(5%)	1(5%)
8-12 hrs	0(0%)	1(5%)	2(10%)
12-16 hrs	1(5%)	0(0%)	0(0%)
16-20 hrs	3(15%)	0(0%)	0(0%)
20-24 hrs	0(0%)	2(10%)	0(0%)

Sore Throat was reported by some patients with different intensity amongst groups. Patients in Group-3 reported a lower pain score of sore throat than those in the other two groups.

Table 6: Pain scores at various time intervals (when Patient in awake state) after surgery (Mean ± SD*)*

Pain Score	Group – 1	Group – 2	Group – 3
0-24 hrs	3.5±2.21	3.45±2.30	3.25±2.76
Inj Diclofenac Sodium(mg)	72±1.2	73.6±2.07	70.8±0.6

Pain Score (VAS Score) was observed amongst three group which was found not to be different significantly statistically. The analgesic consumption was not statistically different significantly between the three groups.

Table 7: Sedation score in all patients (Mean Value)

Sedation Score	Group 1	Group 2	Group 3
0-24 hrs	1.8	1.2	0.9

None of the pts had sedation scores more than 2 (Asleep but respond to verbal command) during post operative period of 24 hrs.

Table 8: Side effects at 24 hrs

	Group – 1	Group – 2	Group – 3
Headache	0	2	0
Sweating	0	0	0
Dizziness	1	0	0
Itching	1	1	0
Rashes	0	0	1

No significant difference was noted in occurrence of side effects amongst three groups.

Discussion

Postoperative nausea and vomiting (PONV) is one of the most common and annoying problem after general anaesthesia and is intractable at time. It may be relatively benign at times and sometimes it can lead to severe sequelae such as aspiration of stomach contents and poor surgical outcome especially after abdominal surgeries.Patients undergoing thyroid surgery are at high risk for development of PONV. The incidence of PONV after thyroidectomy in adult women is relatively high about 76% when no anti emetic was given and the etiology is unknown.[1] Several factors including the age, gender, obesity, previous history of motion sickness or PONV, anxiety, gastroparesis, type and duration of the surgical procedure (e.g., laparoscopy, strabismus, middle ear procedures) , and intense vagal stimulation might be related to PONV. Anesthesiologists have little, if any, control over these surgical factors. However, they do have control over many other factors that influence post operative emesis (e.g., pre anesthetic medication, anesthetic drugs and techniques, and postoperative pain management.[2-4] Most of the currently used antiemetic drugs (e.g. anticholinergics, dopamine receptor antagonist, and antihistamines) have clinically significant side effects. (e.g., dysphagia, restlessness, dry mouth, changes in blood pressure and extra pyramidal symptoms.[1] In this clinical study, the treatment groups were similar with regard to demographics & operative procedure. Patients with history of motion sickness or previous history of emesis were excluded because they had a relatively high incidence of emetic symptoms.[5] Dexamethasone may involve central inhibition of prostaglandin synthesis and/or decrease in serotonin turn over in CNS. Strong anti inflammatory effect of dexamethasone on neck structures may also play a role in its anti emetic effect in patients undergoing thyroidectomy. In these patients, significant oedema and inflammation around the neck may sustain evoked parasympathetic impulses through vagus, recurrent laryngeal and glossopharyngeal nerves to the vomiting centre, thus initiating vomiting responses. Dexamethasone may significantly reduce tissue inflammation around the neck and thus reduces the ascending parasympathetic impulse to the vomiting centre and reduce PONV.[4] Incidence of PONV has been significantly decreased by single dose steroid administration in several studies.[6-8] Dexamethasone has been shown to have anti emetic effect and the dose commonly used is from 5 – 10 mg. Recently, dexamethasone has been proved to be effective in prevention of PONV in females undergoing thyroidectomy and the minimum effective dose is 5 mg.[2] However, patients who received dexamethasone 8 – 10 mg enjoyed a higher chance of complete response and reduction in analgesic requirement than those who received dexamethasone 5 mg.[4,9,10] So we used 10 mg dexamethasone immediately after induction of anesthesia.The long term administration of corticosteroids causes side effects such as increase risk of infection, glucose intolerance, delayed wound healing, superficial ulceration of gastric mucosa, and adrenal suppression.[11] However, these side effects were not related to a single dose of dexamethasone[11-13] We did not have any post operative complication in the form of wound infection or delayed wound healing [14].Dexamethasone was not found to be effective during 0 to 2 hrs after administration because of delayed onset of action. It proved to be effective in the later period. So we used to give it within short period of induction of anesthesia.[12] Dexamethasone has a biological half life of 36 to 72 hours. Thus, the late antiemetic efficacy may be a result of favourable pharmacokinetics. In chemotherapy, there is some evidence that delayed emesis (i.e., beyond 24 hours) is better controlled with dexamethasone compared with classic antiemetics.[15] Propofol is relatively selective modulator of $GABA_A$ receptors. Interaction of propofol with specific components of GABA receptors appear to decrease the rate of dissociation of GABA from the receptor thereby increasing the duration of GABA activated opening of chloride channel causing hyperpolarisation of cells.[16] Low dose of propofol may induce anxiolysis sufficient to modify cortical afferent to the vomiting centre.[17] It has been postulated that antiemetic effect of propofol may be as an antagonist at the $5\text{-}HT_3$ receptor. The antiemetic effect of propofol may be due to modulation of sub cortical pathways.[18] Propofol, in small doses, possesses direct antiemetic properties. Single small dose (0.5 mg/kg) of propofol administered intravenously at the end of surgery before reversal was more effective than traditional anti emetics for prevention of PONV.[19] Subhypnotic dose of propofol was not only superior in comparison with placebo to control the incidence of emesis, but also without unwanted sedative, respiratory or cardiovascular side effects.[18] In our study we did not find any serious side effects amongst patients.Propofol is a cost effective alternative to newer antiemetic drugs for the treatment of refractory postoperative nausea and vomiting.[20] Ondansetron, a selective 5 HT_3 antagonist has been shown to be effective in preventing nausea and vomiting during the perioperative period.[21] Anti emetic effort results from peripheral

blockade of 5 HT_3 receptors, on vagal nerve terminals and central blockade in the area of postrema and nucleus solitaries. This equates with chemoreceptor trigger zone (CTZ) blockade. 5 HT_3 receptor antagonists have no affinity for alpha adrenergic, dopaminergic or histamine receptors. This characteristic eliminates undesirable side effects of sedation, hypotension and extra pyramidal reactions that occur when using other non selective anti emetic agents.[22]The effectiveness of intravenous ondansetron as a prophylactic post operative antiemetic was evaluated in a dose ranging study and it was demonstrated that a single 4 mg dose appeared to be the lowest acceptable dose to prevent PONV.[23-25] However, The optimal intravenous dose of ondansetron to prevent PONV is likely to be 8 mg for long term efficacy.[26] Ondansetron is a highly effective antiemetic that has been used successfully for both the prophylaxis and treatment of postoperative nausea and vomiting. For the efficacy of ondansetron as a prophylactic antiemetic, investigators have administered the drug immediately before induction of anesthesia. Duration of ondansetron's antiemetic efficacy is dose related. Although the timing of administration of ondansetron did not influence the overall incidence of PONV, the need for rescue antiemetic medication in the PACU was significantly decreased in the patients who received ondansetron at the end of surgery.[21] Ondansetron has a relatively short half life of 2.8±0.6 hrs after a single 8 mg intravenous dose.[27] As we used to give ondansetron immediately before induction of anesthesia, we reported some more no. of cases of PONV in first 6-8 hrs postoperatively. In the post operative period both pain and opioids have been reported to increase the incidence of PONV. In the logistic regression models of the risk factors for PONV, the use of post operative opioid was included while the use of intra operative opioid was not. According to the data of today, there is no clear cut association between use of intra operative opioid and PONV.[28,29] So we used intra operative Fentanyl for all our patients undergoing thyroidectomy surgery In our study we found that Propofol in subhypnotic dose was effective to prevent PONV and is associated with fewer requests for rescue antiemetic and sedation in the early phase of recovery. It is equally effective in preventing postoperative nausea as Ondansetron in the first 6 hrs after operation. A single dose of Dexamethasone is safe and is comparable to Ondansetron in preventing PONV. We found that delayed emesis is better controlled with Dexamethasone compared with other groups. All three groups found to be effective in preventing PONV as a complete response in later part of post operative period. There was no significant difference in the demographic parameters amongst three groups. We did not observe significant difference in MAP, Pulse rate, Pain Score, and Total Analgesic consumption in between three groups. No patients had sedation score more than 2. Sedation score was found to be least in Ondansetron and Dexamethasone groups. We found occurrence of sore throat much less in group receiving Dexamethasone. Complications were few and were evenly distributed without any statistically significant difference between the three groups.

Conclusion

Overall incidence of postoperative nausea and vomiting in the 24 hour period after giving propofol, ondansetron and dexamethasone was 35%, 25% and 20% respectively. Statistically significant difference was noted in the incidence of PONV between Group III and Group I and II. Similar efficacy was found in all the three groups for prevention of postoperative nausea and vomiting in patients undergoing thyroidectomy surgery. Ondansetron is effective to prevent postoperative nausea and vomiting. A single low dose of dexamethasone is safe and is comparable to ondansetron to prevent PONV. Prolonged effects of dexamethasone may prove to especially beneficial in limiting PONV. Propofol given at subhypnotic dose significantly decreases the incidence of emetic episodes in patients undergoing thyroidectomy surgery without clinically important adverse events. However, all the three drugs were significantly effective to prevent PONV compared with placebo.

Abbreviations:

ASA - American Society of Anesthesiologist
CTZ - Chemoreceptor Trigger Zone
ECG - Electrocardiogram
GABA - Gamma Amino butyric Acid
Kg - Kilogram
MAP - Mean Arterial Pressure
Max - Maximum
Mcg - Microgram
Mg - Milligram
Min - Minute
PONV - Postoperative Nausea and Vomiting

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