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ORIGINAL ARTICLE

POST OPERATIVE NAUSEA AND VOMITING PROPHYLAXIS: A COMPARATIVE STUDY OF GRANISETRON ALONE AND GRANISETRON PLUS DEXAMETHASONE AFTER ENT SURGERIES

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ABSTRACT: BACKGROUND: Postoperative nausea and vomiting is one of the most frequently occurring side effects affecting one third of the cases. Objective of the study was to compare the efficacy of Granisetron alone and Granisetronplus Dexamethasone in preventing post-operative nausea and vomiting after ENT surgeries. **MATERIALS AND METHODS:** This randomized controlled trial was conducted at the Anaesthesia and ENT departments of Santhiram Medical College and General Hospital, Nandyal from July 2014 to January 2015.60 patients belonging to physical status ASA-I and ASA-II of both sexes were selected (aged between 5-35 yrs).Patients in group-I (n=30) received Granisetron 40 mcg/kg and group –II (n=30) patients received Granisetron 40 mcg/kg and Dexamethasone 150 mcg/kg intravenously just before the start of operation. The whole postoperative period of 24 hrs was divided into 2 phases; early 0-6 hrs and late phase 6-24 hrs. **RESULTS:** Nausea and Vomiting score was significantly higher in group-I patients (P<0.05).The total incidence of nausea and vomiting was reduced from 43% in group-I to 6.6% in group-II which was statistically significant (p<0.05). **CONCLUSION:** Granisetron and Dexamethasone combination is more effective for the prevention of PONV in comparison to Granisetron alone in ENT surgeries.

KEYWORDS: Dexamethasone, Granisetron, ENTsurgeries, Post-operative nausea and vomiting.

INTRODUCTION: Post-operative nausea and vomiting are the most common and distressing side effects encountered by the patients following anaesthetic and surgical procedures [1].The reported incidence of PONV in patients undergoing ENT surgeries (Adenotonsillectomy-36-76% and Middle ear surgery 80%) when no prophylactic antiemetic was given. This incidence may justify the use of prophylactic anti-emetics for the prevention of PONV after ENT surgeries. Patients with PONV may develop medical complications, consume more resources, increased pain at the surgical site and delayed discharge from hospital. Current medical practice entails the use of a combination of antiemetic acting on multiple receptor sites to reduce the risk of PONV in high risk patients. A recent meta-analysis on prevention of PONV suggested that a combination of Dexamethasone with the 5-HT3 receptor antagonists is likely to be the best anti emetic prophylactic regimen among the drugs currently available. Granisetron is a new 5-HT3 receptor antagonist more selective than Ondansetron. It is effective orally as well as intravenously. It blocks the 5-HT3 receptors at both the central and the peripheral sites. It acts on the vagal efferent nerves of the gut and produces blockade of 5-HT3 receptors. It has a half-life of 8-9 hrs[2], hence longer duration of action than Ondansetron which has half-life of 3 hrs.

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Dexamethasone is a 21 carbon compound having a cyclopentanoper hydrophenanthrene (steroid) nucleus. It is very potent and highly selective long acting Glucocorticoid. It has a long half-life of 36-48hrs after a single dose of 8 mg I.V given before induction of anaesthesia[3].The precise mechanism of action is not well understood, but may be due to Prostaglandin antagonism, serotonin inhibition in the gut and release of Endorphins that elevate mood and stimulate appetite. It augments the efficacy of other primary anti emetic drugs like Metoclopramide, Ondansetron and Granisetron. It also serves to reduce certain side effects of the primary antiemetics. We designed this prospective randomized controlled study to compare the efficacy of Granisetron alone and combination of Granisetron and Dexamethasone to prevent PONV in patients undergoing ENT surgeries under General Anaesthesia.

MATERIALS AND METHODS: After obtaining approval from the Ethical committee, the present study has been carried out at Santhiram Medical College & General Hospital, Nandyal. Patients gave a written informed consent.60 patients belonging to physical status ASA-I and ASA-II of both sexes were selected aged between 5-35yrs.

The exclusion criteria were:

a) Patients with ASA-III, ASA-IV.
b) Patients with h/o motion sickness.
c) Patients with past h/o PONV.
d) Patients who received antiemetics within 24 hrs prior to surgery.
e) Patients with known hypersensitivity to Granisetron or Dexamethasone.

All the patients were kept fasting 6-8 hrs and premedicated with tablet Alprazolam 0.25mg in the night before surgery. In the OT, baseline pulse, BP & spo2 were recorded.

Patients were randomly assigned to one of the two study groups (30 in each group) through blocked randomization. Patients in group-I received Granisetron 40 mcg/kg. Patients in group-II received Granisetron 40 mcg/kg with Dexamethasone 150 mcg/kg intravenously. Personnel not involved in the study prepared identical syringes containing the study drug(s). The drugs were administered intravenously slowly just before induction of anaesthesia by the anaesthetist who was blinded to the nature of the drug in the syringe. Pulse, Blood pressure and spo2 were recorded 5 minutes after administration of study drugs.

After preoxygenation for 3min, induction of anaesthesia was done with inj. Fentanyl 2 mcg/kg and inj. Thiopentone 5 mg/kg intravenously. Intubation was done with Suxamethonium 1.5 mg/kg intravenously. IPPV was maintained by Nitrous oxide and Oxygen (50:50). Muscle relaxation was maintained with intravenous Vecuronium 0.1 mg/kg. Incremental doses 1/5th of the loading dose were given to maintain neuromuscular blockade. Anaesthesia was maintained with Sevoflurane in oxygen. At the end of surgery inj. Glycopyrrolate 0.008 mg/kg and inj.Neostigmine 0.05mg/kg were administered intravenously for reversal of neuromuscular block and after complete recovery the patient was extubated. Duration of surgery and anaesthesia was recorded. Postoperative analgesia was provided with inj.Ketorolac 1mg/kg IM 8th hourly.

After surgery patients were observed for 24 hrs postoperatively. Analgesia was provided with Injection Ketorolac 1 mg/kg IM every 8thhourly.Vital signs such as pulse rate, blood pressure

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and respiratory rate were monitored every 1 hour for the first 8 hours and every 2nd hourly for the next 16 hours. The incidence of nausea and vomiting were observed.

Incidence of nausea and vomiting occurring in the first 6 hours post operatively was considered as early nausea and vomiting and incidence of PONV after 6 hours was considered as late nausea and vomiting.

Nausea and vomiting were evaluated on three point ordinal scale.

0 = none, 1 = nausea, 2 = vomiting.

Pain intensity was assessed using 10 cm visual analogue scale (VAS 0 = No pain, 10 = most severe pain).The incidence of nausea and vomiting was analysed using Chi-Square test, p value <0.05 was considered significant.

RESULTS: There were 30 patients in each group. General characteristics of patients in relation to age, weight, sex, duration of surgery and anaesthesia, total amount of opioid used, intraoperative and postoperative haemodynamics which may modify PONV were comparable in the two groups.

Patient characteristics	Mean & SD Group-I	Mean & SD Group-II
Age (years)	14.92±7.947	16.36±8.27
Weight (kg)	40.8±12.23	40.6±11.18
Duration of anaesthesia (min)	50.4±11.63	50.4±16
Duration of surgery (min)	39.2±12.22	39±15.13

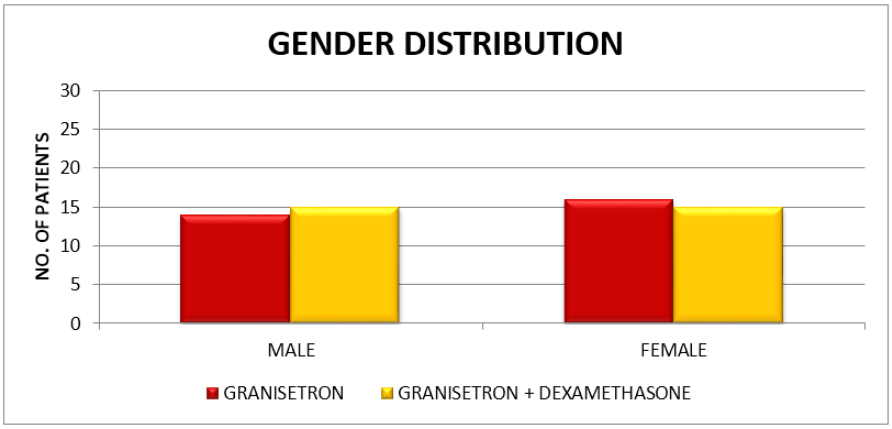
Table 1: Demographic and Anaesthetic Data

No significant difference between both the groups with respect to patient characteristics.

Group	Total number of patients	Total number of male patients	Total number of female patients
Group-I (granisetron)	30	14	16
Group-II (Granisetron + dexamethasone)	30	15	15

Table 2: Gender Distribution

No significant difference with respect to gender of the patient.



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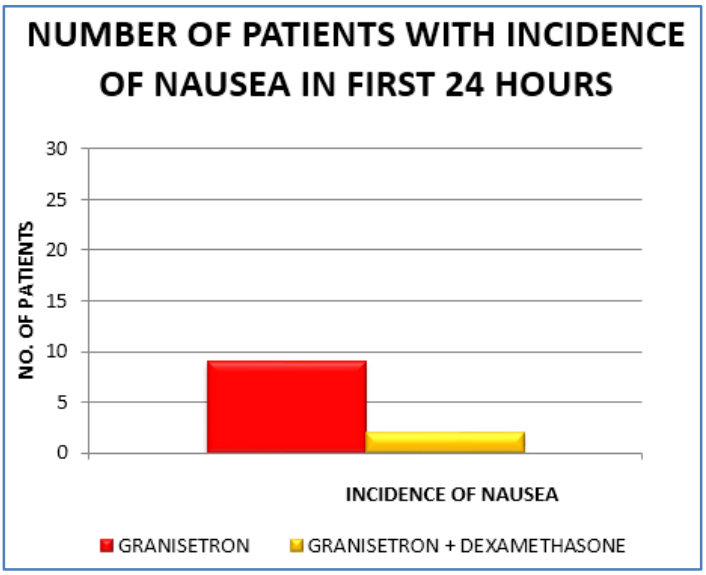
Groups	Total number of patients	Total number of patients with post-operative nausea
Group-I (Granisetron	30	9
Group-II (Granisetron & dexamethasone)	30	2

Table 3: Incidence of Nausea in First 24 Hours

In group-I, 9 patients (30%) had nausea and in group-II, 2 patients (6.6%) had nausea which is statistically significant ($p < 0.05$)



Groups	Total No. of patients	No. of patients with postop vomiting
Group-I (Granisetron)	30	4
Group-II (Granisetron + dexamethasone)	30	0

Table 4: Incidence of vomiting in first 24 hours

In group-I, 4 patients (13%) had vomiting and in group-II no patient had vomiting which is statistically significant ($p < 0.05$)

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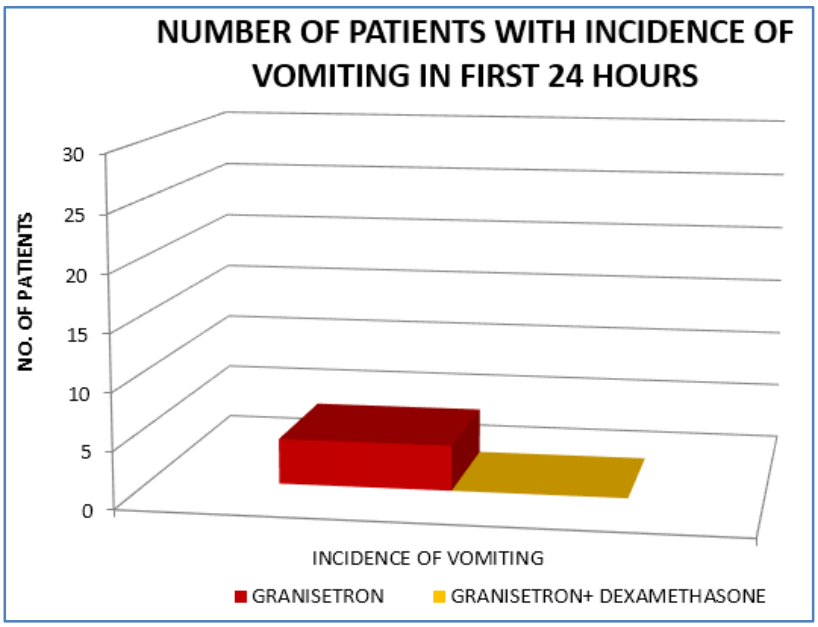
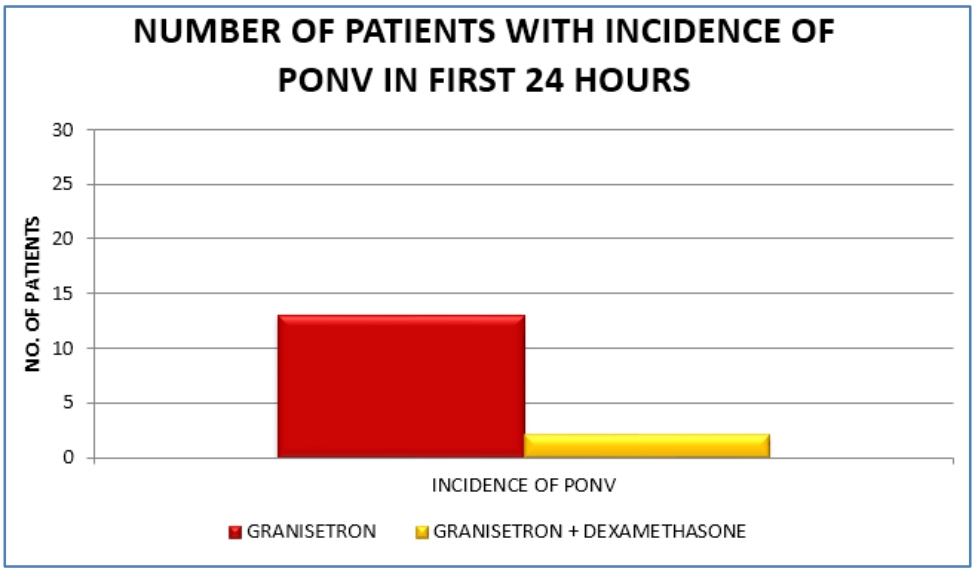


Groups	Total no. of patients	No. of patients with post-operative nausea and vomiting
Group-I (Granisetron)	30	13
Group-II (Granisetron + dexamethasone	30	2

Table 5: Total number of patients with incidence of post op nausea and vomiting in first 24 hours

Total number of patients with post op nausea and vomiting in first 24 hours in group-I is 13 (43%) whereas in group –II, it is 2 (6.6%) which is statistically significant ($p<0.05$).



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DISCUSSION: Nausea and vomiting following General Anaesthesia, has been a distressing problem for the patients and is frequently listed among the most important postoperative concerns, apart from pain.

Inspite of so much advancement in the management of postoperative nausea and vomiting like invention of new drugs, multi modal approaches of management like administering multiple different antiemetic medications, less emetogenic anaesthetic techniques, adequate intravenous hydration, adequate pain control etc., the incidence of PONV remains still high.

Middle ear surgery is associated with a high risk for PONV, because the operation may stimulate the vestibular labyrinth, which is innervated by the vestibular portion of VIII cranial nerve, which in turn activates the Chemoreceptor Trigger Zone (CTZ) in the area postrema.[4] Stimulation of the parasympathetic nerves of pinna during surgical manipulations may induce PONV.[5] Mechanical stimulation of pharynx induces emesis via activation of Glossopharyngeal afferents. The incidence of vomiting after paediatric tonsillectomy may approach 81%. Presence of orotracheal tube may contribute to emesis. It has been reported that the incidence of PONV is greater in patients maintained with an orotracheal tube due to stimulation of pharynx.

There are different types of drugs, which have been used to prevent PONV. In a recent meta-analysis it was concluded that, the best prophylaxis of PONV currently available is by combining Dexamethasone with a selective 5-hydroxy tryptamine type 3 (5-HT 3) receptor antagonist.Such combinations are both safe and efficacious in paediatric, obstetric, breast, ENT and other surgeries associated with a high risk of PONV.[6]

Y. Fujji et al (1996)[7] studied the efficacy of Granisetron in children and concluded that Granisetron is effective in the prevention of retching and vomiting after strabismus repair and tonsillectomy.

CM Bolton et al.,(2006)[8] in their study concluded that Dexamethasone and the serotonergic antagonists Ondansetron, Granisetron, and Tropisetron are clinically effective agents for the prophylactic control of PONV in children after tonsillectomy with or without adenoidectomy.

In 1995 Yoshitaka and Hiroyoshi et al., have done a randomized double blind study in 88 patients undergoing general anaesthesia for major gynaecological surgery[9]. Immediately after recovery from anaesthesia, patients received a single dose of either placebo (saline, n=22) granisetron (20μg/kg, n=22), dexamethasone (8mg i.v., n=22) or combined granisetron and dexamethasone (20μg/kg and 8mg i. v. respectively, n=22). The frequency of postoperative nausea was 32%, 23%, 27% and 5%, whereas the frequency of postoperative vomiting was 23%, 23%, 23% and 5% after administration of placebo, granisetron, dexamethasone and granisetron with dexamethasone combination respectively. They have concluded that prophylactic administration of combined granisetron and dexamethasone is effective in preventing PONV after anaesthesia.

In our study we found that incidence of postoperative nausea in first 24 hrs was 30% in granisetron group and 6.6% in granisetron with dexamethasone combination group ($p<0.05$) clinically and statistically significant. The incidence of postoperative vomiting was significantly lesser in granisetron with dexamethasone group (0 patients) than granisetron group (4 patients, 13%).

In 1998, Y. Fujji, H. Toyookaet al., evaluated the effect of granisetron., dexamethasone and granisetron/dexamethasone combination in the prevention of postoperative nausea vomiting in 120 patients undergoing middle ear surgery.[10] Patients received granisetron 3mg i.v., dexamethasone 8 mg i.v. or granisetron 3mg with dexamethasone 8 mg i.v.(n=40 in each group), immediately before induction of anaesthesia. They have found that a complete response, defined as no PONV and no need for another rescue antiemetic during first 3hrs after anaesthesia, was recorded in 83%, 50% and 98% of patients who had received granisetron, dexamethasone and granisetron/dexamethasone combination respectively. They have concluded that prophylactic use of combined granisetron and dexamethasone was more effective for the prevention of PONV after middle ear surgery.

In our study we found that the incidence of PONV in the first 24 hrs was 43% in granisetron group and 6.6% in granisetron dexamethasone group which is clinically and statistically significant. In 2003, Yoshitaka et al., had conducted randomized double blind study in 120 women undergoing major gynaecologic surgery.[11] Patients received granisetron 40 μg/kg i.v. either alone or in combination with dexamethasone 8 mg, 0-3 hrs after the end of anaesthesia. Patients then were observed for 24 hrs after the study drug administration. They have found that percentage of patients free of emetic symptoms was higher in the granisetron/dexamethasone combination group (95%) than in the granisetron group (80%) ($p=0.012$).

In our study we found that the incidence of PONV is significantly lesser in granisetron dexamethasone group (6.6%) than in granisetron group (43%) with $p< 0.05$.

CONCLUSION: On the basis of the results obtained, it was concluded that Granisetron and Dexamethasone combination is more effective for the prevention of postoperative nausea and vomiting in comparison to Granisetron alone in ENT surgeries.

REFERENCES:

1. Rose JB, Watcha MF. Postoperative nausea and vomiting in paediatric patients. Br. J. Anaesth. 1999; 83(1): 104 – 117.
2. Giglio CA, Soares HP, Caparroz C, Castro PC. Granisetron is equivalent to ondansetron for prophylaxis of chemotherapy induced nausea and vomiting: Results of a meta-analysis of randomized controlled trials. Cancer 2000; 89: 2301-8.
3. Mansour EE. Postoperative nausea and vomiting prophylaxis: The efficacy of a novel antiemetic drug (palonosetron) combined with dexamethasone. Egypt J Anaesth. 2013; 29: 1-7
4. Wathcha MF, White PF. Postoperative nausea and vomiting. Its treatment and prevention. Anaesthesiology 1992; 77: 162-84.
5. Ishizaki H, Pyykko I, Aalto H, Starck J. Tullio phenomenon and postural stability: experimental study in normal subjects and patients with vertigo. Ann Otol Rhinol Laryngol 1991; 100: 976-83.
6. Thomas R, Jones N. Prospective Randomized, double blind comparative study of dexamethasone, ondansetron and ondansetron plus dexamethasone as prophylactic anti emetic therapy in patients undergoing day-case gynaecological surgey.Br J Anaesth 2001; 87: 588-92.

7. Fujji Y. Tanaka H. Granisetron reduces vomiting after strabismus surgery and tonsillectomy in children. Can J Anaesth.1996; 43: 35-38.
8. C.M.Bolton, P.S. Myles et al., Prophylaxis of postoperative nausea and vomiting in children undergoing tonsillectomy: a systematic review and meta-analysis. Br J Anaesth.2006; 97(5): 539-604.
9. Fujji Y, Tanaka H. Granisetron- dexamethasone combination reduces post-operative nausea and vomiting.Can J Anaesth. 1995; 42: 387-390.
10. Fujji. Y, Tanaka H. Toyooka H. Prophylactic antiemetic therapy with a combination of granisetron and dexamethasone in patients undergoing middle ear surgery.Br JAnaesth.1998; 81(5): 754-756.
11. Yoshitaka Fujji MD and Hiroyoshi Tanaka MD. Granisetron vs Granisetron- dexamethasone combination for the treatment of nausea, retching and vomiting after major gynaecological surgery: A randomized double-blind study. Clinical Therapeutics 2003; 25(2): 507-514.

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