



## POSTOPERATIVE EMESIS IN PEDIATRIC PATIENTS: GRANISETRON VS GRANISETRON AND DEXAMETHASONE COMBINATION

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**ABSTRACT** Granisetron is a potent and highly selective 5-HT<sub>3</sub> receptor antagonist with no affinity for dopaminergic or adrenergic receptors. Its antiemetic efficiency increases when it is used in combination with steroids. 60 patients undergoing for tonsillectomy, of ASA 1 and 2, of either sex, of age 6 to 12 yrs were studied for post operative nausea and vomiting. Patients were allocated in two groups of 30 each. Grp A received Inj Granisetron 40µg/Kg while Grp B received combination of Inj Granisetron 40µg/Kg and Inj Dexamethasone 150µg/Kg just after induction. Patients were observed for 24 hrs for incidence of vomiting, retching, need of rescue antiemetic or any other side effect. Complete response was seen in 22(73.4%) patients in Grp A and 29(96.6%) patients in Grp B.

**KEYWORDS :** Granisetron, Dexamethasone, Tonsillectomy, PONV.

### Introduction

Post operative nausea and vomiting (PONV) is the most common distressing and undesirable symptom occurring in 13-42% of all pediatric patients. Severe PONV may be associated with wound dehiscence, pulmonary aspiration of gastric contents, bleeding, dehydration and electrolyte imbalance. Tonsillectomy is a commonly performed pediatric procedure and 70% children experience vomiting in postoperative period leading to delayed hospital discharge and parental dissatisfaction. Combination of antiemetics from different pharmacological classes would provide enhanced efficacy with reduced adverse effects. Granisetron, a selective antagonist of 5-hydroxy tryptamine type 3(5-HT<sub>3</sub>) receptor has more potent and longer acting properties than Ondansetron. Dexamethasone has combined anti-inflammatory and antiemetic property hence useful in tonsillectomy.

A study was designed to compare the efficacy of combination of Granisetron and Dexamethasone with Granisetron alone in the prevention of PONV after tonsillectomy in children.

**Study design:** Prospective, Randomized Double blind clinical trial.

### Aims and Objectives

- 1) To study the efficacy of Granisetron in prevention of PONV in children undergoing tonsillectomy under general anaesthesia.
- 2) To study the efficacy of combination of Granisetron and Dexamethasone in prevention of PONV in children undergoing tonsillectomy under general anaesthesia.
- 3) To compare the efficacy of Granisetron alone with the efficacy of combination
- 4) To study the side effects of both the drugs if any.

### Material and Methods

After obtaining the approval from institutional ethical committee, 60 patients of age group 6-12yrs of either sex belonging to ASA I and II undergoing elective tonsillectomy were included in the study. While patients with history of allergy to any study drug, patients who have consumed antiemetics, antihistaminics, antipsychotics or terfenadine within 24 hrs before surgery, patients with history of motion sickness, or patients having peritonsillar abscess, patients with indication of recurrent tonsillitis were excluded from the study.

Informed written consent was obtained from the parents of patient. Investigations like Hb%, TLC, DLC, Urine analysis Bleeding time, Clotting Time, Blood Grouping, Blood sugar were noted. After confirming the NBM status, subjects were randomly divided into two groups of 30 each.

Group A: Received IV Granisetron 40µg/Kg and saline.  
Group B: Received IV Granisetron 40µg/Kg and IV Dexamethasone 0.15 mg/Kg (max upto 8mg). These drugs were administered IV over 30sec. after induction of anaesthesia.

Both the groups were premedicated with Inj Midazolam 0.03mg/kg IV and Inj Pentazocine 0.3mg/Kg IV. Preoxygenation was done with 100% O<sub>2</sub> for 3 min. After induction with Inj Thiopentone sodium 4-5 mg/Kg, intubation was done under the effect of Inj Succinylcholine 2mg/Kg IV with appropriate sized PVC cuffed or uncuffed endotracheal tube. Anaesthesia was maintained with O<sub>2</sub>/N<sub>2</sub>O and Halothane and Inj. Atracurium as muscle relaxant. Monitoring was done for Heart rate, NIBP, ECG and SpO<sub>2</sub> throughout the procedure. Reversal was done with Inj. Neostigmine 0.05mg/Kg and Inj. Glycopyrrolate 0.008mg/Kg IV. Patients were extubated after return of all reflexes. Postoperatively all episodes of nausea and vomiting were recorded. Inj Metaclopramide 0.15mg/kg IV was used as a rescue antiemetic if two episodes of vomiting occur within 24 hrs after anaesthesia. Patients were enquired about side effects like headache, lightheadedness, drowsiness or diarrhea. Postoperative Pain was treated with per rectal suppository of Acetaminophen 10-15 mg/Kg.

### Statistics

Patient demographic data, duration of fasting, duration of anaesthesia and surgery were analysed by unpaired Student's t test. The frequency of postoperative vomiting, need for rescue antiemetics and incidence of adverse effects were analysed using Fishers exact test and Chi square test. P value of <0.05 was deemed statistically significant.

### Results

Both groups were compared for mean age, sex, weight and were found to be nonsignificant (p=>0.05)

**Table 1: Comparison between duration of anaesthesia and surgery.**

Duration	Group A	Group B	P value
Mean duration of anaesthesia(min)	76.8(SD-7.5)	80(SD-6)	0.072(NS)
Mean duration of surgery(min)	61.9(SD-8.28)	64.73(SD-6.02)	0.135(NS)

Both parameters were found to be nonsignificant.

**Table 2: Comparison of incidence of vomiting and retching between two groups.**

Drug	Children having vomiting	Children having retching	Children having vomiting or retching
<b>Group A</b> Granisetron 40µg/kg	7(23.3%)	1(3.3%)	8(26.6%)
<b>Group B</b> Granisetron 40µg/kg +Dexamethasone 150 µg/kg	1(3.3%)	0	1(3.3%)
<b>P value</b>	0.026(S)	0.50(NS)	0.022(S)

Incidence of vomiting between two groups was compared with

Fisher's exact test. Incidence of early as well as late vomiting was significantly reduced statistically when combination of drugs was used. ( $p < 0.05$ ).

Incidence of retching was not significant ( $p > 0.05$ ) However combined incidence of vomiting and retching when compared with two groups was found to be statistically significant. ( $p < 0.05$ ).

Children having two or more episodes of vomiting were given Inj. Metoclopramide 0.15mg/kg IV as rescue antiemetic. No patient in Grp B and only one patient in Grp A required rescue antiemetic. P value obtained was 0.5 which was statistically nonsignificant.

**Table 3: Side effects.**

Groups	Headache	Diarrhoea	Drowsiness	Others
<b>Group A (Granisetron) n=30</b>	3(10%)	2(6.6%)	0	1
<b>Group B (Granisetron +Dexamethasone) n=30</b>	4(13.3%)	1(3.3%)	0	1

Incidence of side effects among the two groups was compared using the Fisher's exact test. There was no statistically significant difference in either grp ( $p > 0.05$ ).

### Discussion

With the change in emphasis from inpatient to outpatient care and possibility of delayed discharge or unexpected hospital admission, PONV has been called the Big little problem<sup>1</sup>. PONV affects the economics of medical care, as well as the degree of patient's satisfaction, comfort and quality of life. PONV has gained importance in prevention and treatment because of increase in ambulatory and office based anaesthesia, newer techniques, antiemetics, use of multimodal therapy etc.

The present study compares the efficacy of combination of Granisetron and Dexamethasone with Granisetron alone in the prevention of postoperative nausea and vomiting after tonsillectomy in children. The incidence in preschool children is 20% while in school going age group it is 34-50% with rising trends in girls. As age itself is independent risk factor for PONV, prophylactic antiemetic is advocated in pediatric age group.<sup>2,3</sup> Obesity poses a special problem as adipose tissue acts as a reservoir for anaesthetic agents and may show increased incidence in recovery period<sup>4</sup>.

Duration of anaesthesia is an important parameter for nausea. The rise in incidence from 17.5% to 46% is seen when duration is more than one hour.<sup>5</sup> Although full stomach patients are likely to vomit in postoperative period, increased duration of fasting also increases the incidence.<sup>6</sup>

In our study we selected pediatric patients undergoing tonsillectomy. PONV is one of the most common and significant complication in tonsillectomy with or without adenoidectomy demanding delayed discharge, incidence being upto 70%. It is possible that surgical technique may influence the PONV, but there is no evidence to support this hypothesis. The anaesthetic technique has an important bearing over degree of PONV. Among the intravenous agents Propofol has least incidence of PONV compared to Ketamine. Inhalational agents like Sevoflurane or Isoflurane show minimal degree of PONV. Anticholinesterase like Neostigmine can cause vomiting due to muscarinic effect by increasing the gastric motility. All these agents demand prophylactic use of antiemetics.

In our study we use Granisetron and Dexamethasone as antiemetics. 5-HT<sub>3</sub> receptor antagonists are devoid of any side effects or drug interactions, hence their discovery is a major advance for treatment of PONV. The peak plasma concentration of IV Granisetron is 30 min. with elimination half life of 6.3 hrs.<sup>7</sup> Fujii et al in a study concluded that Granisetron given in a dose of 40µg/kg is adequate to prevent PONV.<sup>8</sup>

In our study 8 (26.6%) children who received Granisetron alone had one or more episodes of vomiting and retching requiring rescue antiemetic in first 24 hrs postoperatively. It indicates that 73.4 % children had complete response with Granisetron prophylaxis.

Dexamethasone in a dose of 0.15mg/Kg is an effective antiemetic with plasma half life of 4hrs. Combination of Granisetron with Dexamethasone has been used with more efficiency as steroids may reduce the levels of 5-Hydroxytryptophan, prevent release of serotonin in gut and potentiate action of antiemetics by sensitizing pharmacological receptors<sup>9</sup>. In our study 96.6% children had complete response when combination was used as only one patient had vomiting in first 24 hrs.

The common side effects seen with Granisetron are headache, vomiting, diarrhoea and constipation<sup>10</sup>. Long term use of corticosteroids is associated with adrenal suppression or avascular necrosis of hip, but single dose is considered safe. However in our study only few patients had mild headache which was relieved without any medicines. No other complications were seen in either group.

### Conclusion

Combination of Granisetron and Dexamethasone significantly lowers the incidence of postoperative emesis. However the incidence of need of rescue antiemetics or any other side effects is similar when Granisetron is used alone or in combination.

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