

Addition of Dexamethasone to Prophylactic Granisetron in Children Undergoing Ocular Surgeries – A Randomised Controlled Double-Blind Trial

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ABSTRACT

BACKGROUND

Postoperative nausea and vomiting are highly prevalent after ophthalmic surgeries in the paediatric age group. In this randomised, double-blind prospective clinical trial, we studied and compared the efficacy of granisetron and combination of granisetron with dexamethasone to prevent postoperative nausea and vomiting after paediatric ocular surgeries.

METHODS

Sixty paediatric patients (06 - 12 yrs. of age) undergoing elective ocular surgeries were randomly allocated to one of the two groups of 30 patients each. Group (G) received granisetron 40 mcg kg⁻¹ intravenously as a bolus before induction of anaesthesia. Group (G + d) received granisetron 40 mcg kg⁻¹ & dexamethasone 0.1 mg kg⁻¹ intravenously as a bolus before induction. Student t-test, Fisher exact test were used wherever applicable for statistical analysis using SPSS version 15.0.

RESULTS

A complete response (defined as no post-operative nausea and vomiting and no need for another rescue antiemetic) was achieved in 63.3 % of patients who received granisetron alone and in 96.7 % of patients who received granisetron plus dexamethasone. We found nil difference in complications between the two groups.

CONCLUSIONS

We found that addition of dexamethasone to granisetron is more effective and beneficial than granisetron alone in preventing postoperative emesis in 1st 24 hours.

KEYWORDS

Post-Operative Nausea and Vomiting, Anaesthesia, Granisetron, Dexamethasone

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BACKGROUND

Post-operative nausea and vomiting, one of the most worrying complication after anaesthesia, can occur after both general and regional anaesthesia. The incidence of postoperative emesis in many studies has been reported to be in 20 - 30 %.¹ Incidence of postoperative nausea and vomiting without prophylaxis is 41 % - 88 %.^{2,3} It is very troublesome symptom after postoperative pain, persistence of post-operative nausea and vomiting can result in raised intraocular pressure, subconjunctival haematoma, suture dehiscence, prolonged hospital stay and increased economic costs. We have chosen paediatric ocular surgeries as the incidence of post-operative nausea and vomiting as it is high among the paediatric population. Of all operations, surgeries for strabismus⁴ glaucoma, cataract have a high prevalence of post-operative nausea and vomiting, and very few studies are there in paediatric ocular surgeries. granisetron⁵ a selective 5-hydroxytryptamine type 3 (5-HT₃) receptor antagonist, is an effective and long-acting antiemetic. In most of the studies showed dose of granisetron for prevention of post-operative nausea and vomiting was 40 mcg kg⁻¹, while dexamethasone they have used 0.15 mg kg⁻¹ for post-operative nausea and vomiting prophylaxis.⁶ There are conflicting results in few studies about addition of dexamethasone to 5-hydroxytryptamine type 3 antagonists, so our primary objective is to find out the effectiveness of addition of dexamethasone with granisetron and granisetron alone in preventing post-operative nausea and vomiting and secondary objective is to find out any adverse effects in postoperative period.

METHODS

We obtained ethical clearance from our institutional ethical and scientific committee, and informed consent from parents, we conducted a comparative, prospective randomised, double-blinded controlled study in 60 paediatric patients undergoing elective ocular surgeries. The study was conducted in our institute from January 2013 to June 2014. Research protocol was submitted and approved from the National Board of Examinations, New Delhi, and then proceeded with our study. Randomisation was done by computer generated tables, and opaque sealed covers were opened by parents of children who participated in study. Study drugs were diluted to a fixed volume of 5 ml by anaesthesia technician. The anaesthetist and observer were not aware of the group of the children. The study was done on children of 6 - 12 yrs. of age, ASA 1, 2. Patients with known hypersensitivity to granisetron, patients with a history of motion sickness or previous post-operative nausea and vomiting, patients who have taken anti-emetic drugs within 24 hrs before surgery, patients with a history of renal diseases or liver diseases were excluded from the study. Children were allowed food 6 hrs prior to surgery. In the operating room standard monitoring like electrocardiogram, non-invasive blood pressure, and pulse oximeter were

connected. The drugs were given 5 minutes before induction of anaesthesia by an anaesthetist who is not involved in the study, for making the study double blinded. Anaesthesia was induced after preoxygenation with 100 % O₂ for 3 min with intravenous thiopentone 5 mg kg⁻¹ and fentanyl 2 mcg kg⁻¹, and vecuronium bromide 0.1 mg kg⁻¹ for muscle relaxation and oral cuffed endotracheal tube was inserted. Anaesthesia was maintained with N₂O 66 %, O₂ 33 %, halothane and intermittent doses of vecuronium bromide and fentanyl were administered. Ventilation was controlled mechanically, intermittent positive pressure ventilation. After the end of the procedure, the residual neuromuscular blockade was reversed by neostigmine 50 mcg kg⁻¹ and glycopyrrolate 10 mcg kg⁻¹.

All incidences of post-operative nausea and vomiting in the first 24 postoperative hours were recorded at the intervals of 0 - 6 hrs. and 6 - 24 hrs. The severity of post-operative nausea and vomiting over the first 24 postoperative hours was assessed using the numeric scoring system for post-operative nausea and vomiting.

0 = No nausea or vomiting,
1 = Nausea but no vomiting,
2 = Vomiting once,
3 = Two or more episodes of vomiting.

Adverse effects were observed for in the 1st 24 hours. Nausea is defined as the unpleasant sensation associated with urge to vomit. Vomiting is defined as the act or instance of forceful expulsion of gastric contents from the mouth. Nausea was assessed by self-reporting and observing. These were assessed by nausea and vomiting score. Rescue antiemetic (metoclopramide 150 mcg / Kg) was used if the patient had nausea or vomiting.

RESULTS

Age in Years	Group G		Group G + D	
	No	%	No	%
1 - 6	0	0.0	4	13.3
7 - 12	30	100.0	26	86.7
Total	30	100.0	30	100.0
Mean ± SD	8.90 ± 1.84		8.97 ± 1.92	

Table 1. Age Distribution of Patients Studied

Samples are Age-Matched with P = 0.891

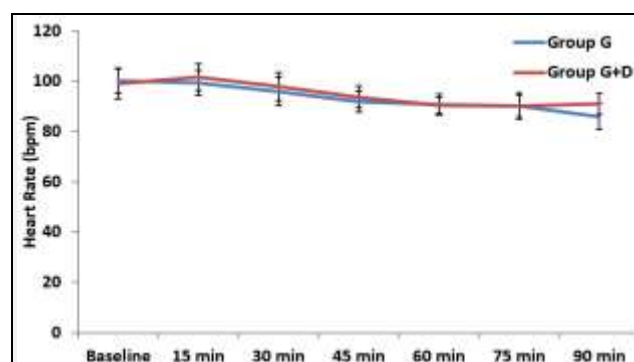


Figure 1. Comparison of Heart Rate between the Two Groups Studied

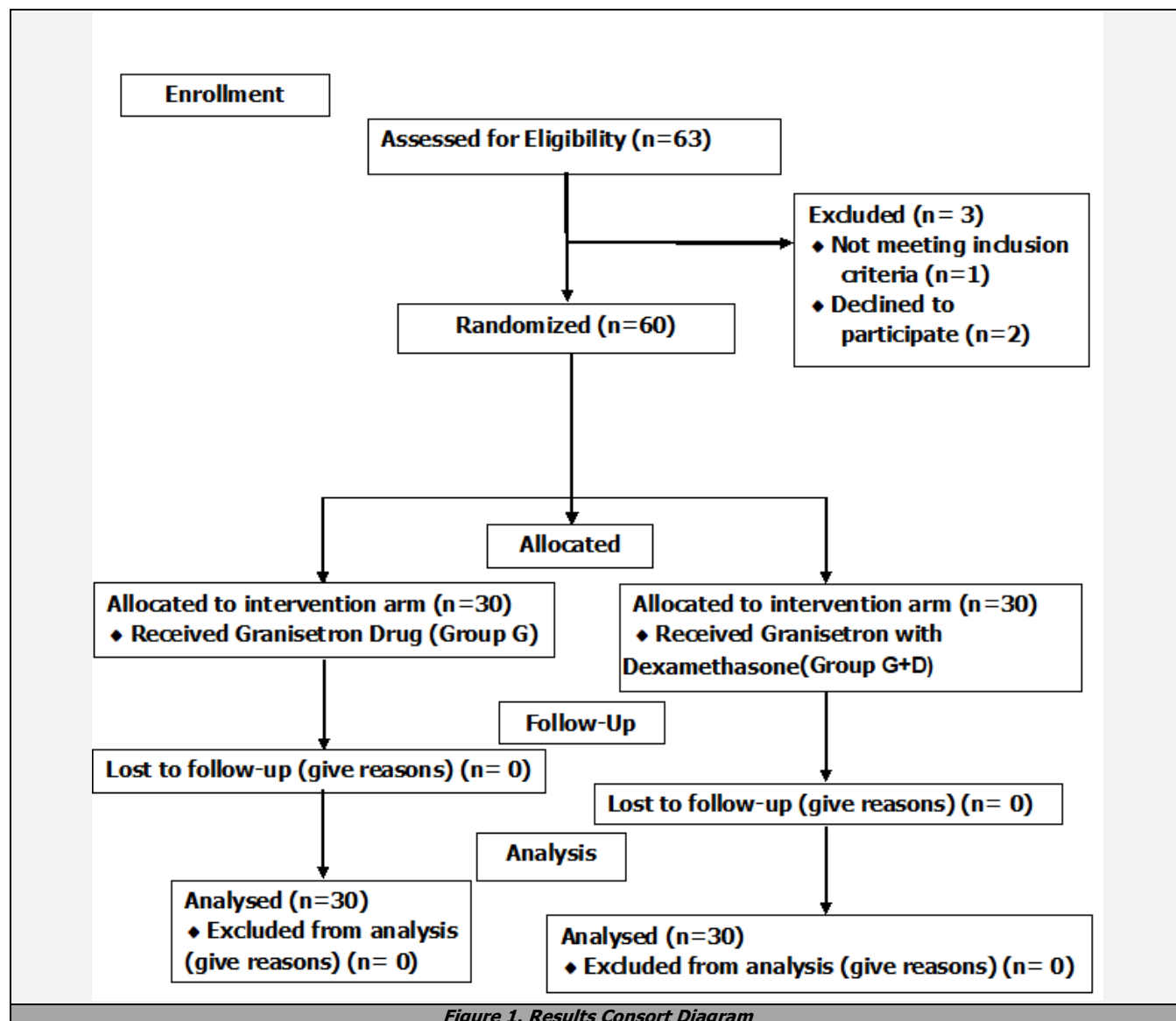


Figure 1. Results Consort Diagram

Nausea	0 - 6 Hrs. (n = 30)	6 - 24 Hrs. (n = 30)	% Change
Group G			
• No	23 (76.7 %)	27 (90.0 %)	+ 6.7
• Yes	7 (23.3 %)	3 (10 %)	- 6.7
Group G + D			
• No	29 (96.7 %)	29 (96.7 %)	0.0
• Yes	1 (3.3 %)	1 (3.3 %)	0.0
P-value	0.050*	0.612	

Table 2. Comparison of Frequency of Nausea in the Two Groups of Patients Studied

Vomiting	0 - 6 Hrs. (n = 30)	6 - 24 Hrs. (n = 30)	% Change
Group G			
• No	26 (86.7 %)	28 (93.3 %)	+ 6.6
• Yes	4 (13.3 %)	(6.7 %)	- 6.6
Group G + D			
• No	30 (100.0 %)	30 (100.0 %)	0.0
• Yes	0 (0 %)	0 (0 %)	0.0
P-value	0.112	0.492	-

Table 3 Comparison of the Frequency of Vomiting in the Two Groups of Patients Studied

Statistical Analysis

We have used Student t-test (two-tailed, independent) to find the significance of study parameters on continuous scale between two groups (intergroup analysis) on metric parameters. We have used Fisher exact test to find the significance of study parameters on a categorical scale between two or more groups. Suggestive significance (p-value: less than 0.05). We have used SPSS 15.0 for the analysis of the data and Microsoft Word and Excel have been used to generate graphs, tables etc.

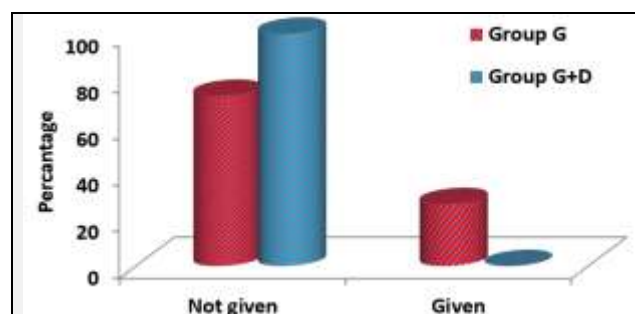


Figure 2. Rescue Antiemetic between the Two Groups

DISCUSSION

In our double-blinded randomized controlled study, we found that combined therapy of granisetron with dexamethasone is more effective than granisetron alone. A complete response (defined as no post-operative nausea and vomiting and no need for another rescue antiemetic) was attained in 73.3 % of patients who received granisetron alone and in 96.7 % of patients who received granisetron plus dexamethasone. We found No difference in adverse events was observed in the two groups.

Postoperative nausea and vomiting are approximately twice as frequent amongst children as adults with an incidence of 13-42 % in all paediatrics patients,⁸ Of all the ocular surgeries strabismus surgery has high incidences of post-operative nausea and vomiting of any surgical procedure. Most of the events of vomiting occur during 1st 24 hrs time, so we have studied post-operative nausea and vomiting in paediatric ocular surgeries in 1st 24 hours; we felt it is unethical to add placebo arm in our study as ocular surgeries have high incidence of post-operative nausea and vomiting.

post-operative nausea and vomiting aetiology is multifactorial, nausea and vomiting can cause suture dehiscence^{1,4} raised intra ocular pressure, prolonged hospital stay and increased economic costs, so preventing post-operative nausea and vomiting is always better than treating it.

Pushplata Gupta and Jain⁹ used granisetron at 40mcg kg⁻¹ for post-operative nausea and vomiting prophylaxis in breast cancer surgeries. De Orange et al.¹⁰ used dexamethasone at 150 mcg kg⁻¹ in children, and we have also used the same dose in our study. Mathew et al.¹¹ concluded that dexamethasone is effective in preventing postoperative nausea and vomiting following strabismus surgeries in children.

In this study, we tried to avoid confounding variables like opioid prescription, and we used the same type of opioid in both groups; thus, both groups are similar in nature, in age and gender distribution (Table 1). In our study, both groups received similar anaesthetic medications.

In a study conducted by S. Gombar¹² et al., they observed that complete response was achieved significantly more so in children who received a combination of granisetron and dexamethasone (96.7 %) than in those who got granisetron alone (80 %) which is an almost similar finding in our study. A complete response (defined as no post-operative nausea and vomiting and no need for another rescue antiemetic) was attained in 73.3 % of patients who received granisetron alone and in 96.7 % of patients who received granisetron plus dexamethasone.

In a study conducted by Pusplata et al.⁹ also they found that the incidence of complete response (no post-operative nausea and vomiting, no rescue medication) was 96 % with granisetron and dexamethasone combination (G + D), as compared with 86 % with granisetron alone and 4 % with ondansetron group during 0 - 3 hrs. after surgery which was clinically significant.

Whereas contrary to our findings Renu Sinha et al.¹³ found that complete response to postoperative nausea and

vomiting in 24 hours was observed in 75 % (51 / 68) of children in group granisetron and 76.9 % (50 / 65) of children in group granisetron with dexamethasone, which was comparable statistically. They found that granisetron is as equally competent enough as a combination of granisetron with dexamethasone.

In our study, we found that only during 0 - 6 hours there was a statistically significant difference between both groups in nausea (Table 2), but there was no statistically significant difference between both groups in vomiting (Table 3) unlike the study by Pushpalata¹² et al., where they found that statistically significant difference in both nausea and vomiting in combination therapy. Study done by Renu Sinha¹³ et al. found that both groups' combination and granisetron monotherapy showed almost similar results which are statistically insignificant.

This difference of results may be due to different study design, patient characteristics, anaesthesia related factors, type of surgery and anaesthesia duration.

In group G, six patients were given rescue antiemetic (Figure 2) where none in group G + D.

Two patients had a headache one in each group, which is insignificant. Most of the haemodynamic variables were normal in both the groups (Figure 1). But in both of the groups, two in each group developed intraoperative arrhythmias which was transient; we have taken 12 lead electrocardiogram strip; we could not find any QT prolongation. Still, we should always monitor for electrocardiogram changes till at least 12 hours and caution required in cardiac patients.

There are a few drawbacks in our study lack of control group (placebo) in our study is a drawback. However, conducting surgery with a high incidence of post-operative nausea and vomiting, without any prophylactic antiemetic was not acceptable ethically. We could not assess the antiemetic efficacy of dexamethasone alone, and as we conducted a study in paediatric population subjective assessment of nausea was difficult. As we conducted a study on paediatric ocular surgeries, we could get an only sample size of 60 patients, further research needed in large sample sizes would be more beneficial.

CONCLUSIONS

Incidences of post-operative nausea and vomiting after paediatric ocular surgeries is high. In our study, the combination (granisetron plus dexamethasone) was found to be better in attaining a complete response than granisetron alone, even though we found no significant difference in nausea during 1st 24 hrs.

Symbols & Abbreviations

SI No: Serial Number

Ip No: Inpatient Number

ASA Gr: ASA Grade

Anes Du Min: Anaesthesia Duration in Minutes

Surg Du: Surgery Duration

M: Male

F: Female

MmHg: Millimetre of Mercury

BPM: Beats per Minute

Min: Minutes

Hrs: Hours

PONV: Postoperative Nausea and Vomiting

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

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