

A Comparative Study: Dexamethasone Versus Granisetron in Prevention of Post Operative Vomiting in Pediatric Patients Undergoing Strabismus Surgery

¹Hala M.B. Abdel Hakim, ¹Dalia S. Tawfik, ¹Rehab M.S. Abdelaziz and ²Mohamed A. Mahmoud

¹Department of Anaesthesia in Research Institute of Ophthalmology, Giza and

²Department of Anaesthesia in National Hepatology and Tropical Medicine Research Institute, Cairo, Egypt

Abstract: Background: This study evaluated the antiemetic effectiveness and clinical usefulness of granisetron in comparison to dexamethasone in the prevention of postoperative vomiting in children undergoing strabismus surgery. Methods: A total of 90 patients, allocated in three groups, 30 each were scheduled for elective strabismus surgery, with age varying from 3-6 years, ASA physical status I or II. After induction of anesthesia with sevoflurane and 100% oxygen, children either received, granisetron (40 mic/kg), dexamethasone (0.25 mg/kg) or placebo. Results: There is no difference between groups as regard the demographic and clinical data. The incidence of 24-h of post operative retching and vomiting was significantly decreased in granisetron group 21.1% compared with placebo 75.7%. but this incidence decreased insignificantly in dexamethagon group 42.4%. The number of children who suffered severe vomiting (2 times or more) were 14,13,3 in placebo, dexamethazon and granisetron group and it was found that it was reduced significantly in granisetron group. The duration of PACU stay was significantly shorter in granisetron group compared with placebo. Conclusion: The prophylactic use of granisetron is effective in preventing post operative retching and vomiting and improving the outcome measareas after strabismus repair in children.

Key words: Dexamethasone, Granisetron, Post Operative Vomiting, Pediatric Patients, Strabismus Surgery.

INTRODUCTION

Postoperative retching and vomiting remains a distressing and common problem after strabismus repair, despite the use of different antiemetics (Abramowitz *et al.*, 1983). Dexamethasone is a potent synthetic member of glucocorticoids class of steroid drugs. It acts as anti inflammatory. The first clinical trail that dexamethasone may prevent post operative nausea and vomiting was published by Baxendale *et al.* (1993). Granisetron is a selective 5-hydroxy tryptamine type 3 (5-HT₃) receptor antagonist and proved to be more potent and had longer acting activity against cisplatin-induced emesis than ondansetrone (Andrews, 1992). It has been proved that it is also effective for prevention of post operative vomiting in children undergoing strabismus surgery (Fujii *et al.*, 1996).

This prospective, randomized double-masked, placebo-controlled study was designed to compare dexamethasone versus granisetron in prevention of post operative retching and vomiting in pediatric patients undergoing strabismus surgery.

MATERIALS AND METHODS

The study was done after obtaining institutional approval and informed parental consent from parents of 90 children, ASA physical status I or II, between the age of 3 and 6 years old undergoing strabismus surgery. Exclusion criteria for subjects included:

1. Any patients received any type of preoperative antiemetic therapy at least in last 24 hours.
2. Patients with clinically notable GIT, renal or hepatic disease.

Children did not consume milk on solid food for at least 6 hours before operation, clear fluids were allowed 2 hours before induction. No premedication given.

Corresponding Author: Hala M.B. Abdel Hakim, Department of Anaesthesia in Research Institute of Ophthalmology, Giza, Egypt.
E-mail: halabahy@hotmail.com

Anesthesia has been induced by inhalation of sevoflurane in oxygen via a face mask, then atracurium 0.4-0.5 mg/kg was given to facilitate endotracheal anaesthesia was maintained Isoflurane 0.5-1% and 100% O₂. Ventilation was controlled mechanically, and the patients were monitored by basic monitoring devices; ECG, pulse oximeter, capnography, dynamap and temperature. The subjects received in a randomized double-blinded manner, a single I.V dose of either dexamethasone 0.25 mg/kg, granisetron 40 mic/kg or placebo (saline) two minutes after induction of anesthesia and prior to surgical procedure. At the end of surgical procedure, atropine sulphate 0.02 mg/Kg and neostigmine 0.04 mg/Kg were administered I.V for reversal of muscle relaxation, and the trachea was extubated when the patients were awake. Postoperative analgesia was provided by acetaminophen 10-15 mg/Kg per rectal of mild pain and pentazocine 0.3 mg/Kg I.V for severe pain.

All episodes of retching and vomiting in the first 24 h of the post operative period in the hospital at the intervals 0-2h, 2-6h, 6-24 hours were evaluated using a numeric scoring system (0= no retching or vomiting, 1 = retching but no vomiting, 2 = vomiting once in 30 minutes, 3 = two or more episodes of vomiting in 30 minutes) by PACU and ward nursing staffs, who were aware of the nature of the study but blind to the study group. Any child having a score of 3 was considered to have severe vomiting and was treated with 150 mic/kg intravenous metoclopramide as a rescue antiemetic.

Retching was defined as the process of straining to expel the stomach contents without producing any thing whereas vomiting was defined as the act of expelling the stomach contents by an active process. Nausea was not assessed in this study due to young age of patients.

The criteria for discharge from the PACU to the ward are maintenance of patient air way without assistance, stable vital signs, adequate pain control, and no retching and vomiting in the first 2h after surgery. Those children who had retching and vomiting in first 2 h of stay were observed in PACU until they remained free for 1h. The details of any adverse effects throughout the study were recorded by a follow up nurse who interviewed the parents of the subject.

Statistical Analysis:

Two samples, t tests and Mann-Whitney tests were used to compare the age; weight; duration of anesthesia, surgery, recovery, and PACU stay; and analgesic requirements. The incidence and severity of vomiting from 0-6 and 0-24 h, the duration of PACU stay were compared for each group with every other group. Severity of post operative vomiting between dexamethasone, granisetron and placebo was compared by chi-square analysis and the fisher exact test with a Yates continuity correction wherever appropriate. Over all p value < 0.05 were considered to be statistically significant, and data are presented as the mean ± SD unless other wise specified.

Results:

The demographic and clinical data such as patient's age, sex, weight, physical status, duration of surgery and anesthesia, analgesic requirements and recovery time were similar in all groups (Table 1).

As regard the 24-h incidence of postoperative retching and vomiting there is a decrease in dexamethasone group than placebo group but the decrease is insignificant. A significant reduction in the incidence was observed in granisetron group (p< 0.0001) compared with placebo. Also the incidence of post operative reacting and vomiting in the early post-operative period (0-2 and 2-6 h) was reduced significantly only at granisetron group (P < 0.001) (Table 2).

Table 1: Patients demographic data.

Demographic and clinical data	Placebo group (n = 30)	Dexamethasone group (n = 30)	Granisetron group (n = 30)
Age (yr)	4.3 ± 1.7	4.8 ± 1.8	3.9 ± 2.1
Sex (m/F)	15/15	13/17	16/14
Weight (kg)	16.1 ± 0.6	16.9 ± 7.2	17 ± 8.4
ASA status I/II	28/2	29/1	30/0
Duration of:			
-Anesthesia (min)	60.1 ± 15.1	47.2 ± 15.7	62.2 ± 15.7
-Surgery (min)	49.4 ± 16.3	62.4 ± 9.3	50.4 ± 11.2
Recovery time (min)	20.7 ± 16.7	18.3 ± 15.3	16.1 ± 6.6
Analgesics post operatively:			
Acetamenophen	23/30	22/30	23/30
Pentazocine	2/30	2/30	2/30

-Age, weight, anaesthetic, surgical and recovery times were represented as the mean ± SD. ASA, physical status, sex, post operative analgesics were represented as the number of children.

-The demographic and clinical data are comparable in all groups.

Table 2: Incidence of post operative retching and vomiting.

Post operative retching and vomiting measures	Placebo group (n = 30)	Dexamethasone group n = 30	Granisetron group (n= 30)
	P.O. retching and vomiting (%)		
0-2 h	39.1	23.3	5.6
2-6h	59.1	29.5	20.6
6-24h	29.1	12.9	2.6
0-6 h	65.7	38.8	20.8
0-24h	75.7	42.4	21.1

-The incidence of post operative retching and vomiting at various intervals were presented as the percentage of children with post operative retching and vomiting.

-The 24-h post operative retching and vomiting incidence was less in granisetron group ($P < 0.001$) compared with placebo group.

Table 3: Severity of post operative vomiting.

Severity of post operative vomiting	Placebo (n=30)	Dexamethasone (n=30)	Granisetron (n=30)
Children who received I.V meto clopromide	14/30	13/30	3/30

-Rescue antiemetic requirements has been reported as the number of children.

-The adverse effects commonly observed in this study were headache, drowsiness and others (constipation, muscle pain) (Table 4).

Table 4: Adverse effects.

Side effects	Placebo (n=30)	Dexamethasone (n=30)	Granistrone (n=30)
Headache	2	2	2
Drowsiness	2	2	2
Others	0	1	1

-The incidence of side effects were presented as the number of children.

-The duration of PACU stay was significantly shorter in graniestrone group ($P < 0.001$) compared with the placebo group (Table 5).

Table 5: Duration of PACU stay.

Duration of PACU stay (min)	Placebo n =30	Dexamethasone n =30	Granisterone n =30
	154.3 ± 43.1	139.5 ± 16.5	128.3 ± 11

-Duration of PACU stay was presented as mean ± SD.

-The duration of PACU stay was shorter in granisetron group ($P < 0.001$) compared with the placebo.

The number of children who required metoclopramide as the rescue antiemetic were 14, 13, 3, in the placebo, dexamethasone and granisetron group respectively the requirements was reduced significantly only in granstrone group ($P > 0.01$).

The incidence of adverse effects postoperatively were not different among the three groups.

Discussion:

The reported incidence of vomiting after strabismus surgery in children varies from 48% to 85% when no antiemetic treatment is given (Abramowitz *et al.*, 1983). The etiology of postoperative vomiting is not exactly known, but it is probably multifactorial (Watcha and White, 1992). These factors include age, sex, obesity, history of motion sickness or postoperative vomiting, anesthetic technique and post operative pain. Surgical factors also include the impulse from the extrinsic eye muscles related to the vestibular nuclei via nuclei III, IV, VI of the medial longitudinal fascicule (Warner *et al.*, 1988). These vestibular nuclei lie in the brainstem reticular formation and are closely associated anatomically to the vomiting centers (Watcha and White, 1992). In this study, however, the factors that increase the incidence of post operative vomiting are well balanced among all the groups, so that the difference in the incidence of post operative vomiting among them can be attributed to the differences to the drugs administered. Fujil *et al.* (1996) found that granisetron reduces the incidence of vomiting following strabismus surgery and tonsillectomy in children. In this study with the administration of placebo, dexamethasone and granisetron we found that there is a significant reduction in the 24 h incidence post operative retching and vomiting in graniestrone group compared with placebo, but the reduction is insignificant in dexamethasone group.

This study also showed that who had received placebo and who had received dexamethasone required another rescue antiemetic drug (e.g., metoclopramide) for the treatment of severe vomiting (score of 3) where as only 3 who had received granisetron needed this agent.

Thus, the ability of granisetron to attenuate the severity of post operative vomiting following strabismus repair may be as important as its ability to reduce the incidence of vomiting per se. The present investigation also found that prophylactic granisetron was more effective in reducing the duration of PACU stay and in improving comfort after strabismus surgery in children. As regard the side effects, the incidence of the adverse effects postoperatively were not different among the three groups. Yaker *et al.* (1994) also found that granisetron lacks the sedative, dysphoric and extrapyramidal symptoms associated with non-5-HT₃ receptor antagonists (e.g., droperidol, metoclopramide, Yaker *et al.*, 1994).

Granisetron can be used also orally and it was found that preoperative oral granisetron 40mg/kg is effective in preventing vomiting after strabismus surgery in children. Increasing the dose to 80 mg/Kg provides no demonstrable additional benefit (Yoshitaka *et al.* 1999).

The role of dexamethasone in the surgical setting is less well understood. The first clinical trial suggesting that dexmethasone may prevent PONV was published in 1993. Subsequent studies indicated that dexamethasone alone (Henzi *et al.*, 2009) or in combination with a 5-HT3 receptor antagonist (Mousa and Oregan, 2007; Mitsunari *et al.*, 2007 and Fujii, 2000) may indeed be an interesting alternative for the control of emetic symptoms in the post operative period.

REFERENCES

- Abramowitz, M.D., T.H. Oh, B.S. Epstein, U.E. Ruttimann, D.S. Friendly, 1983. The antiemetic effect of droperidol following outpatient strabismus surgery in children, *Anesthesiology*, 59: 579-83.
- Andrews, P.L., P. Bhandari, P.T. Devey, *et al.* 1992. Are all (5-HT3) receptor antagonist the same? *Eur. J. Cancer*, 28A suppl., 52-6.
- Baxendale, B.R., M. Vater, K.M. Lavery, 1993. Dexamethasone reduces pain and swelling following extraction of third molar teeth. *Anaesthesia*, 48: 961-4.
- Fujii, S.Y., H. Tanaka, H. Toyook, 2000. Granisetron dexamethasone combination for the prevention of postoperative nausea and vomiting after the laparoscopic cholecystectomy. *Eur. J. Anaesthesiol.*, 17(1): 64-8.
- Fujii, Y., H. Tanaka and H. Toyooka, 1996. Granisetron reduce vomiting after strabismus surgery and tonsillectomy in children. *Can. J. Anaesth.*, 43: 35-8.
- Henzi, I., B. Walder and M.R. Tramer, 2000. Dexamethasone for the prevention of post operative nausea and vomiting. A quantitative systematic Review. *Analg.* 90: 186-194(s).
- Mitsunari, H., E. Ashikari and K. Tanaka, 2007. The use of droperidol decreases post operative nausea and vomiting after gynecological Laparoscopy, 21(4): 507-9(s).
- Mousa, A.A. and P.J. Oregan, 2007. Prevention of post operative nausea and vomiting in patients undergoing laparoscopic bariatric surgery granisetron alone Vs, granisetron combined with dexamethazone/droperidol. *Eur. J. Anaesthesiol.*, 19(2): 357-67(s).
- Warner, L.O., M.D. Rogers, L.D. Martino, *et al.* 1988. Intravenous Lidocaine reduces the incidence of vomiting in children after surgery to correct strabismus. *Anesthesiology*, 68: 618-21.
- Watcha, M.F. and P.F. White, 1992. Post operative nausea and Vomiting treatment and prevention. *Anesthesiology*, 77: 162-84.
- Yarker, Y.E., Mc D. Tavish, 1994. Granisetron, An update of its therapeutic use in nausea and vomiting induced by antineoplastic therapy. *Drugs*, 48: 761-93.
- Yoshitaka, F., T. Hirojoshi and I.T.O. Mutsuko, 1999. Preoperative oral granisetron for the prevention of vomiting after strabismus surgery in children. *Ophthalmology*, 106: 1713-1715.