PROPHYLACTIC METOCLOPRAMIDE ADMINISTERED IMMEDIATELY AFTER THE INDUCTION OF ANESTHESIA HAS NO EFFECT ON THE INCIDENCE OF POSTOPERATIVE EMESIS AFTER STRABISMUS SURGERY

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Objective: *To evaluate the efficacy of metoclopramide (0.25 mg/kg) administered IV immediately after induction of general anesthesia for the prevention of postoperative emesis in children undergoing, elective strabismus surgery. Design: Double blind, randomized. Setting: Operation-theater. Subjects and Interventions: Seventy six non premedicated children of ASA class 1 and 2 were randomly allocated to receive either normal saline or metoclopramide immediately after the induction of general anesthesia. All children received a standardized similar anesthetic technique. Postoperative analgesia consisted of oral indomethacin.* ***Results:*** *The incidence of postoperative emesis in the metoclopramide group was 60% versus 71 % in a placebo group ($p < 0.05$). The incidence of severe emesis (2 or >2 vomiting) was similar in the placebo group (34.20%) and metoclopramide group (21.05%). There were no adverse reactions like excessive sedation, extrapyramidal signs and hemodynamic depression in either placebo or metoclopramide group.* ***Conclusion:*** *Metoclopramide in a dose of 0.25 mg/kg administered intravenously prior to manipulation of eyeball is devoid of side effects but is not effective in preventing postoperative emesis in children undergoing strabismus surgery.*

Key words: *Metoclopramide, Postoperative emesis, Strabismus.*

CORRECTIVE strabismus surgery in pediatric patients is associated with a high incidence of postoperative emesis(l). In common with the treatment of postoperative pain, there has been a recent resurgence of interest in the prevention and treatment of emesis associated with surgery. This has got humanitarian as well as economic benefits. Metoclopramide is a dopaminergic antagonist that possesses intrinsic central antiemetic actions, it is also shown to accelerate gastric emptying and to increase lower esophageal sphincter tone(2). Reports on utility of metoclopramide for prophylaxis against postoperative emesis in high risk surgical population have been mixed(3-6). We evaluated the efficacy of metoclopramide administered prophylactically prior to start of surgery as an antiemetic agent in pediatric patients undergoing elective strabismus surgery.

Subjects and Methods

Seventy-six pediatric patients of ASA class I and 2 of either sex (40M : 36F) and

age between one to twelve years, scheduled for elective strabisnvus surgery at the Rajendra Prasad Center for Ophthalmic Sciences, New Delhi, India were included in study after obtaining permission from institutional ethical committee. Patients predisposed to nausea and vomiting secondary to gastrointestinal reflux, motion sickness, inner ear disorder or CNS disorders were excluded. None of the children received any premedication. All children were prohibited from eating solid food or drinking milk products after midnight. However, children younger than 5 years of age were permitted to consume clear fluids up to 4 hours prior to surgery. General anesthesia consisted of a standardized anaesthesia technique.

Patients received either saline (P) or metoclopramide 0.25 mg/kg (M) made up to equal volume of 5 ml in the identical syringes, immediately following induction of general anesthesia according to randomized assignment list. The author (MH) who followed up the patients was blinded to the agent given, as he was not involved with anesthesia management. All the patients received lactated ringer to replace preoperative deficits and to provide the maintenance requirements. At the termination of surgery an orogastric tube was passed briefly and gastric contents emptied. All patients were monitored intraoperatively for vital signs, SPO_2, ECG and ETCCX,. Tracheal extubation was performed after reversing the patients adequately with neostigmine 50 micrograms/kg and atropine 20 micrograms/kg after which patients were transpored to Post-Anesthesia Care Unit (PACU).

The patients were evaluated for responsiveness according to method of Steward and emesis by numeric rank score. Each episode of emesis that occurred was recorded(7) 0 to 2 hours, 2-6 hours and 6-24 hours after surgery and were scored as 0= No nausea and vomiting, 1 = Nausea but no vomiting, 2 = One vomiting, 3 = 2 or >2 vomiting. We followed up patients for twenty four hours as postoperative emesis can continue to be significant for the first 24 hours(4,8). Any child having two or more episodes of vomiting was considered to have severe vomiting.

A significant episode of oculocardiac reflex (OCR) was defined as an acute decrease in heart rate of 30% or greater associated with traction on eye muscle. If heart rate did not return to baseline after release of the muscle traction or OCR recurred, atropine 0.01 mg/kg was administered intravenously. Postoperative analgesia if required consisted of oral indomethacin.

Data were analyzed for the incidence of vomiting and severity of vomiting between two groups at various time intervals by Chi-squared test. Pre-study power analysis based on previously published study(4,5) indicated that in order to decrease the incidence of vomiting by 50% using 50% significance test, with 90% power we needed 38 patients in each group.

Results

Patient characteristics were comparable in both the groups *(Table I)*. The overall incidence of postoperative emesis for first twenty-four hours in the metoclopramide group was 60% as compared to 71% in placebo group. The incidence of emesis was statistically similar at 0-2 hours, 2-6 hours and 6-24 hours in both the groups. Although the incidence of severe vomiting was less in metoclopramide group (21.05) as compared to placebo (34.2%), the difference was statistically not significant *(Table II)*. There were no adverse reactions like excessive sedation, extra-pyramidal signs and hemodynamic depression either

TABLE I–*Comparison of Baseline Characteristics (Mean±SEM)*

Characteristic	Placebo (n=38)	Metoclopramide (n=38)
Age (Yrs)	6±3 63	6.87±3.34
Sex (M·F)	20.18	20:18
Weight (kg)	19.84±12.09	21.69±11.16
No. of Muscles	2.07±0.81	2.36±0.81
Anesthesia Time (min)	64.23±32.25	65.12±31.02
Surgery duration (min)	58.55±27.75	60.55±28.90

None of the differences between the groups were significant.

TABLE II–*Incidence and Severity of Post-operative Emesis (Emesis Score 0-3 Range)*

Characteristic	Placebo (n=38)	Metoclopramide (n=38)
Severe vomiting	13/38 (34.3)	8/38 (21.1)
Time Period		
0-2h	17/38 (44.7)	11/38 (28.9)
2-6h	19/38 (50 0)	10/38 (28.9)
6-24h	6/38 (15.8)	6/38 (15.8)
0-24h	27/38 (71.0)	23/38 (60.0)

Figure in parantheses indicate percentages.
None of the differences in the two groups were statistically significant (p >0.05).

to metoclopramide or placebo. Recovery evaluated by recovery room scoring was similar in both the groups.

Discussion

The incidence of postoperative emesis following strabismus surgery in children who have not received any form of prophylactic antiemetic treatment has been reported to range from 59-88%(4,5,8,9). Our observed incidence of 71% in the placebo group is generally consistent with previous studies. Metoclopramide even though observed to be very effective in reducing the postoperative emesis by some investigators(4,5,9) has performed poorly in well controlled clinical trials(3,10). In our study the observed incidence of 60% in the metoclopramide treated children was statistically similar to the placebo group.

Metoclopramide probably reduces postoperative nausea and vomiting through several mechanisms like antagonizing dopamine receptors in the chemoreceptor trigger zone (CTZ)(2) and in higher doses metoclopramide also appears to antagonise 5 HT3 receptors(11,12). The most important peripheral antiemetic effect of metoclopramide may be it's ability to increase gastric motor activity(2). Previous studies have shown that both timing of metoclopramide administration and total dose may be important variables in the control of postoperative vomiting in the children undergoing strabismus surgery(5,10). We

decided to give meto-clopramide prior to surgical incision, presuming that early blockade of receptors in chemoreceptor trigger zone (CTZ) prevents their activation during surgery and thus reduces vomiting postoperatively(5). The recommended dose of metoclopra-mide(2) for children less than 14 years of age is 0.1 mg/kg but not to exceed 0.5 mg/kg. In the present study we chose 0.25 mg/kg as this dose was shown to be effective in this population(5).

In the present study, metoclopramide failed to demonstrate significant efficacy in attenuating the severity and reducing the incidence of postoperative emesis following strabismus surgery. This can be attributed to various factors like: *(a)* Half life of metoclopramide; *(b)* Time of administration of antiemetic; and (c) Use of atropine either for the treatment of OCR or reversal of residual neuromuscular blockade in conjuction with anticholinesterase. The half-life of intravenously administered metoclopramide is only 2.6 to 4.6 hours in adults(2). In the present study as metoclopramide was administered at induction of anesthesia and before the manipulation of eye ball, the rapid redistribution of metoclopramide after intravenous administration must have resulted in low plasma concentrations in the postoperative period leading to higher incidence of emesis. Rapid distribution of metoclopramide after intravenous administration has been reported (T alpha 1/2 = 4.9 min)(13). Broadman *et a*\.(4), probably because of brief duration of action of metoclopramide, administered it at the completion of surgery and found it to be effective in reducing the incidence of vomiting in their population (M35% *vs* P 59%). There are mixed reports in the literature regarding efficacy of metoclopramide in relation to the time of administration. According to Broadman *et al*.(4) metoclopramide (0.15 mg/kg) when administered at the end of surgery effectively reduced the incidence of vomiting while Vanden Berg *et al.{6)* did not find it effective in the same dose administered at the end of surgery. In another study, metoclopramide proved very effective when given before surgery in a dose of 0.25 mg/kg. but failed in a dose of 0.15 mg/kg(5). In view of so much variability associated with regard to the time of administration and efficacy(10), clearly further work needs to be done to establish the optimal time for administration of metoclopramide as a prophylactic antiemetic.

The most important peripheral effect of metoclopramide may be its ability to increase gastric motor activity. This effect probably prevents gastric relaxation which must precede the act of vomiting. Preanesthetic medication with atropine and use of atropine in conjunction with anticholinesterase agents may reduce the antiemetic efficacy of metoclopramide by blocking the metoclopramide induced inhibition of gastric relaxation that must precede vomiting(2). However, anticholinergics have been shown to antagonise the gastric stimulation effects of metoclopramide(9,14). Sixteen patients in placebo group and 19 patients in metoclopramide group demonstrated OCR, out of which fifteen patients in metoclopramide group and twelve patients in placebo group required atropine for the treatment of OCR, as well we used atropine with neostigmine for the reversal of neuromuscular block in all the patients. This might have contributed to the higher incidence of postoperative emesis in metoclopramide group in our study as compared to previous reports(4,5). An earlier study(5) suggested a dose response relationship. However, whether higher doses will prove more efficacious remains to be determined. We were reluctant to use higher dose because of possibility of extrapyramidal side effects.

In summary, we have shown that

metoclopramide 0.25 mg/kg administered intravenously prior to the manipulation of eyeball is not effective in attenuating the severity of vomiting and preventing post-operative emesis in the children undergoing strabismus surgery. No adverse reactions were noted in either metoclopramide or placebo group.

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