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A Double-blinded Comparison of Metoclopramide and Droperidol for Prevention of Emesis Following Strabismus Surgery

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Vomiting in the postoperative period is common in children after strabismus surgery. One hundred ten pediatric patients, ages 8 months to 14 yr, admitted for outpatient strabismus surgery were enrolled in a randomized, double-blinded study to compare droperidol and metoclopramide to placebo for the prevention of postoperative emesis. Each child was prospectively assigned at random to one of four treatment groups: metoclopramide 0.15 mg/kg, metoclopramide 0.25 mg/kg, droperidol 0.075 mg/kg, or saline control. Drugs were administered intravenously immediately after induction of inhalation anesthesia. No neuromuscular blocking agents were used. Tracheal extubation was performed while patients were still deeply anesthetized. Acetaminophen and meperidine were given in standard doses for postoperative pain to all children. The incidence of vomiting was less in both the droperidol (33%) and metoclopramide 0.25 mg/kg (29%) groups when compared to controls (88%) ($P < 0.01$). Patients receiving metoclopramide 0.15 mg/kg had a 68% incidence of vomiting (P not significant). The mean frequency of emesis was reduced in all treatment groups compared with control ($P < 0.05$). Patients receiving droperidol and metoclopramide 0.25 mg/kg also had decreased postoperative stays (metoclopramide 201 min; droperidol 213 min) *versus* control (258 min, $P < 0.05$). No child exhibited extrapyramidal symptoms, excessive drowsiness, or agitation. We conclude that metoclopramide in a dose of 0.25 mg/kg, administered prior to the start of surgery, is at least as effective as droperidol in preventing postoperative emesis and can reduce the time to patient discharge compared to control. (Key words: Anesthesia: outpatient; pediatric. Surgery: ophthalmologic. Vomiting: antiemetics.)

CORRECTIVE STRABISMUS SURGERY in the pediatric patient is associated with a high incidence of postoperative emesis.[1] Prophylactic administration of droperidol has been shown to reduce postoperative vomiting significantly in this population.[2-4] However, there remains concern regarding the sedating effects of this agent, which may prolong recovery room stays or necessitate overnight hospitalization.[2,4,5]

Metoclopramide is a dopaminergic antagonist that possesses intrinsic central antiemetic actions.[6] It also acts to promote gastric emptying and increase lower esophageal sphincter tone, both of which may serve to further reduce vomiting. Reports on the utility of metoclopramide for prophylaxis against postoperative emesis in high-risk surgical populations have been mixed.[5,7-9] We undertook this study to compare the efficacy of metoclopramide at two doses (0.15 and 0.25 mg/kg) with that of droperidol 0.075 mg/kg (a dose previously shown to reduce vomiting)[4] for the prevention of postoperative emesis after strabismus surgery.

Materials and Methods

One hundred ten pediatric patients, ASA physical status 1 or 2, scheduled for elective strabismus surgery were studied over a 6-month period. Patients were not excluded if they had a history of motion sickness, previous eye surgery, or prior postoperative nausea and vomiting. The parents or guardians of each child gave informed consent, and the protocol was approved by our Institutional Review Board. Patients were prospectively randomized to receive one of four treatments: saline (control), metoclopramide 0.15 mg/kg, metoclopramide 0.25 mg/kg, or droperidol 0.075 mg/kg, administered intravenously. The investigator and observers were blinded as to the agent given.

Patients consumed nothing by mouth prior to operation; children less than 2 yr of age were permitted clear fluids up to 4 h prior to surgery, whereas older children were restricted for 6 h.[10] No preoperative medication was administered. Anesthesia was induced with halothane and 60% nitrous oxide in oxygen administered by mask. Each patient's trachea was intubated without the use of a muscle relaxant. The antiemetic agent was given immediately after induction and prior to surgical incision. Anesthesia was maintained with halothane and nitrous oxide; in rare cases the halogenated agent was changed to isoflurane because of ventricular ectopy. All patients received a minimum of 10 ml/kg intravenous fluid. At the termination of surgery, an orogastric tube was passed briefly and the gastric contents emptied. Tracheal extubation was performed under deep anesthesia after which the patients were transported to the postanesthesia care unit (PACU).

Upon arrival to the PACU patients were scored on a scale of 0-6 for responsiveness according to the method of Steward (table 1).[11] Patients were reevaluated at 5, 15, and 30 min, and again upon discharge. All patients were given acetaminophen 10 mg/kg rectally and meperidine 0.5 mg/kg intravenously on admission. Each episode of emesis that occurred prior to discharge was recorded. Retching was not considered emesis. Promethazine 1 mg/

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TABLE 1. Recovery Room Scoring System

Factor	Score
Consciousness	
Awake	2
Responding to stimuli	1
Not responding	0
Airway	
Coughing or crying	2
Maintaining good airway	1
Airway requiring maintenance	0
Movement	
Moving limbs purposefully	2
Nonpurposeful movements	1
Not moving	0

Recovery score is the sum of the three factors (range 0–6). Adapted from Steward.[11]

kg through the rectum was administered as an adjunctive antiemetic if a second episode of vomiting occurred. Patients were considered ready for discharge when they were awake and tolerating oral fluids. All children were observed for a minimum of 2 h.

Of the 110 subjects initially randomized, data were incomplete or missing from 4 subjects, and these patients were excluded from analysis. Variability between treatment groups with respect to age, sex, weight, number of muscles repaired, and anesthetic duration was determined using one-way analysis of variance (ANOVA) or chi-squared tests, as appropriate. Comparison of intergroup differences in the incidence of emesis was performed using chi-squared analysis with Yates's continuity correction. A one-way ANOVA was used to compare the duration of postoperative stays between groups, with Scheffé's procedure for multiple comparisons used where the null hypothesis was rejected. Recovery scores were analyzed using a two-way ANOVA for repeated measures, with Fisher's protected least significant difference tests used where the interaction proved significant. A P value of less than 0.05 was considered significant.

Results

There were no statistically significant differences in patient characteristics or operative procedure between groups (table 2). The incidence of postoperative emesis in the control group was 88%, whereas that of the high-dose metoclopramide group (0.25 mg/kg) was 29% and that of the droperidol group was 33% (fig. 1). These differences were significant at the $P < 0.01$ level. Similarly, the mean number of emesis episodes experienced prior to discharge was higher in the control group than in the study groups (fig. 2). Patients receiving the lower dose of metoclopramide (0.15 mg/kg) had a 68% incidence of vomiting (P not significant), although their average of 1.7 vomiting episodes was significantly less than the 2.9 episodes for controls ($P < 0.05$).

Patients receiving droperidol tended to have lower recovery scores when compared to other treatment groups. These differences were significant at 5, 15, and 30 min ($P < 0.05$) but resolved by time of discharge from the PACU (fig. 3). No patient required overnight admission for excessive sedation.

Overall hospital stays were shorter in those patients receiving metoclopramide 0.25 mg/kg and droperidol 0.075 mg/kg (mean postoperative stay 201 and 213 min, respectively) when compared to controls (258 min, $P < 0.05$). There was no significant difference in hospital stay between the high-dose metoclopramide and the droperidol groups (fig. 4).

There was no statistical association between age, sex, or number of muscles repaired and the incidence of emesis (data not shown). Extrapyramidal symptoms such as torticollis, dystonia, or oculogyric crisis were not observed in any patient. Restlessness was likewise not noted.

Discussion

The incidence of postoperative emesis after strabismus surgery in pediatric patients who have not received prophylactic antiemetic therapy has been reported to range from 41 to 85%.[2,3,8,12–14] Our observed incidence of 88% in the control group is generally consistent with previous studies. Several investigators administered atropine, either prophylactically or in conjunction with neuromuscular reversal agents, which may have contributed to the lower incidence of emesis cited in some earlier studies; atropine,

TABLE 2. Patient Demographic Characteristics

	Saline (n = 26)	Metoclopramide 0.150 mg/kg (n = 25)	Metoclopramide 0.250 mg/kg (n = 28)	Droperidol 0.075 mg/kg (n = 27)
Age (months)	54 ± 32	62 ± 40	43 ± 30	57 ± 29
Sex (M/F)	16/10	8/17	14/14	11/16
Weight (kg)	18 ± 7	20 ± 10	16 ± 6	19 ± 8
Number of muscles repaired	2.4 ± 0.8	2.2 ± 0.7	2.3 ± 0.8	2.4 ± .8
Anesthetic duration (min)	62 ± 17	58 ± 14	55 ± 16	62 ± 18

Values are mean ± SD.

No statistically significant differences observed between groups ($P < 0.05$).

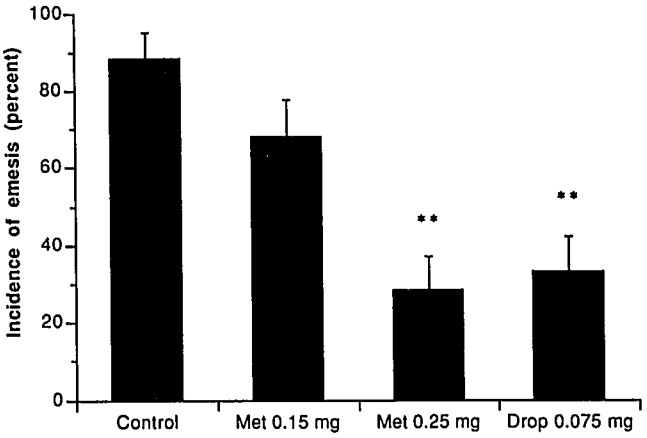

FIG. 1. Incidence of postoperative emesis (mean ± SEM) following strabismus repair, displayed by treatment group. Metoclopramide 0.25 mg/kg and droperidol 0.075 mg/kg administered at the outset of anesthesia significantly reduced the incidence of emesis. **Significant difference from control ($P < 0.01$).

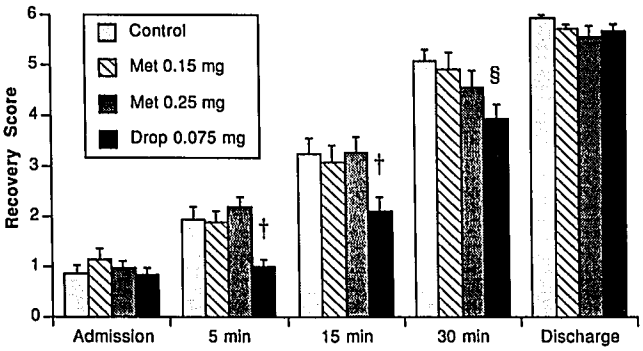

FIG. 3. Recovery scores (mean ± SEM) in the postanesthesia care unit by treatment group. Patients receiving droperidol 0.075 mg/kg were significantly more sedated than patients in other treatment groups. This difference was resolved by time of discharge. †Significant difference from all other groups ($P < 0.05$). §Significant difference from control and metoclopramide 0.15 mg/kg ($P < 0.05$).

like scopolamine, possesses antiemetic properties.[15,16] Our use of meperidine postoperatively may have contributed to an increased incidence of emesis, since opioids themselves can cause nausea and vomiting.[16–18] Based on our clinical experience, however, we believed it inappropriate not to provide opioid analgesia to these patients. The confounding effect of the opioid was minimized by administering the same dose, on a per-kilogram basis, to all patients across study groups.

The etiology of the unusually high incidence of postoperative emesis after strabismus surgery remains uncertain. It is hypothesized to result either from altered visual perception after muscle resection or from a central response arising from manipulation of the eye muscles (the so-called oculoemetic reflex),[19] similar to the oculocardiac reflex. The chemoreceptor trigger zone, located in the area postrema of the medulla, is believed to be the final common pathway and the site of action of most antiemetic agents.[20] Various neurotransmitters are believed to play a role in the mechanism of vomiting. Dopamine antagonists, acting at the D_2 receptor, are known to possess strong antiemetic properties. Other neurotransmitter sites of clinical significance include histamine (H_1 receptors), 5-hydroxytryptamine (5-HT_3 receptors), and acetylcholine (central muscarinic receptors). Both droperidol and metoclopramide are believed to act *via* antagonism at dopaminergic sites; at higher doses, such as those used for prevention of emesis after chemotherapy (1.5–3.0 mg/kg), metoclopramide also appears to antagonize 5-HT_3

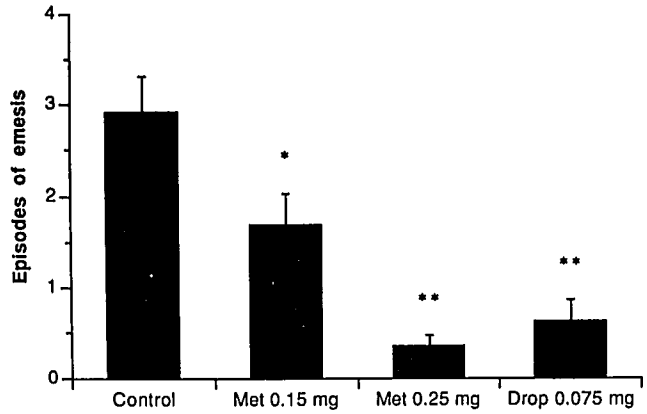

FIG. 2. Episodes of emesis per patient (mean ± SEM) by treatment group. Metoclopramide reduced the frequency of vomiting in a dose-dependent fashion. Droperidol similarly reduced the frequency of emesis. *Significant difference from control ($P < 0.05$). **Significant difference from control ($P < 0.01$).

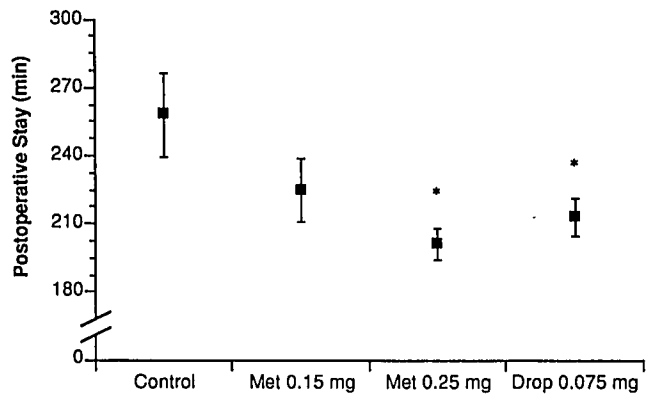

FIG. 4. Postoperative recovery time (mean ± SEM) by treatment group. Metoclopramide 0.25 mg/kg and droperidol 0.075 mg/kg both significantly reduced the time from admission to the postanesthesia care unit to hospital discharge. *Significant difference from control ($P < 0.05$).

receptors,[21,22] which may contribute to its antiemetic activity.

The timing of the administration of antiemetic treatment has been postulated to affect the incidence of postoperative emesis.[4] The presumption is that early blockade of receptors in the chemoreceptor trigger zone prevents their activation during surgery and thus reduces vomiting postoperatively. This suggests that antiemetic agents that work by this mechanism should be administered prior to manipulation of the globe. However, several studies have also shown these drugs to be effective when given immediately after completion of surgery.[2,8,13]

Postoperative vomiting can also continue to be a significant problem for the first 24 h after surgery.[3,4,23] Previous investigators have reported that as many as 14% of patients not receiving prophylactic antiemetics will vomit only after discharge from the hospital.[3] Although we attempted to follow up all study patients after 24 h, the response rate was not sufficient to achieve clinical significance.

In this study, treatment with metoclopramide reduced the incidence of postoperative vomiting when compared with control. Although the benefit observed was not statistically significant at the lower dose studied (0.15 mg/kg), it became so at the higher dose (0.25 mg/kg), suggesting a dose–response relationship. Whether higher doses will prove more efficacious remains to be determined; we were reluctant to increase the dose because of the potential for extrapyramidal side effects. Dystonic reactions from metoclopramide, caused by excessive dopamine antagonism, are rare but do occur.[6]

Previous reports on the ability of antiemetics to reduce recovery room stays have been mixed. Several earlier studies suggested droperidol 0.075 mg/kg does not decrease and may actually prolong time to discharge.[2,4,24] Recently, Broadman and associates showed a reduction in discharge times in children treated with metoclopramide in the recovery room when compared to controls.[8] In our study, patients receiving droperidol or metoclopramide 0.25 mg/kg were discharged significantly earlier than patients in the control group. There was no significant reduction in recovery times in patients given the lower dose of metoclopramide (0.15 mg/kg).

Patients receiving droperidol were significantly less responsive than those treated with metoclopramide or saline in the early recovery period. However, these differences had resolved by the time patients were discharged. Because patients receiving droperidol were actually discharged earlier than controls, it appears that although droperidol may be sedating, the degree of sedation is not sufficient to interfere with discharge. While comparisons between studies are difficult because of varying institutional discharge criteria, clearly agents that shorten hospital stay are of interest in today's economic climate.

To our knowledge this is the first study to demonstrate that metoclopramide, given prior to surgical stimulus, is effective at reducing postoperative emesis after pediatric strabismus surgery. Metoclopramide is at least as effective as droperidol for this indication and appears to be less sedating postoperatively. Like droperidol, metoclopramide shortens recovery room time and overall hospital stay when compared to controls, presumably by reducing the frequency of emesis and decreasing the time to oral intake of fluids. We conclude that metoclopramide 0.25 mg/kg, administered intravenously prior to manipulation of the eye, reduces postoperative emesis and recovery time without significant side effects.

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