

# Dimenhydrinate Decreases Vomiting After Strabismus Surgery in Children

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Dimenhydrinate, a H<sub>1</sub>-receptor antagonist, has been used to both prevent and treat postoperative vomiting (POV) in children for several decades. However, its effectiveness for POV after strabismus surgery remains anecdotal. This study was designed to determine the effectiveness and side effects of dimenhydrinate for the prevention of POV in children after strabismus surgery. Eighty ASA physical status I or II children, ages 1–12 yr inclusive, who were undergoing strabismus surgery, were prospectively and randomly allocated to receive either dimenhydrinate 0.5 mg/kg intravenously (*n* = 40) or placebo (*n* = 40) at induction of anesthesia. The incidence of POV and the times to arousal and discharge from the recovery room and hospital were recorded postoperatively in a double-blinded manner.

For 24 h after discharge from the hospital, all emetic episodes and medications given were recorded by the parents. Demographic data did not differ between the groups. Children who received dimenhydrinate had significantly less POV both in-hospital (10%) and overall (30%) than those who received placebo (in-hospital 38%, *P* < 0.008; overall 65%, *P* < 0.003). The times to arousal and discharge from the hospital did not differ between the two groups. Dimenhydrinate (0.5 mg/kg) is an effective, safe, and inexpensive antiemetic in children undergoing strabismus surgery. It significantly reduces the incidence of vomiting for 24 h postoperatively and is not associated with prolonged sedation or other adverse effects.

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**P**ostoperative vomiting (POV) is common after strabismus surgery in children, with a frequency that ranges from 34% to 88%, depending on the anesthetic technique and other less well-defined factors (1–8).

Dimenhydrinate is a H<sub>1</sub>-receptor antagonist that is the theoclate salt of diphenhydramine (9). It is available over the counter in oral preparation in the United States as Dramamine. In Canada, dimenhydrinate is sold as Gravol in adult and pediatric formulations and as a rectal suppository. Dimenhydrinate is available as a parenteral formulation (50 mg/mL, Schein Pharmaceuticals, Phoenix, AZ) for intravenous and intramuscular injections.

Dimenhydrinate has been used to treat motion sickness, labyrinthine dysfunction, and vestibular diseases, as well as postoperative nausea and POV.

Dimenhydrinate was first used to treat POV in the 1950s after its effectiveness for control of motion sickness was recognized by the military during World War II (10–12). Since then, dimenhydrinate has been used for POV, although few studies have documented its effectiveness in this regard (13). In 1989, Bidwai et al.\* reported that intravenous dimenhydrinate, 20 mg, in adults undergoing outpatient surgery significantly decreased nausea from 34% to 8%.

Pykko (14) speculated that the efficacy of dimenhydrinate in motion sickness and inner ear diseases may be caused by inhibition of the integrative functioning of the vestibular nuclei by reducing the vestibular and visual input. Manipulation of the extraocular muscles in strabismus surgery may trigger an "oculo-emetic" reflex similar to the well-described oculo-cardiac reflex (15). If the afferent arc of this reflex is also dependent on the integrity of the vestibular nuclei apparatus, then dimenhydrinate may attenuate or block this reflex and decrease the incidence of POV.

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\* Bidwai AW, Meuleman T, Thatte WP. Prevention of postoperative nausea with dimenhydrinate (dramamine) and droperidol (inapsine) [abstract]. *Anesth Analg* 1989;68(Suppl):S25.

One objective of this study was to determine the antiemetic efficacy of dimenhydrinate 0.5 mg/kg intravenously given at induction of anesthesia, compared with the placebo in children undergoing outpatient strabismus surgery. Another objective was to document any side effects using this dosage and route in children, including prolongation of time spent in the postanesthesia care unit or a delay in discharge to home.

## Methods

With approval from the Research Ethics Board, informed, written consent was obtained from the parents of 80 children undergoing strabismus surgery. Verbal assent was also obtained from study patients 8 yr of age or older. All children were ASA physical status I or II, between the ages of 1 and 12 yr, and without a history of emesis or antiemetic usage in the 24 h prior to surgery. This study was conducted in a prospective, randomized, double-blind, placebo-controlled manner.

All children were fasted at least 3 h and were not premedicated. Each child was randomly assigned to either dimenhydrinate (0.5 mg/kg up to a maximum of 25 mg) or placebo (normal saline), using random number tables to yield a block design. Dimenhydrinate (50 mg/mL) was diluted with normal saline to a total volume of 10 mL. The volume of diluted dimenhydrinate administered to each child was 0.1 mL/kg. In the placebo arm, 0.1 mL/kg normal saline was infused. Dimenhydrinate or placebo was administered intravenously immediately after induction of anesthesia, but before the start of surgery.

After standard monitors (electrocardiogram, noninvasive blood pressure cuff, and a pulse oximeter probe) were applied in the operating room, 70% N<sub>2</sub>O in O<sub>2</sub> was administered by face mask to facilitate intravenous catheter placement. Anesthesia was induced with intravenous sodium thiopental (5 mg/kg) premixed with atropine (15 μg/kg). This was followed immediately by succinylcholine (2 mg/kg) intravenously to facilitate tracheal intubation, after which ventilation was manually assisted until spontaneous ventilation resumed. Anesthesia was maintained with halothane (1%–2% inspired) and 70% N<sub>2</sub>O in O<sub>2</sub>. End-tidal CO<sub>2</sub> and inhalational drug concentrations were monitored continuously using a Datex monitor (Datex Division of Instrumentarium Corp., Helsinki, Finland). At the completion of surgery, the pharynx was suctioned, and the trachea was extubated under deep anesthesia with halothane in 100% O<sub>2</sub> with spontaneous respiration. Evacuation of gastric contents was not performed routinely. A minimum of 20 mL/kg of lactated Ringer's solution was administered intravenously to each patient in the perioperative period.

Acetaminophen (10–20 mg/kg) was administered per rectum to all children on arrival in the recovery room. Intravenous morphine sulfate (0.1 mg/kg) was administered to treat postoperative pain at the discretion of the recovery room nursing staff, in consultation with the attending anesthesiologist. Rescue dimenhydrinate 0.5 mg/kg was administered intravenously to all children who experienced two or more episodes of POV in the recovery period while still in the hospital. The children were discharged from the recovery room to a step-down unit when they were awake and pain free.

During emergence from anesthesia, the time intervals between discontinuation of anesthesia and arousal (spontaneous eye opening or purposeful movement) and discharge from the postanesthetic recovery unit were recorded. The incidences of POV and the sites where it occurred were recorded. Emetic episodes were recorded as distinct incidents when they were separated by periods of at least several minutes without retching or emesis. All medications administered were recorded by the nursing staff, who were unaware of the treatment assignment.

Criteria for discharge from the step-down unit included stable vital signs and an awake or easily rousable patient. Oral fluid intake was voluntary and was not required for discharge home.

The frequency and time of all emetic episodes and medications given during the first 24 postoperative hours were recorded in a diary by the parents. On the day after discharge from the unit, each parent was telephoned by one of the investigators. Diaries were returned either by mail or during their first postoperative visit.

Before commencing the study, sample size was determined using power analysis. The sample size calculation was based on four assumptions: 1) an incidence of vomiting of 60% in the placebo group; 2) an incidence of 25% in the dimenhydrinate group; 3)  $\alpha_2 = 0.05$ ; and 4)  $\beta = 0.2$ . The required sample size was 36 children/group. The control incidence of 60% was based on previous investigations at our institution. A goal of at least a 50% reduction in emetic episodes was considered by the investigators to be reasonable evidence of a clinically significant decrease in vomiting.

*Post-hoc* statistical analysis of the data was performed using Student's *t*-test, Fisher's exact test, and linear regression where appropriate.  $P < 0.05$  was accepted as statistically significant.

## Results

Demographic data for the two groups were similar for age (66 ± 36 mo in the dimenhydrinate group vs 68 ± 28 mo in the control [mean ± SD]), weight (21 ± 11 kg vs 22 ± 9 kg), and gender (18 males and 22 females in the dimenhydrinate group and the same in the control

**Table 1.** Arousal and Discharge Times and Medication Use

	Dimenhydrinate	Placebo
End-tidal halothane at extubation (%)	1.6 ± 0.7	1.5 ± 0.7
Morphine administration in recovery room	11/40	18/40
Time to arousal	33 ± 17	30 ± 16
Time to PAR discharge	68 ± 20	67 ± 20
Time to discharge home (overall)	178 ± 49	178 ± 69
Patients with no emesis in hospital (n)	172 ± 3 (36)	151 ± 45 (25)
Patients with emesis in hospital (n)	234 ± 7* (4)	223 ± 80† (15)
Rescue dimenhydrinate (Y/N)	3/40	9/40

All times are in minutes. Data are means ± SD, except where indicated. PAR = postanesthetic recovery; Y = yes; N = no.

\*  $P < 0.013$ , compared with dimenhydrinate patients without emesis. No intergroup comparisons were significant.

†  $P < 0.001$ , compared with placebo patients without emesis. No intergroup comparisons were significant.

group). The median number of muscle repairs in both groups was two, with a range of 1–4. The specific extraocular muscles repaired in both groups were similar in number (i.e., inferior oblique, medial rectus, etc.), as was the duration of anesthesia.

The time intervals to arousal and discharge from the recovery room and step-down unit did not differ between the two groups (Table 1). The time spent in recovery prior to discharge home for children who vomited in both groups was significantly greater than the recovery time for children in the same group who did not vomit (Table 1).

The overall incidence of POV in the dimenhydrinate group was significantly less than that in the placebo group ( $P < 0.003$ ) (Table 2). This difference was significant both in-hospital (10% with dimenhydrinate vs 38% in the placebo group,  $P < 0.008$ ) and postdischarge (23% vs 58%, respectively,  $P < 0.002$ ) (Table 2). Four children in the placebo group were lost to follow-up despite repeated telephone calls. In-hospital data for these children were included in the analysis. To be conservative, we assumed that none of these children vomited after discharge from the hospital.

Rescue dimenhydrinate in the dimenhydrinate group (3 of 40) was administered three times less frequently than it was to the placebo group (9 of 40) postoperatively, but this difference was not significant. Morphine administration in the two groups was statistically similar between groups, and there was no

**Table 2.** Incidence of Emesis

	Dimenhydrinate	Placebo	P value
In hospital	4/40 (10%)	15/40 (38%)	0.008
After discharge (to 24 h)	9/40 (23%)	21/36 <sup>a</sup> (58%)	0.002
Overall emesis	12/40 (30%)	26/40 <sup>a</sup> (65%)	0.003

<sup>a</sup> Four patients in the placebo group were unavailable for follow-up. Data are number of patients with emesis/total number of patients.

correlation by regression analysis with emesis in either group separately or as pooled data. There were no problems noted with airway obstruction in the recovery room after deep extubation in this study.

## Discussion

This study demonstrates that intravenous dimenhydrinate (0.50 mg/kg) given at induction of anesthesia significantly decreases the incidence of POV for up to 24 hours after surgery, compared with placebo. Furthermore, dimenhydrinate does not appear to delay discharge from the recovery room or hospital, and there were no adverse side effects observed with this dose of dimenhydrinate.

Although sedation is a common effect reported with dimenhydrinate, there was no evidence of it found in this study. The time to discharge from the hospital for patients who received dimenhydrinate was similar to that for those who received the placebo.

Perioperative control of nausea and vomiting after strabismus surgery in children has been the subject of numerous studies; droperidol, lidocaine, lorazepam, promethazine, metoclopramide, propofol, ondansetron, and even acupuncture have all been investigated (2–4,16,17). The continuing search for the optimal antiemetic may reflect the inadequacy of vomiting control with any one therapy, a high incidence of side effects at effective doses, or medication costs.

Several factors have been found to contribute to the incidence of perioperative nausea and vomiting after strabismus surgery. Some of these include the patient's age and gender, premedication, anesthetic technique, gastric suctioning, early oral intake, and timing of ambulation (3). Consequently, an incidence of emesis between 34% and 88% in the placebo arms of the various investigations is not surprising. It is not possible to control all of these factors during surgery for strabismus repair. One can, however, lessen nausea and vomiting by the use of an antiemetic and consequently also lessen the in-hospital recovery time.

When considering antiemetic prophylaxis, the cost of the antiemetic must be addressed. On the basis of

body weight, dimenhydrinate is one of the least expensive, but effective, antiemetics with a cost of \$0.02/kg. This amount is based on the average wholesale price of the drug (\$2.22/50-mg vial).† The cost per kilogram assumes that the drug is diluted as described herein according to the manufacturer's recommendation and then dispensed to multiple patients as needed. The average wholesale price of a drug usually reflects what the hospital charge to the patient is and not the cost to the pharmacy. In addition, a dispensing fee is generally charged to the patient as well. In the hypothetical situation that the child is charged for the entire vial and the unused portion is discarded, dimenhydrinate remains very inexpensive.

The costs associated with postoperative emesis may be substantial. These include a prolonged recovery room stay, pharmacy charges, equipment and laundry expenses, and more intensive nursing acuity. Rarely, postoperative emesis may lead to an unexpected hospital admission for intravenous hydration. Our data demonstrated that children who vomit may remain in the recovery room and hospital longer than those without any emesis.

With all of the drugs studied for prevention of POV, there is a finite percentage of children who are resistant to prophylactic antiemetic therapy. Dimenhydrinate significantly reduced POV at a rate comparable with other antiemetics that have been studied at a cost that is significantly less than many other antiemetics and without serious side effects noted at the dosage we used. In summary, the results of this study demonstrate that, when dimenhydrinate 0.5 mg/kg intravenously is given at induction of anesthesia, it is an effective antiemetic for children undergoing outpatient strabismus surgery for up to 24 hours postoperatively.

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† Drug prices are courtesy of the Pharmacy Department, All Children's Hospital, St. Petersburg, FL, as of October 1995.

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