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The Antiemetic Effect of Lorazepam after Outpatient Strabismus Surgery in Children

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The high incidence of postoperative emesis after strabismus surgery in pediatric outpatients can be reduced by the prophylactic administration of droperidol 75 μg/kg intravenously. However, this may be associated with profound sedation, delayed discharge, dysphoria, agitation, and extrapyramidal symptoms in this population. Because lorazepam used as an antiemetic in children during chemotherapy decreased the incidence of nausea and vomiting, we compared the antiemetic effects of lorazepam and droperidol in a randomized, double-blind, placebo-controlled study of 129 healthy children undergoing surgical correction of strabismus. The children, aged 1–13 yr, were randomly allocated into three groups. The children in group 1 received droperidol 75 μg/kg intravenously; those in group 2 received lorazepam 10 μg/kg intravenously; and those in group 3 received placebo. Anesthesia consisted of halothane, nitrous oxide in oxygen, and atracurium. Study drugs were administered intravenously after induction of anesthesia but before surgery. In children 3–13 yr old, administration of either lorazepam or droperidol was associated with a lower ($P < 0.024$) incidence of postoperative vomiting. There was no difference between the antiemetic effect of lorazepam and that of droperidol. The incidence of postoperative agitation was greater in the droperidol group ($P < 0.001$) than in the lorazepam and placebo groups. Postdischarge vomiting was less ($P < 0.009$) in children younger than 3 yr of age. Lorazepam, similar to droperidol, has an antiemetic effect in outpatient children 3–13 yr old undergoing strabismus correction, but it is associated with less postoperative agitation than is droperidol. (Key words: Anesthesia: pediatrics. Anesthetics, gases: nitrous oxide. Anesthetics, volatile: halothane. Antiemetics: droperidol; lorazepam. Complications, postoperative: agitation; vomiting. Surgery: strabismus.)

THE INCIDENCE OF VOMITING after strabismus surgery in pediatric outpatients can be as great as 85%.[1] Several medications and techniques including droperidol,[1–6] lidocaine,[7,8] metoclopramide,[9,10] P6 acupressure,[11] propofol,[12] and dixyrazine[13] have been tried as antiemetics with variable results and success. Intravenous (iv) droperidol 75 μg/kg administered prophylactically (about 10 min before the surgical stimulus) reduces the incidence of vomiting[2] but also may lead to dysphoria, agitation, extrapyramidal symptoms, and delayed discharge from the hospital. Small doses of droperidol are ineffective as antiemetics and may also be associated with delayed discharge.[3–6]

Lorazepam, when used alone or in conjunction with other antiemetics, has reduced the incidence of nausea and vomiting associated with chemotherapy.[14–20]

The purpose of this study was to evaluate lorazepam as an antiemetic and to compare it to droperidol in outpatient children undergoing strabismus surgery.

Materials and Methods

We studied 129 children, ASA physical status 1 or 2 and ages 1–13 yr, scheduled for elective strabismus correction as outpatients. The study was approved by the Committee for the Protection of Human Subjects of the University of Texas Medical School at Houston. Written, informed consent was obtained from the parents of the children. The study was double-blind, and the children were allocated randomly to one of three groups. The patients in group 1 received droperidol 75 μg/kg iv; group 2 received lorazepam 10 μg/kg iv; and group 3 received placebo. The patients received neither food nor clear liquids after midnight the evening before surgery and were not premedicated.

Anesthesia was induced with nitrous oxide (60%) in oxygen and halothane 0.5–4% *via* a face mask. Monitoring included precordial stethoscope, automated blood pressure, ECG, pulse oximetry, esophageal temperature probe, and mass spectrometry. After induction of anesthesia, an iv cannula was placed in an arm vein, and atropine sulfate 20 μg/kg iv was administered to prevent an oculocardiac reflex. Atracurium 0.5 mg/kg iv was administered to facilitate orotracheal intubation, followed by the iv administration of 2 ml of the study solution, which was prepared by the pharmacist. An iv bolus of lactated Ringer's solution equal to half the calculated maintenance fluid deficit was infused during the 1st h of surgery. No sedatives, opioids, or other antiemetics were administered intraoperatively.

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At the end of surgery, gastric contents were suctioned. Atropine sulfate 20 μg/kg iv and neostigmine 70 μg/kg iv were administered to counteract any residual muscle paresis. The children were allowed to breathe spontaneously, and when their breathing became regular and they regained their upper airway protective reflexes, the endotracheal tube was removed. An acetaminophen suppository (15 mg/kg) was placed for postoperative pain relief. The patients then were transferred to the recovery room while in the lateral position.

An independent observer evaluated the incidence of vomiting in the operating room, the recovery room, and the day-surgery unit after the patients' discharge from the recovery room. Vomiting was defined as the forceful expulsion of gastric contents. Nausea and retching without expulsion of gastric contents were not considered vomiting. The number of episodes of vomiting was not evaluated. If a patient vomited more than once, droperidol 10 μg/kg iv was administered. In the recovery room, if patients were agitated, either an opioid or physostigmine was administered. Generally, patients in pain received an opioid, and patients who were more disoriented received physostigmine. The patients were discharged when they were able to drink, retain fluids, and ambulate. Telephone contact was made with the patients' parents to determine the incidence of postdischarge vomiting in the first 24 h after surgery.

The primary variables of interest were postoperative vomiting (in the hospital, after discharge, or either) and postoperative agitation (irrational, uncontrollable excitement and movement) evaluated in the recovery room. Possible confounding variables included age; weight; gender; ASA physical status; anesthesia duration (the time from the start of induction until the termination of the inhalation anesthetic—"anesthesia end"); surgery duration (the time from incision until the last surgical stitch); extubation time (the time from anesthesia end until extubation); awakening time (anesthesia end until the child responds to verbal commands); and duration of recovery room stay, duration of day-surgery unit stay, and combined recovery room and day-surgery unit stay. Confounding variables were tested for differences between treatment groups using analysis of variance techniques. Because of some concern that children less than 3 yr of age are less prone to vomit postoperatively,[21] data were stratified by age group (age 3 yr and older *vs.* younger than 3 yr).

Significance of effects of drug treatment on vomiting and agitation and the effect of age group on the incidence of vomiting was determined using standard contingency chi-square tables. A P value of less than 0.05 was taken to be significant. After testing the primary hypothesis of interest regarding the effect of treatment *versus* placebo, we then examined three pairwise comparisons (droperidol *vs.* placebo, lorazepam *vs.* placebo, and droperidol *vs.* placebo). To correct for the multiple comparisons, a more conservative P value of 0.017 is appropriate to judge simultaneous significance.[22]

Results

There was no difference among the groups with respect to age, gender, ASA physical status, weight, height, duration of anesthesia, and duration of surgery (table 1). In addition, the extubation time (8 ± 4 min, range 1–24 min), awakening time (49 ± 21 min, range 8–125 min), recovery room time (61 ± 24 min, range 30–150 min), day-surgery unit time (104 ± 58 min, range 15–360 min) and combined recovery room and day-surgery unit time (174 ± 66 min, range 60–410 min) were not different among the groups.

When all patients were included in the analysis of postoperative vomiting, whether the patients received placebo or drug, the incidence of vomiting at the hospital, after discharge, or either was not different among the groups (fig. 1). However, when postoperative vomiting was compared between subjects 3 yr of age and older and those less than 3 yr of age, the incidence of postdischarge vomiting was less (10% *vs.* 32%) ($P < 0.013$, Fisher's exact test) in the younger group (fig. 2).

In the 3–13-yr-old group, the administration of either lorazepam or droperidol was associated with a lower ($P < 0.024$) incidence of postoperative vomiting compared to the placebo group. This same effect was also observed for in-hospital vomiting ($P < 0.043$) and postdischarge vomiting ($P < 0.008$) for either treatment *versus* placebo. Pairwise contrast probabilities (presented in fig. 3) are consistent with these findings. There was no difference between the antiemetic effect of lorazepam and droperidol in these groups (fig. 3).

The incidence of postoperative agitation was greater ($P < 0.001$) in the droperidol group, compared to the lorazepam and placebo groups (fig. 4).

TABLE 1. Demographic Data

	Group		
	Droperidol 75 μg/kg	Lorazepam 10 μg/kg	Placebo
Number	43	41	43
Age (yr)	5 ± 3	5 ± 4	5 ± 3
Age (<3 yr)	15	12	12
Sex (F/M)	22/21	21/20	20/23
Weight (kg)	20 ± 9	21 ± 11	20 ± 11
Height (cm)	112 ± 19	109 ± 24	106 ± 22
ASA physical status 1/2	38/5	39/4	32/11
Anesthesia duration (min)	61 ± 18	66 ± 17	60 ± 14
Surgery duration (min)	42 ± 16	45 ± 19	42 ± 14

Values are mean ± SD or number.

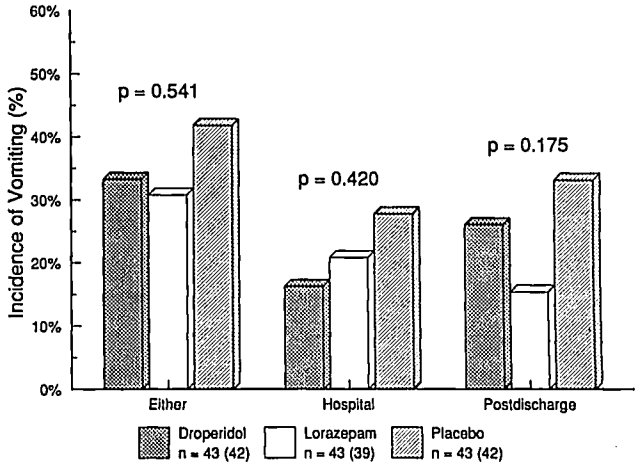

FIG. 1. Postoperative vomiting (age 1–13 yr). There was no difference in the incidence of postoperative vomiting among the groups, whether it occurred at the hospital or postdischarge. (Numbers in parentheses indicate number for whom postdischarge vomiting was assessed.)

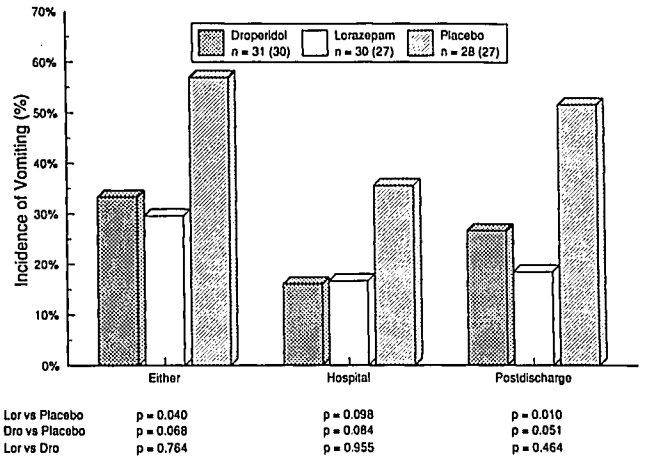

FIG. 3. Postoperative vomiting (age 3–13 yr). Both lorazepam and droperidol decreased postoperative vomiting, whether it occurred in the hospital or postdischarge, and there was no difference between the antiemetic effect of both drugs. Numbers in parentheses indicate number for whom postdischarge vomiting was assessed.

In the recovery room, 14 children were extremely agitated: these included 9 in droperidol group, 4 in the saline group, and 1 in the lorazepam group. To control the agitation, opioids were administered to 11 of these children—6 in the droperidol group, 4 in the saline group, and 1 in the lorazepam group. Six of these children vomited either in the hospital or after discharge. Because of the known emetic effect of opioids, all analyses were repeated with exclusion of those who vomited after opioid administration. There were no differences in results based on this analysis. The three other agitated children in the droperidol group were more disoriented and received physostigmine. They were not excluded from the analysis.

In the recovery room, 10 children vomited more than once and received droperidol 10 μg/kg iv, which did not affect the incidence of postdischarge vomiting.

We were unable to contact the parents of six children, one in the younger age group, to inquire about postdischarge vomiting.

In the droperidol group, two children, 4 and 6 yr old, developed extrapyramidal symptoms on emergence from anesthesia; these resolved spontaneously.

None of the children developed an oculocardiac reflex or required additional atropine sulfate.

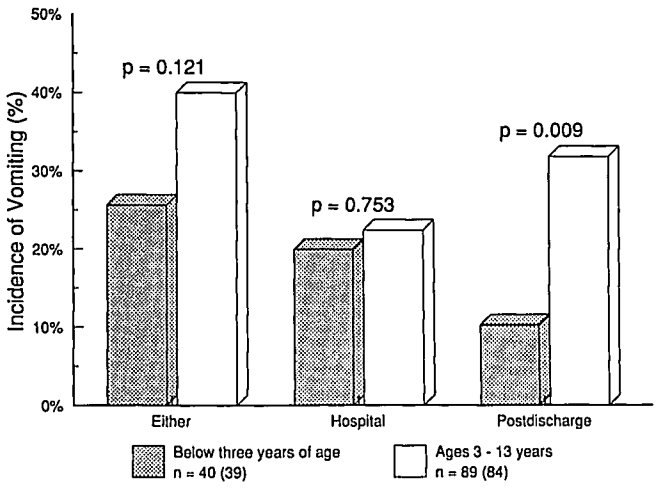

FIG. 2. Postoperative vomiting: effect of age. The incidence of postdischarge vomiting was less ($P < 0.009$) in children 2 yr old and younger, compared to children 3–13 yr old. Numbers in parentheses indicate number for whom postdischarge vomiting was assessed.

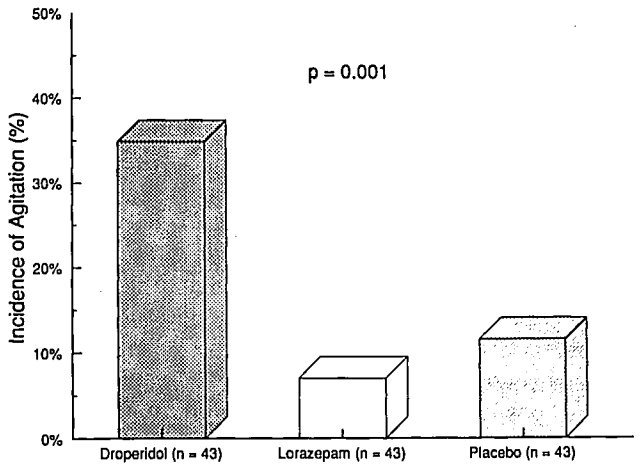

FIG. 4. Postoperative agitation. The postoperative agitation was higher ($P < 0.001$) in the droperidol group compared to the lorazepam and placebo groups.

Discussion

This study demonstrates that lorazepam 10 μg/kg iv decreased the incidence of postoperative vomiting when prophylactically administered to outpatient children 3–13 yr old undergoing strabismus correction during general anesthesia. The antiemetic effect of lorazepam was similar to that of droperidol.

Lorazepam is used by itself and combined with other agents as an antiemetic in patients having chemotherapy.[14–20] The antiemetic effect of lorazepam may be secondary to its ability to decrease anxiety, induce hypnosis, provide retrograde amnesia, and/or simply provide a specific antiemetic effect. In this study, because lorazepam was given to the children after they were asleep, its antiemetic effect may not have been related to decreasing anxiety or induction of hypnosis. A previous study demonstrated that there was no correlation between the degree of lorazepam sedation and antiemetic effect.[16] Because lorazepam is a central nervous system depressant, it could be expected to influence the chemoreceptor trigger zone and/or the emetic center.[18]

Lorazepam 50 μg/kg orally proved to be a safe and effective sedative in children.[23] In a prestudy trial we compared the effect of lorazepam 20 μg/kg iv *versus* 10 μg/kg iv on the incidence of postoperative vomiting and recovery time in outpatient children undergoing strabismus correction. Lorazepam 20 μg/kg iv was associated with prolonged recovery time and was not associated with a lower incidence of postoperative vomiting; therefore, in this study we evaluated the antiemetic effect of lorazepam 10 μg/kg iv.

In this study, the incidence of postoperative agitation in the droperidol group was significantly higher than in the lorazepam and placebo groups ($P < 0.001$). Because perioperative opioids were not administered routinely, this could have contributed to a high incidence of agitation in the droperidol group. However, 11 of the children were extremely agitated, and opioids were required for adequate control. Three other agitated and disoriented children responded favorably to the iv administration of 0.5 mg physostigmine.

In children less than 3 yr of age, the incidence of postdischarge vomiting was (10%), significantly less compared to children 3–13 yr old (32%). Our findings are consistent with a previous study demonstrating that children less than 3 yr of age are less prone to vomit postoperatively.[21] In several previous antiemetic studies using droperidol,[1,2,5,6] children 2 yr of age and younger were excluded, to avoid possible side effects of droperidol. In the current study, children 1 and 2 yr old were included, and they did not react differently to droperidol than did children 3–13 yr old.

Although in previous studies, the administration of 25, 50, or 75 μg/kg droperidol iv was associated in some children with somnolence and delayed discharge,[1,5,6] in our study there was no difference among the groups regarding recovery room stay, day-surgery unit stay, or combined recovery room and day-surgery unit stay. No patient required hospital admission for excessive somnolence or severe vomiting.

In conclusion, we recommend the prophylactic administration of lorazepam 10 μg/kg iv as an antiemetic to outpatient children 3–13 yr old undergoing strabismus correction, because it decreases postoperative vomiting. Similarly, the prophylactic administration of droperidol 75 μg/kg is effective in decreasing the postoperative vomiting, but, unlike lorazepam, it is associated with a higher incidence of postoperative agitation.

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