calcemia and hyperphosphatemia. Persistent elevations of creatine phosphokinase indicate that he may have some form of muscular dystrophy. The fact that he sustained cardiac arrest on induction of anesthesia could be related to either of these two states as well as the use of succinylcholine, which has been documented to produce sinus arrest after repeat administration in children and adults.

Whatever the cause or causes of cardiac arrest in this patient, it is of concern that he was being brought to surgery as an outpatient, a category reserved for patients only in the best of health. His electrolyte imbalance was unsuspected, as was his possible muscular dystrophy. In retrospect, this patient does not fit the ASA Class I patient group. The chronic use of any medication, even enemas, should have made this patient ineligible for outpatient surgery. If admitted the night before surgery, he would not necessarily have had the benefit of electrolyte screening. It should stand as encouragement to anesthesiologists to have a high index of suspicion regarding the chronic use of any drug or substance, even enemas, and to check for abnormalities accordingly.

REFERENCES


The Antiemetic Effect of Droperidol Following Outpatient Strabismus Surgery in Children

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Although strabismus surgery is performed readily in an ambulatory setting, persistent vomiting following anesthesia may delay the patient’s discharge from the hospital or may even lead to hospitalization. In our institution, as well as others, patients undergoing general anesthesia for strabismus surgery have a higher incidence of postoperative vomiting than those receiving the same anesthesia for other types of ambulatory surgical procedures. In addition to discomfort to patients, vomiting often presents many risks, such as dehydration, electrolyte imbalance, tracheal aspiration, and wound contamination particularly for those with no eye dressing placed after surgery.

In a preliminary investigation we studied the antiemetic effects of droperidol in children undergoing strabismus surgery. We found that approximately 80% of the children not receiving any antiemetic vomited after strabismus surgery and that droperidol 50 mcg/kg iv administered during the surgery was not totally satisfactory in reducing the frequency and severity of vomiting. We speculated that better results might have been produced if a higher dose had been used. In this study, we, therefore, extended our clinical experiments to investigate the effect of higher doses of droperidol.

METHODS

Fifty-two ASA physical status I patients (ranging from 2 to 13 yr of age) scheduled for correction of strabismus were studied. On admission to our ambulatory surgical center, parents were questioned for a history of motion sickness and vomiting after previous ophthalmic surgery in their children. Patients who had received any drug or who had viral or bacterial infections within the 2 weeks
before the study were excluded. Informed consent was obtained from the parent. This study was approved by our Institutional Review Board.

Anesthesia was induced by inhalation of nitrous oxide and halothane via a face mask and Jackson–Rees system. No premedication was given. Ventilation was assisted while asleep. Tracheal intubation was performed under deep anesthesia without the use of muscle relaxants. Gastric contents were aspirated after tracheal intubation. Blood pressure, temperature, and heart rate were monitored. Dextrose 5% with 0.3% saline was infused iv until patients could retain oral fluid in the postoperative period. Each patient received either droperidol or saline iv approximately 30 min before the end of surgery in a double-blind, randomized sequence. The endotracheal tube was removed under deep anesthesia. Gastric contents were aspirated again before extubation of the trachea.

In order to evaluate the severity and frequency of vomiting, a scoring system was devised; score 0: no vomiting; score 1: mild vomiting, once per observation period; score 2: moderate vomiting, two or three times per observation period; score 3: severe vomiting, four or more per observation period; and score 4: persistent vomiting regardless of treatment. Retching was considered as vomiting. Nausea was not evaluated. Using this system, an observer collected data at 15-min intervals (one observation period) for a maximum of 8 h postoperatively. The same observer made all these evaluations.

Recovery from anesthesia was assessed by an Aldrete recovery score, which was based on adequacy of airway, blood pressure, heart rate, consciousness, and movement (scale 0–10; the higher, the more stable) while patients stayed in the recovery room. When an Aldrete score of 10 was obtained, the patient was transferred to a hospital room, where observation of possible vomiting and its severity was continued.

If vomiting became severe and protracted, a decision to break the study code was made on two preestablished criteria: 1) score of 2 or 3 for three consecutive 15-min observation periods in the recovery room; and 2) a cumulative score of 6 or more during the observation in the hospital room. Thus, two subgroups of patients who received droperidol were identified at the conclusion of the trial: a prophylactic group, which received droperidol approximately 30 min before the end of surgery; and a therapeutic group, which was given droperidol for excessive postoperative vomiting either in the recovery or hospital room. Any patient who could not meet all discharge criteria in a maximum of an 8-h observation period was admitted to the hospital overnight. Patient discharge criteria included 1) stable vital signs; 2) all reflexes (swallow, gag, cough) present; 3) ability to walk alone; 4) clear state of consciousness; 5) no respiratory distress; 6) minimal nausea, vomiting, or dizziness; and 7) ability to tolerate oral fluids.

Initially we designed the study such that 80% of the patients receiving droperidol would be given 75 mcg/kg iv, and the rest, 100 mcg/kg. The reasons for the administration of the latter dose were twofold. First, it provided the opportunity for assessing any possible side effects of a relatively high dose of droperidol for an outpatient, and, secondly, it furnished a pilot sample to be used for the design of a further study in case the dose of 75 mcg/kg should not prove to be efficacious.

Using the dose of 75 mcg/kg only, a restricted sequential decision plan was designed with a two-sided overall significance level of 2α = 0.05. Our preliminary data indicated that approximately 80% of the children not receiving the drug vomited. A decrease of this incidence rate to 50% after droperidol administration was considered clinically relevant, and desired to be detected, if present, with a power of 1-β = 0.95. This design requires a maximum of 40 untied patient pairs. One patient of each pair received droperidol (75 mcg/kg), and the other, placebo in a double-blind randomized pattern. The response criterion for the decision to stop the trial was the number of observed preferences in the formed pairs, either toward droperidol or placebo. The patients who received droperidol 100 mcg/kg iv and their corresponding control were interspersed randomly in this design, but not included in the decision plan.

Results

After 11 untied treatment pairs, the trial using 75 mcg/kg iv was stopped with 10 preferences in favor of droperidol and one in favor of the placebo (fig. 1). Ten pairs were tied. There were no significant differences between the droperidol and placebo groups for age, sex, previous history of ophthalmic surgery and motion sickness, total surgery time, and duration of recovery room stay.

The number of patients with and without vomiting and their respective recovery times are compared in table 1. Vomiting occurred only in nine patients (45%) in the group that received droperidol, 75 mcg/kg, prophylactically compared with 22 in the placebo group (85%). The mean difference of the proportion between the two groups was 42% with a 95% confidence interval of this difference ranging from 17 to 67%. In addition, none of the nine patients in the prophylactic group vomited severely enough to require breaking the study code; however, in the placebo group, 10 out of 22 vomited so excessively that the study code was broken and droperidol (75 mcg/kg iv) given therapeutically (table 2). This difference in severity of vomiting is statistically significant (P = 0.002, Fisher’s exact test).

The ancillary study of children receiving droperidol at a dose of 100 mcg/kg yielded a sample of five patients. Three out of these five patients vomited but required no
further medication. While this sample is too small to provide conclusive data, it is very unlikely that the higher dose would lead to a substantial reduction of the vomiting incidence rate as compared with the lower dose. Computations showed that if the true vomiting incidence for the 100 mcg/kg dose were 20%, the observed result with three out of five patients vomiting could have occurred with a chance of only $P = 0.05$. Further study of the use of a higher dose was terminated with the conclusion of this study.

For comparison of the discharge time, the patients were subdivided further according to whether or not they vomited. For the patients who vomited, there was no statistically significant difference ($P > 0.6$) in the recovery time between the prophylactic droperidol group and the placebo group (348 min vs. 361 min). One patient in the droperidol group was admitted to the hospital overnight and therefore was not used in the computation of the recovery time. In the placebo group the patients who did not vomit were discharged earlier than those in the droperidol group (211 min vs. 284 min); however, this difference was not statistically significant (Student's $t$ test, $t_{14} = 1.79, P > 0.09$). The patients whose vomiting was severe enough to receive droperidol therapeutically required the longest recovery time (369 min, table 2). The overall recovery time of the placebo group tended to be longer than that of the droperidol group (338 min vs. 309 min); however this was not statistically significant ($P > 0.1$). For comparison, the discharge time $\pm$ SEM in those five patients who received 100 mcg/kg droperidol prophylactically was 323 $\pm$ 27.0 min.

Three patients in each group had a history of motion sickness. All three in the placebo group vomited so extensively that they required therapeutic droperidol. Only one in the droperidol group vomited but required no further treatment.

All but one parent was reached for the follow-up telephone interview. There were no major complications in either group other than vomiting following discharge. No vomiting occurred at home in any of 10 children who were treated with droperidol therapeutically after surgery. Neither abnormal behavior nor prolonged somnolence was reported.

**DISCUSSION**

The incidence of vomiting following pediatric strabismus surgery is higher than that following any other "minor" surgical procedure.$^2,3$ Vomiting is not only an unpleasant experience for children but also one of the most

**TABLE 1. The Incidence of Vomiting and Time (Mean $\pm$ SEM) for Recovery in the Droperidol and Placebo Groups**

<table>
<thead>
<tr>
<th></th>
<th>Droperidol Group (n = 21)</th>
<th>Placebo Group (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>8</td>
<td>22</td>
</tr>
<tr>
<td>Time (min)</td>
<td>348 $\pm$ 21.4* (stayed overnight)</td>
<td>361 $\pm$ 13.1</td>
</tr>
<tr>
<td>No vomiting</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>Time (min)</td>
<td>284 $\pm$ 22.6</td>
<td>211 $\pm$ 18.0</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>309 $\pm$ 17.1</td>
<td>338 $\pm$ 15.6</td>
</tr>
</tbody>
</table>

* Stayed overnight.
TABLE 2. The Severity of Vomiting and Time (Mean ± SEM) for Recovery in Both Groups

<table>
<thead>
<tr>
<th></th>
<th>Droperidol Group (n = 21)</th>
<th>Placebo Group (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Time (min)</td>
</tr>
<tr>
<td>Severe vomiting*</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent or mild vomiting</td>
<td>21</td>
<td>309 ± 17.1</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>309 ± 17.1</td>
</tr>
</tbody>
</table>

* Study code broken, droperidol given therapeutically († in recovery room, ‡ in the hospital room).

important factors delaying discharge from the hospital on the day of surgery.

Many antiemetics have been evaluated in the treatment of postoperative nausea and vomiting. Droperidol has been used as a potent antiemetic for many years. Its beneficial effect has been demonstrated in various surgical procedures, however, these study populations usually were limited to adults. Rita et al. reported in a double-blind study that droperidol 0.005 mg/kg was effective in lowering the incidence of postoperative vomiting significantly in children 11–15 years of age hospitalized following orthopedic surgery. These authors were reluctant to advocate or study higher doses because of extrapyramidal symptoms reported in children when droperidol was used in the recommended dose range (100 mcg/kg) for premedication.

In an earlier study of pediatric outpatient strabismus surgery at our institution, droperidol 50 mcg/kg was studied, which was 10 times the dose used by Rita et al. The children in the droperidol group tended to have a lower incidence of vomiting than the placebo group, but the difference between the two groups was not statistically significant. Therefore, in the present study we increased the dose of droperidol to 75 mcg/kg. The results showed that a dose of 75 mcg/kg was effective in decreasing the incidence of vomiting from 85% in the placebo group to 43% in the droperidol group. This decrease was statistically and clinically significant. Furthermore, a reduction in severity of vomiting also was demonstrated, as evidenced by the fact that no patient who received the drug prophylactically required its use therapeutically. We even increased the dose to 100 mcg/kg for a small portion of the study population; however, this dose was considered to be associated with more risk than benefit and was not extended to a larger portion of the study population.

Although the overall recovery time was not delayed significantly, in the five patients who received droperidol, 100 mcg/kg iv, three vomited, and it is unlikely that its antiemetic effect would have been more satisfactory than with the lower doses.

Our experiment was unique for several reasons. It was designed to control some of the variables of other investigations, because it was limited to one surgical procedure and one anesthetic technique. Observation bias was controlled by administering the study drug in a double-blind randomized fashion and by using only one observer who adhered to a strict scoring protocol during the postoperative period. The application of a restricted sequential decision plan permitted us to stop the trial as soon as sufficient statistical evidence had accumulated, requiring fewer patients than a fixed sample size design. The breaking of the blind study code for those patients who vomited severely enough to receive droperidol therapeutically did not interfere with the statistical analysis of the sequential decision plan, yet allowed us to reduce protracted vomiting for those in whom it occurred. Because the outcome of the treatment of each patient is known within a short time, this study design appeared ideal for the investigation of the prevention of vomiting or its treatment.

Some anesthesiologists have been reluctant to use an antiemetic such as droperidol in outpatients because of prolonged drowsiness. In our study, hypotension and extrapyramidal side-effects were not observed, and somnolence was less important in delaying discharge than vomiting. Our strict discharge criteria have been adopted and evaluated in our short-stay recovery unit for 8 yr. Although recovery for discharge of 4–6 h after surgery might be considered prolonged in children following myringotomy or herniotomy, this time is common after surgical procedures such as in patients with orchiopexy and strabismus. Because it is the policy of some insurance carriers to require that the latter procedure be performed in an outpatient setting, reduction in the frequency and severity of vomiting within an acceptable period of time suitable for same-day discharge is highly desirable. One patient from the prophylactic droperidol group was admitted to the hospital after an 8-h observation period. Admission was considered prudent because of inability to tolerate oral fluids rather than a result of sedation or vomiting that was not extensive enough to require further treatment.

Four out of 26 patients did not vomit and never received droperidol prophylactically. They were discharged
from the hospital earlier than any other study group. Some effort should be made to define preoperatively those factors that predict vomiting so that only those who need prophylaxis receive an antiemetic. However, if all patients receive droperidol prophylactically, their average discharge time still may be less than those without prophylaxis (309 min vs. 338 min), because patients who vomit take longer to meet criteria for discharge home.

We conclude that droperidol used prophylactically in a dose of 75 mcg/kg iv is very effective in decreasing the incidence and severity of vomiting in children undergoing outpatient surgery for correction of strabismus without significantly delaying discharge home. Their postoperative course is more comfortable yet not more complicated.

The authors acknowledge the assistance of Deidre Boswell and Martha Wallis.

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Bronchospasm Following Intraocular Injection of Acetylcholine in a Patient Taking Metoprolol

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Systemic effects produced by locally absorbed ophthalmic agents have been observed in patients with both normal and abnormal cardiopulmonary systems. For instance, 10% phenylephrine eye drops, commonly used in the perioperative period for pupillary dilatation and hemostasis, have produced hypertension and coronary artery spasm. Two previous reports of hypertension, one of which occurred in association with bradycardia, were attributed to the instillation of acetylcholine chloride (Miochol® intraocular) into the anterior chamber of the eye during routine cataract surgery. We observed a case of bronchospasm following acetylcholine injection into the anterior chamber of the eye of a patient taking metoprolol for hypertension, suggesting an interaction between acetylcholine and a beta-adrenergic blocking drug.

REPORT OF A CASE

The patient was a 76-year-old woman with a long history of hypertension, obstructive pulmonary disease, and stable angina, who was...