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Effect of Propofol on the Incidence of Postoperative Vomiting after Strabismus Surgery in Pediatric Outpatients

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Vomiting is a common problem after strabismus surgery in pediatric outpatients. We compared the effects of propofol with and without N_2O and droperidol to the effects of a conventional regimen consisting of halothane–N_2O–droperidol on the recovery characteristics and the incidence of postoperative emesis after strabismus surgery in 120 ASA physical status 1 or 2 children. After induction of anesthesia with halothane–N_2O, patients were randomly assigned to one of four groups. Group A (control) received halothane, 66% N_2O, and droperidol 75 $\mu g \cdot kg^{-1}$; group B, propofol 2 $mg \cdot kg^{-1}$ bolus followed by infusion of 160 $\mu g \cdot kg^{-1} \cdot min^{-1}$; group C, propofol (as in group B) and 66% N_2O; and group D, propofol (as in group B), 66% N_2O (as in group C), and droperidol 75 $\mu g \cdot kg^{-1}$. Patients in group B had more episodes of intraoperative oculocardiac reflex responses than patients in group A, but had shorter times to extubation, oral intake, ambulation, and discharge, as well as a lower incidence of postoperative emesis ($P < 0.05$). The addition of N_2O to the propofol anesthetic regimen (group C) was associated with an increased incidence of emesis ($P < 0.05$), whereas the addition of droperidol to the propofol–N_2O regimen (group D) did not affect the incidence of emesis compared to the other three groups. We conclude that maintenance of anesthesia with a total intravenous regimen using propofol results in a more rapid recovery and less postoperative emesis than with a halothane–N_2O–droperidol regimen. (Key words: Anesthesia: pediatrics. Anesthetics, gases: nitrous oxide. Anesthetics, intravenous: propofol. Anesthetics, volatile: halothane. Anesthetic technique: continuous infusion; inhalational. Antiemetics: droperidol. Complications: postoperative vomiting. Surgery: strabismus.)

THE INCIDENCE OF POSTOPERATIVE VOMITING after strabismus surgery in pediatric patients has been reported to be 50–80%.[1–8] Droperidol 75 $\mu g \cdot kg^{-1}$ given intravenously (iv) has been shown to be effective in reducing the incidence of emesis in this patient population. However, it can produce profound sedation and may contribute to a delayed discharge.[4–7] Smaller doses of droperidol, from 25 to 50 $\mu g \cdot kg^{-1}$ iv, produced less sedation but were not as effective in preventing vomiting.[2,5] Propofol is a rapid and short-acting intravenous anesthetic agent used for adult outpatient anesthesia.[9–13] It provides for a rapid recovery and is associated with a low incidence of postoperative vomiting compared to standard anesthetic techniques when intravenous induction is followed by inhalation agents for maintenance of anesthesia.[9–13] However, there are only limited data available on the use of propofol infusions for maintenance of anesthesia in children.[14,15]

The recovery characteristics and the incidence of postoperative vomiting after the use of propofol with and without N_2O and droperidol for the maintenance of anesthesia was compared to a conventional anesthetic regimen with halothane–N_2O–droperidol in children undergoing elective strabismus surgery.

Materials and Methods

We studied 120 ASA physical status 1 or 2 children, ages 6 months to 12 yr, scheduled for elective strabismus surgery. This study was approved by the Human Studies Committee of the Washington University, and written informed consent was obtained from the parents or legal guardians of the subjects. Patients were not excluded if they had a history of previous eye or other surgery, a history of motion sickness, or inner ear disorders or other conditions predisposing to vomiting, or if they had vomited after previous eye or other surgery. No solid foods or milk products were permitted after midnight of the evening prior to surgery. Clear liquids were permitted up to 4 h prior to surgery in infants and up to 6 h prior to surgery in older children.

No child received preanesthetic medication. Anesthesia was induced with N_2O (66%) in oxygen and 1–3% halothane *via* face mask. After loss of consciousness, iv access was obtained, and all patients received atropine 0.01 $mg \cdot kg^{-1}$ iv, morphine 0.1 $mg \cdot kg^{-1}$ iv, and vecuronium 0.1 $mg \cdot kg^{-1}$ iv. When neuromuscular blockade was fully established, the trachea was intubated and end-tidal carbon dioxide tension was maintained between 32 and 45 mmHg using positive-pressure ventilation. The time from the start of induction of anesthesia to tracheal intubation was recorded.

After intubation, patients were randomly assigned to one of four maintenance anesthetic regimens: group A received N_2O 66%, halothane 1–3%, and droperidol 75 $\mu g \cdot kg^{-1}$ iv (to a maximum dose of 2.5 mg); group B received propofol 2 $mg \cdot kg^{-1}$ iv bolus over 30–60 s, followed by a continuous infusion at an initial rate of 160 $\mu g \cdot kg^{-1} \cdot$

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min^{-1}; group C received propofol as in group B plus N_2O 66%; and group D received propofol and N_2O as in group C plus droperidol 75 $\mu g \cdot kg^{-1}$ iv (to a maximum dose of 2.5 mg). The dose of propofol or halothane was adjusted as required to the lowest dose that would prevent signs of inadequate anesthesia (tachycardia or hypertension). Heart rate and blood pressure were maintained within 20% of the preinduction values. Intravenous fluids were administered to replace the preoperative deficits and to provide for maintenance requirements. Neuromuscular blockade was maintained with supplemental doses of vecuronium as required.

A significant episode of the oculocardiac reflex (OCR) was defined as an acute decrease in heart rate of 15% or greater associated with traction on an eye muscle. If the heart rate did not return to baseline after release of the muscle traction or if the OCR reflex recurred, additional atropine, 0.01 $mg \cdot kg^{-1}$ iv, was administered.

After the surgical procedure was completed, neuromuscular block was reversed with edrophonium 1 $mg \cdot kg^{-1}$ iv and atropine 0.01 $mg \cdot kg^{-1}$ iv; the stomach was aspirated; and the anesthetic drugs were discontinued. Adequate reversal of neuromuscular blockade was evaluated by the tactile and visual demonstration of a 5-s sustained tetanic contraction after a 50-Hz stimulus. The trachea was extubated when protective airway reflexes had returned, and the patient was breathing spontaneously and making purposeful movements. Because of the milky-white appearance of propofol and the method of administration (iv), it was not possible to blind the anesthesiologist as to the group to which a specific patient was assigned. However, the personnel gathering data in the postoperative period were not aware of the intraoperative therapeutic group assignments.

In the postoperative period, children were permitted access to oral fluids upon request. Pain and discomfort usually was treated with acetaminophen 10 $mg \cdot kg^{-1}$ orally or rectally. If postoperative pain persisted or became more severe, additional morphine, 0.05 $mg \cdot kg^{-1}$ iv, was administered. The time from the end of surgery until extubation of the trachea, eye opening, response to verbal commands, ambulation, and first oral intake, as well as the timing of each vomiting episode, were recorded by a blinded nurse observer. Vomiting or emesis was defined as the forceful expulsion of stomach contents. Nausea, coughing, and retching without expulsion of gastric contents were not considered to be vomiting. If the patient vomited twice in 1 h or three or more times while in the recovery room, the vomiting was classified as severe, and the patient received metoclopramide 0.15 $mg \cdot kg^{-1}$ iv. If vomiting persisted, the patient was administered rectal trimethobenzamide (100 mg for children between 4–15 kg and 200 mg for children between 15–45 kg).

Patients were discharged when they satisfied the following discharge criteria: stable vital signs, responsiveness to parents, administration of last medication at least 1 h prior to discharge, minimal vomiting (no or only one episode of vomiting in the 90 min prior to discharge), and ability to tolerate clear fluids. Telephone contact was made with the parent the following day to determine the incidence of vomiting during the first 24 h after surgery. Patients who vomited more than once in the 24-h postoperative period were considered to have recurrent emesis.

Age, weight, sex, duration of surgery (time from incision to placement of dressing), induction time (time from start of induction to tracheal intubation), duration of administration of maintenance anesthetic medications (time from tracheal intubation to the discontinuation of maintenance anesthetic drugs), and the total duration of anesthesia (time from start of induction to arrival in the postanesthetic care unit) were compared among the four groups by a one-way analysis of variance and by a Student's *t* test with a Bonferroni correction for multiple comparisons. The time from the end of surgery to tracheal extubation, eye-opening, the first response to commands, the first oral intake, ambulation, and discharge also were compared by a one-way analysis of variance and by a Student's *t* test with a Bonferroni correction. If the null hypothesis was rejected, a Fisher's least-protected-difference test was performed to compare group means. Chi-squared analyses with a Yates's correction and a Fisher's exact test were used to compare, between the control group and the three other groups, the incidence of OCR, the number of patients requiring atropine therapy of OCR, the need for supplemental morphine and antiemetic therapy in the postoperative period, and the incidence of vomiting during the first 24 h after the operation. A P value of < 0.05 was considered significant. Data are presented as means ± standard deviations.

Results

There were no significant differences among the four groups with respect to age, gender, weight, history of previous eye muscle or other surgery, history of emesis after previous surgery, or the number of eye muscles operated on during the study. Patients in group A (control) had a significantly shorter mean duration of surgery compared to the other groups but did not differ significantly in the induction time, duration of administration of maintenance anesthetic drugs, or total duration of anesthesia (table 1). The incidence of OCR and the requirements of additional atropine therapy were greater in the group receiving only intravenous drugs for maintenance of anesthesia (group B) compared to the control group. There were no significant differences in the incidence of OCR between the control group and the groups receiving

TABLE 1. Demographic Characteristics of the Four Study Groups

	Group and Anesthetic Agents Used for Maintenance of Anesthesia			
	A Halothane + N_2O + Droperidol	B Propofol	C Propofol + N_2O	D Propofol + N_2O + Droperidol
Number	30	30	30	30
Age (yr)	4.7 ± 3.7	4.9 ± 4.3	4.3 ± 2.5	4.8 ± 3.1
Sex (M/F)	16/14	17/14	17/13	15/15
Weight (kg)	22.1 ± 18.8	21.8 ± 17.7	18.1 ± 8.8	22.6 ± 14.8
Number of operated muscles: median (range)	2 (1–4)	2 (1–4)	2 (1–4)	2 (1–4)
Surgical time (min)	42.7 ± 14.9	54.3 ± 20.2*	52.9 ± 16.2*	54.2 ± 20.2*
Induction time (min)	8.8 ± 3.6	7.8 ± 3.5	8.7 ± 3.5	8.9 ± 4.0
Maintenance anesthesia time (min)	62.0 ± 15.7	70.2 ± 18.3	69.3 ± 17.1	69.6 ± 19.2

All values are mean ± SD. See text for definition of surgical, induction, and maintenance anesthesia times.

* $P < 0.05$ compared to group A.

N_2O–propofol with or without droperidol (groups C and D, respectively). As expected, patients receiving N_2O with propofol required a lower average infusion rate of propofol compared to those receiving propofol alone (table 2).

Emergence from anesthesia was more rapid in patients receiving propofol alone as an alternative to halothane–N_2O–droperidol. The times from the end of surgery to tracheal extubation, acceptance of oral intake, ambulation, and fitness for discharge were shorter in patients receiving total intravenous maintenance anesthesia compared to times in the control group (table 3). The incidence of postoperative pain and discomfort treated with acetaminophen or with morphine was not significantly different among the four groups (table 4).

There was a statistically significant decrease in the incidence of vomiting in the 24-h postoperative period in children who received propofol alone (group B) compared to the incidence in those treated with halothane (table 4). Supplementing the iv propofol regimen with N_2O (group C) significantly increased the incidence of emesis. However, patients receiving droperidol in addition to the propofol–N_2O regimen (group D) did not have a significantly different incidence of emesis compared to any of the other groups (table 4). There were no statistically significant differences among the four groups in the incidence of severe vomiting, recurrent vomiting, or vomiting in hospital or after discharge (table 4). There was an inverse relationship between early oral intake and emesis ($r^2 = 0.037$; $P = 0.035$).

Discharge from the hospital occurred earlier in patients receiving propofol alone compared to those receiving halothane–N_2O–droperidol for the maintenance of anesthesia. In addition, the tracheas of patients receiving propofol–N_2O (group C) were extubated earlier, and these patients followed commands and accepted oral intake earlier than did those in the control group (table 3). However, the discharge times in groups A and C were similar because our discharge criteria included the ability to accept oral intake with minimal vomiting, and the incidence of emesis was not different between the two groups (tables 3 and 4). All patients receiving droperidol (groups A and D) had delayed times to oral intake and discharge compared to those times in group B (table 3).

TABLE 2. Intraoperative Events

	Group and Anesthetic Agents Used for Maintenance of Anesthesia			
	A Halothane + N_2O + Droperidol	B Propofol	C Propofol + N_2O	D Propofol + N_2O + Droperidol
Incidence of oculocardiac reflex: n (%)	10 (30%)	17 (54.8%)*	11 (33%)	13 (43.3%)
Required atropine treatment: n (%)	3 (10%)	11 (35.5%)*	5 (16.7%)	7 (23.3%)
Average propofol infusion rate ($\mu g \cdot kg^{-1} \cdot min^{-1}$)	0	175 ± 43	149 ± 36.7†	150 ± 37.6†

Shown are comparison of the incidence of oculocardiac reflex (number and percentage of patients), and number and percentage of patients requiring atropine therapy of the oculocardiac reflex (OCR), and the average propofol infusion rates during surgery in the four treatment groups.

* $P < 0.05$ compared to group A.

† $P < 0.05$ compared to group B.

TABLE 3. Comparison of the Recovery Characteristics from Anesthesia in the Four Groups

	Group and Anesthetic Agents Used for Maintenance of Anesthesia			
	A Halothane + N_2O + Droperidol	B Propofol	C Propofol + N:i2O	D Propofol + N_2O + Droperidol
Extubation time (min)	14.7 ± 7.3	9.4 ± 7.6*	9.5 ± 4.4*	9.6 ± 5.6*
Time to eye-opening (min)	38.4 ± 22.3	25.7 ± 25	33.4 ± 38	25.9 ± 16.5
Time to following commands (min)	84 ± 67.3	54 ± 52	48 ± 35*	57 ± 55
Time to oral intake (min)	220 ± 94.5	135 ± 77.3*	131 ± 53*	199 ± 111†
Time to ambulation (min)	247 ± 90.2	175 ± 72*	190 ± 109	218 ± 138
Time to discharge (min)	357 ± 86.5	279 ± 117*	313 ± 113	342 ± 110†

All values are mean ± SD.
* $P < 0.05$ compared to group A.
† $P < 0.05$ compared to group B.

Discussion

In children, propofol has been used both for induction and for maintenance of anesthesia.[14–18] Even though it does not cause venous irritation, its use is associated with pain or movement or both on injection.[14–16] Since children do not tolerate painful injections, we induced anesthesia with halothane and N_2O in all four groups and then evaluated four different maintenance anesthetic regimens. Recovery from anesthesia was more rapid with a total intravenous anesthetic technique and was associated with a decreased incidence of vomiting, even though patients receiving the standard anesthetic technique (halothane–N_2O–droperidol) had shorter surgical procedures.

Patients undergoing strabismus surgery have a high incidence of postoperative vomiting, which probably is multifactorial in origin.[3–8,19] Our control group had a higher incidence of emesis than did a previously reported group that also received halothane–N_2O–droperidol.[5] However, in that study, anesthesia was induced with thiopental, and perioperative opioids were avoided. The incidence of emesis in our control group was similar to that in other studies in which anesthesia was induced and maintained by halothane–N_2O and in which droperidol was administered prior to surgical manipulation of the eye.[3,4,6,7] Differences in the incidence of emesis between our control group (group A) and a similar group in a study by Eustis *et al.* may be attributed also to our use of morphine.[5]

In the current study, the incidence of emesis was significantly less when a propofol infusion was the only anesthetic agent used for maintenance of anesthesia. Although data from this and other studies indicate that propofol is associated with a lower incidence of postoperative vomiting than are other anesthetic techniques, this does not prove that propofol has a specific antiemetic action.[11,12,18] Such claims for an antiemetic action initially were made for halothane when the incidence of postoperative emesis after its use was demonstrated to be less than that with trichloroethylene, ether, and other older inhalation agents.[20] There are no data available on the effects of propofol on the chemoreceptor trigger zone or on central dopaminergic receptors.

A prominent feature of recovery from propofol anesthesia is the absence in the early recovery period of a residual "hang-over" effect, which often is seen with the use of halogenated inhalation agents.[9,13,20] Patients who have received propofol appear to be more clear-headed and occasionally euphoric in the early recovery period, and this may explain the earlier oral intake and ambulation in patients in this group compared to those receiving the standard inhalational anesthetic technique.[12,13] Although it has been suggested that withholding fluids and delaying ambulation reduce the incidence of postoperative

TABLE 4. Comparison of the Incidence of Postoperative Pain, Discomfort, and Emesis Between the Four Anesthetic Groups

Group	A	B	C	D
Postoperative emesis during first 24 h	15 (50%)	7 (23%)*	18 (60%)†	13 (43%)
Severe postoperative emesis	4 (13%)	4 (13%)	5 (17%)	2 (7%)
Emesis in hospital	7 (23%)	5 (16%)	14 (47%)†	10 (33%)
Emesis after discharge	8 (27%)	5 (16%)	10 (33%)	9 (30%)
Recurrent emesis (> 1 episode in 24 h)	6 (20%)	3 (10%)	11 (37%)	6 (20%)
Acetaminophen given	10 (33%)	6 (20%)	14 (47%)	13 (43%)
Postoperative pain treated with morphine	1 (3%)	3 (9%)	2 (7%)	0 (0%)

Values shown are number of patients; percentages are in parentheses.
See text for definitions of anesthetic groups.
* $P < 0.05$ compared to group A.
† $P < 0.05$ compared to group B.

emesis,[19,21,22] we noted an inverse relationship between the time of the first oral intake and the incidence of emesis after strabismus surgery. In a previous study, postoperative oral fluid restriction did not alter the incidence of vomiting after ophthalmic surgery.

In the current study, the addition of N_2O decreased the average propofol infusion rate required to maintain satisfactory anesthesia by only 15% but significantly increased the incidence of vomiting (tables 2 and 3). This may explain why other investigators were unable to find a significant difference in the incidence of vomiting in children undergoing strabismus correction surgery with either propofol–N_2O or enflurane–N_2O anesthesia.[17] It is unclear if the increased emesis with propofol–N_2O compared to propofol alone is a reflection of the effects of N_2O or of the reduced dose of propofol. There are few data comparing total intravenous anesthesia with propofol to a propofol–N_2O combination. In a study involving young women undergoing gynecologic surgery, the incidence of nausea during propofol, propofol–N_2O, and enflurane–N_2O anesthesia were 0, 3.4, and 9.4%, respectively.[10]

In contrast to our findings with propofol, the addition or elimination of N_2O from a halothane-based anesthetic does not appear to alter the incidence or severity of emesis after pediatric strabismus surgery or tonsillectomy–adenoidectomy procedures.[23,¶] The induction time was not different among groups B, C, or D, indicating that the period of exposure to halothane was similar for groups receiving propofol with or without N_2O. Therefore, differences in the recovery characteristics among these groups cannot be attributed to the brief exposure to halothane during induction. Additional studies are necessary to determine if the induction technique (inhalational or intravenous propofol) alters the recovery characteristics and the incidence of postoperative emesis after strabismus surgery. Confirming a previous report,[17] our study found that intravenous infusions of propofol were associated with a higher incidence of OCR. Cross *et al.* have demonstrated that the chronotropic effect of submaximal doses of atropine were significantly decreased during propofol–N_2O anesthesia compared to enflurane–N_2O anesthesia, suggesting that the former is associated with a predominance of vagal influences.[24] Although the incidence of reflex-induced bradycardia after eye manipulation (OCR) was greater in patients receiving propofol, no patient in our study had additional episodes of OCR after a second dose of atropine, 0.01 $mg \cdot kg^{-1}$ (total dose 0.02 $mg \cdot kg^{-1}$), was administered. Therefore, we speculate that an atropine dose of 0.02 $mg \cdot kg^{-1}$ might prevent the occurrence of OCR during ophthalmic surgery under propofol anesthesia.

In conclusion, maintenance of anesthesia with an intravenous infusion of propofol after a conventional halothane–N_2O induction is associated with earlier recovery from anesthesia and a lower overall incidence of postoperative emesis than maintenance with a standard halothane–N_2O–droperidol regimen in children undergoing strabismus correction surgery. The incidence of emesis in the first 24 h after surgery was less in a group receiving propofol alone compared to that in a group receiving propofol with N_2O but was not different from a similar group of children receiving droperidol with propofol and N_2O. However, patients in the group receiving propofol alone recovered and were discharged earlier than were those receiving propofol–N_2O–droperidol. The use of propofol alone may be associated with less postoperative emesis, but decreases in heart rate after traction on an eye muscle occurred more commonly with propofol than with a standard halothane–N_2O anesthetic technique. Additional studies are required to determine if the incidence of emesis after maintenance of anesthesia by a total intravenous technique with propofol is decreased further by the addition of other antiemetic drugs, by the avoidance of opioids, or by induction with intravenous propofol.[3,5–18]

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