Propofol anaesthesia reduces early post-operative emesis after paediatric strabismus surgery

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Propofol anaesthesia may reduce postoperative emesis. The purpose of this study was to compare the incidence of emesis after propofol anaesthesia with and without nitrous oxide, compared with thiopentone and halothane anaesthesia, in hospital and up to 24 hr postoperatively, in outpatient paediatric patients after strabismus surgery. Seventy-five ASA class I or II, unpremedicated patients, aged 2–12 yr were randomly assigned to one of three groups: Thiopentone, 6.0 mg · kg^{-1} iv induction followed by halothane and N_2O/O_2 for maintenance (T/H); propofol for induction, followed by propofol and oxygen for maintenance (P/O_2); and propofol for iv induction, followed by propofol infusion and N_2O/O_2 for maintenance (P/N_2O). All received vecuronium, controlled ventilation, and acetaminophen pr. Morphine was given as needed for postoperative analgesia. There were no differences in age, weight, number of eye muscles operated upon, duration of anaesthesia or surgery. The P/N_2O group (255 ± 80 μg · kg^{-1} · min^{-1}) received less propofol than the P/O_2 group (344 ± 60 μg · kg^{-1} · min^{-1}) ($P \leq 0.0001$) and had shorter extubation ($P < 0.001$) and recovery ($P < 0.01$) times. Emesis in the hospital, in both the P/N_2O (4.0%) and P/O_2 group (4.0%) was less than in the T/H group (32%) ($P < 0.01$). Antiemetics were required in four patients in the T/H group (16.0%). Overall emesis after surgery was not different among the groups: T/H (48%), P/O_2 (28%) and P/N_2O (42%). The use of propofol anaesthesia with and without N_2O decreased only early emesis. This supports the concept of a short-acting, specific antiemetic effect of propofol.

On attribue au propofol des propriété anti-émétiques postopératoires. Cette étude a pour objectif de comparer l'incidence des vomissements après l'anesthésie au propofol avec ou sans protoxyde d'azote, comparativement à l'anesthésie au thiopentone-halothane. Cette étude est réalisée à l'hôpital et jusqu'à 24 heures après l'opération chez des patients ambulatoires après chirurgie pour strabisme. Soixante-quinze patients ASA I et II, non prémédiqués, âgés de 2 à 12 ans sont assignés au hasard à un de trois groupes: induction au thiopentone, 6,0 mg · kg^{-1} avec maintien à l'halothane-N_2O, (T/H); induction avec maintien au propofol-oxygène (P/O_2) et induction au propofol avec maintien au protoxyde-oxygène (P/N_2O). Tous reçoivent du vécuronium, une ventilation contrôlée et de l'acétaminophène rectal. De la morphine est administrée au besoin pour contrôler la douleur postopératoire. Il n'y a pas de différence d'âge, du poids, du nombre de muscles opérés et de durée anesthésique et chirurgicale. Les patients du groupe P/N_2O (255 ± 80 μg · kg^{-1} · min^{-1}) reçoivent moins de propofol que le groupe P/O_2 (344 ± 60 μg · kg^{-1} · min^{-1}, $P < 0,001$), sont intubés moins longtemps ($P < 0,0001$) et s'éveillent plus rapidement ($P < 0,01$). A l'hôpital, les vomissements dans les deux groupes P/N_2O (4,0%) et P/O_2 (4,0%) sont moins fréquents que dans le groupe T/H (32%). Des antiémétiques sont requis chez quatre patients du groupe T/H (16%). L'incidence générale des vomissements après la chirurgie est la même pour tous les groupes: T/H (48%), P/O_2 (28%) et P/N_2O (42%). L'utilisation du propofol en anesthésic avec ou sans N_2O ne diminue que l'incidence des vomissements précoces, ce qui supporte le concept d'une activité anti-émétique brève et spécifique.

Key words
ANAESTHESIA: outpatient, paediatric, ophthalmologic;
ANAESTHETICS, GASES: nitrous oxide;
ANAESTHETICS, INTRAVENOUS: propofol, thiopentone;
ANAESTHETICS, VOLATILE: halothane;
VOMITING: incidence.

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Postoperative emesis accounts for one third of the post-anaesthetic morbidity in paediatric patients,[1] and vomiting is the most common reason for unanticipated admission to hospital in paediatric ambulatory surgical patients.[2] In children undergoing strabismus surgery,

propofol anaesthesia has been reported to reduce the incidence of postoperative vomiting from 30–50% to 4–23%.[3,4] Despite the multifactorial origins of emesis,[5] the wide variation in the frequency of reported vomiting in these studies may have resulted from the use of premedication, narcotics, nitrous oxide (N_2O) and antiemetics.

This study examined the incidence of emesis after propofol anaesthesia with and without nitrous oxide, compared with thiopentone and halothane anaesthesia, in hospital and up to 24 hr after surgery, in outpatient paediatric patients after strabismus surgery.

Methods

Following institutional approval and informed written, parental consent, 75 healthy children, ASA physical status I or II, aged 2–12 yr, scheduled for elective outpatient, strabismus surgery were studied. Patients were assigned to receive one of three anaesthetic regimens: thiopentone, 6.0 mg · kg^{-1} *iv* induction followed by halothane 0.5–1.5% and nitrous oxide 70%/oxygen for maintenance (T/H); propofol, 5.0 mg · kg^{-1} *iv* followed by propofol and oxygen (P/O_2); and propofol, 5.0 mg · kg^{-1} *iv* followed by propofol and nitrous oxide 70%/oxygen maintenance (P/N_2O).

Routine fasting instructions were followed, with solid foods allowed up to six hours and clear fluids allowed up to four hours preoperatively. Patients were unpremedicated. A local anaesthetic cream, EMLA®, was applied to the dorsum of the hands one to two hours before surgery. Retrograde amnesia was tested in children greater than four years by showing a picture of an animal to the child 30–60 min before induction and testing for recall one to two hours after discontinuation of the anaesthetic.

At induction of anaesthesia, an intravenous infusion of Ringer's Lactate solution was commenced through a 22° or 24° cannula inserted on the dorsum of the hand. All patients received atropine, 0.02 mg · kg^{-1} *iv* and lidocaine 0.3 mg · kg^{-1} *iv* prior to the assigned induction agent. The induction was observed for the presence of largyngospasm, bradycardia, hypotension (BP $<$ 20% of baseline), and pain on injection. Tracheal intubation was facilitated by muscle relaxation with vecuronium, 0.1 mg · kg^{-1} *iv*.

Routine monitoring was established with a precordial stethoscope, ECG, oxygen saturation monitor, end-tidal carbon dioxide monitor, automated oscillometric blood pressure recorder, temperature probe and peripheral nerve stimulation. Rectal acetaminophen 15 mg · kg^{-1} was given after induction. All patients received Ringer's Lactate, 10 ml · kg^{-1} over one hour followed by maintenance fluid at a rate of 4.0 ml · kg^{-1} · hr^{-1} for the first 10 kg, an additional 2.0 ml · kg^{-1} · hr^{-1} for body weight between 10 and 20 kg and an additional 1.0 ml · kg^{-1} · hr^{-1} for above 20 kg.

Anaesthesia was maintained according to group randomization with controlled ventilation to maintain normocapnia ($P_{ET}CO_2$ 35–40 mmHg). Incremental doses of vecuronium (0.025–0.05 mg · kg^{-1} *iv*) were given to maintain surgical relaxation. In the propofol groups, an intravenous infusion of propofol was commenced at 300 μg · kg^{-1} · min^{-1} and then titrated (150–400 μg · kg^{-1} · min^{-1}) as needed to maintain clinically satisfactory anaesthesia. Halothane or propofol were discontinued at the time of the last conjunctival manipulation. Nitrous oxide was continued in the T/H and P/N_2O groups until residual neuromuscular blockade was reversed with edrophonium 0.5 mg · kg^{-1} and atropine 0.01 mg · kg^{-1}. The trachea was extubated when the patient was swallowing and making purposeful movements such as reaching up for the endotracheal tube.

All patients were observed for two hours after discontinuation of the anaesthetic by recovery room nursing staff who followed the usual protocols including offering clear fluids or frozen fluids (Popsicles®) to the patients. Morphine 50 μg · kg^{-1} *iv* up to three doses, was given as needed at the nurse's discretion.

Postoperative antiemetic therapy was given after the second emesis with metoclopramide 0.15 mg · kg^{-1} *iv*. After a third episode of emesis and at least 15 min after the first antiemetic, dimenhydrinate 0.5 mg · kg^{-1} *iv* was given.

At discharge, patients over four years were asked if they could recall the picture shown preoperatively. Parents were instructed to give their children oral acetaminophen 10 mg · kg^{-1} and codeine 1.0 mg · kg^{-1} for analgesia if necessary and also to give dimenhydrinate 1.0 mg · kg^{-1} orally or rectally if necessary for excessive emesis after discharge from hospital. The parents were telephoned the day after surgery to ascertain if their child had vomited. Parents and the patient were not informed of the anaesthetic technique until the conclusion of the telephone interview.

Data collected

The age, weight and sex of the patients were recorded. The type of surgery, (i.e., recession, resection myectomy), number of eye muscles operated upon, and whether the surgery was unilateral or bilateral was recorded. The anaesthetic time was calculated from the time of intravenous induction to discontinuation of the nitrous oxide (T/H and P/N_2O) or propofol infusion (P/O_2). The surgical time was measured from the time of the first conjunctival incision until the last conjunctival manipulation. The time to extubation was measured from the time of discontin-

TABLE I Demographic data

Parameter	*Thio/Hal*	*Propofol/O_2*	*Propofol/N_2O*	*P value*
Number of patients*	25	25	25	
Age (yr)†	6.2 ± 2.2	6.3 ± 1.9	5.1 ± 2.5	0.11
Weight (kg)‡	21.1 (11–42)	20 (14–50)	18 (10–47)	0.18
Sex (M/F)*	7/18	11/14	9/16	0. 5
Eyes (1/2)*	4/21	8/17	8/17	0.34

Thio = thiopentone Hal = halothane.
*Count.
†Mean ± SD.
‡Median (range).

uation of anaesthetic agents (end anaesthesia) to the time of tracheal extubation.

In the recovery room, recovery and emesis were observed by trained, recovery room nursing staff who were blinded to the group assignment. Recovery time was measured using the Steward[6] recovery score at five-minute intervals until the maximum score of six was obtained. The time from arrival in the post-anaesthetic recovery room (PACU) until a score of six was achieved was recorded as the recovery time. The eye opening time was measured as the time from extubation to the time of first eye opening in response to voice command.

A modified Abramowitz[7] emesis score was performed at 15 min intervals (0 = none, 1 = mild, once in a 15 min period; 2 = moderate, two or three times in a 15 min period; 3 = severe, four or more times in a 15 min period; 4 = persistent and severe emesis despite treatment with metoclopramide or dimenhydrinate). Involuntary retching was scored as emesis but nausea was not evaluated.

The length of stay in the PACU and the day care unit (DCU) were recorded. These times were added to give a duration of hospital stay. The time to oral intake was measured from the time of discontinuation of the anaesthetic to the time of first oral intake. Morphine utilization was measured by recording the number and the time of administration. The time to first morphine administration was measured from the time of discontinuation of the anaesthetic. Any antiemetic administration was also recorded.

Emesis after discharge from hospital was recorded by telephone interview for the following intervals; during transport home, during the first 12 hr after discharge, and during the second 12 hr after discharge. Overall emesis was defined as the total incidence of emesis at any of the study intervals.

Data analyses

Sample size calculation was based on a power analysis, using values of $\alpha = 0.05$ and $\beta = 0.2$. An 80% incidence of emesis was predicted in the T/H group and a 50% reduction in the incidence of emesis expected in the propofol groups. The sample size required was 23 subjects per treatment. Normally distributed data were summarized using means and standard deviations. Skewed data were expressed as medians and ranges. Categorical data were expressed as counts. Continuous variables that were normally distributed were analyzed by one-way analysis of variance with Newman-Keuls test for multiple comparisons and skewed continuous data were analyzed with the Kruskal-Wallis test using Dunn's test for multiple comparisons.

Categorical data were analyzed with Chi-square test or Fisher's exact test when expected frequencies were <5. Bonferroni's correction was used for multiple intergroup comparisons in contingency tables. The mean doses of propofol in the propofol groups were compared using an unpaired t test. A P value of <0.05 was considered significant.

Results

Seventy-five patients were enrolled in the study, 25 in each group. Complete data were obtained with the following exceptions. Discharge was delayed for surgical reasons in one patient in the P/N_2O group. Recovery data relating to times of discharge and emesis data after discharge in this patient were excluded from analysis. Four patients, two in the T/H group and one in each of the propofol groups were discharged before two hours postoperatively, at 100–119 min. These data are included.

There were no differences among the three groups with regard to age, weight, sex, number of eye muscles repaired or number of eyes operated upon (Table I). Most surgical procedures were bilateral, two muscle repairs involved a combination of recessions and resections (Figure 1). There were a total of twenty different surgical procedure categories performed by five different surgeons.

Intravenous cannulation on the dorsum of the hand was achieved in all patients. The incidence of pain on injection of propofol was 18.4%. No bradycardia, hypotension or laryngospasm was observed during induction.

TABLE II Anaesthetic, surgery, and recovery times

Parameters	*Thio/Hal*	*Propofol/O_2*	*Propofol/N_2O*	*P value*
Duration of surgery†	32 ± 13	29 ± 9	29 ± 9	0.52
Duration of anaesthesia†	44 ±13	40 ± 10	41 ± 10	0.50
Time to extubation†	10 ± 5	11 ± 5	6 ± 3	0.0005*
Time to eye opening‡	32 (10–51)	26 (12–99)	14 (3–59)	0.0001*
Time to recovery score of 6†	36 ± 12	33 ± 11	24 ± 13	0.0037*
Time to first oral intake‡	69 (28–153)	72 (24–154)	58 (31–138)	0.43
Duration of PACU stay†	65 ± 23	70 ± 21	64 ± 16§	0.52
Duration of DCU stay‡	85 (50–180)	85 (20–164)	79 (54–180)§	0.63
Duration of hospital stay‡	155 (102–260)	148 (118–230)	140 (100–236)§	0.35

Thio = thiopentone Hal = halothane.
*$P < 0.05$, propofol/N_2O vs thio/hal and propofol/N_2O vs propofol/O_2.
†Mean ± SD.
‡Median (range).
§$N = 24$.

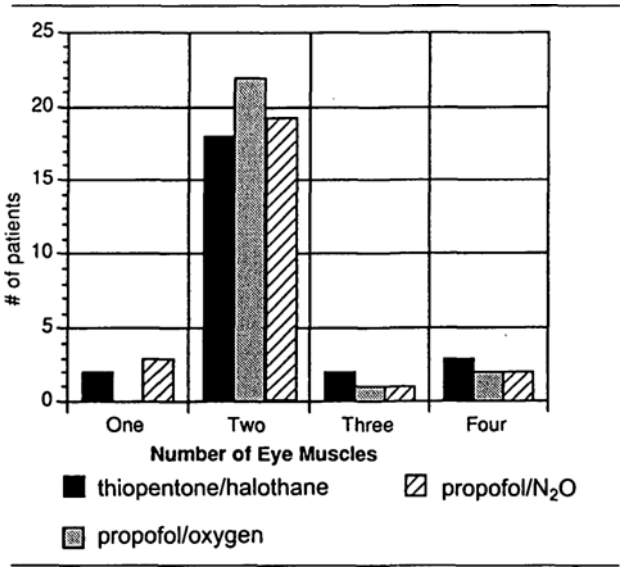

FIGURE 1 Number of eye muscles operated upon.

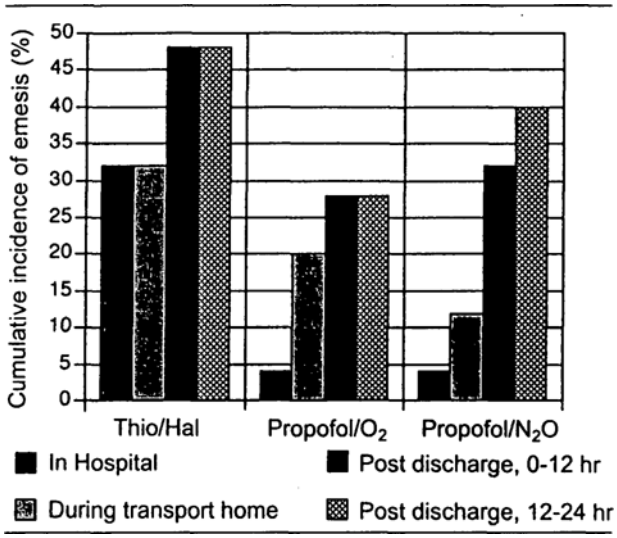

FIGURE 2 The cumulative incidence of postoperative emesis.

The P/N_2O group received a lower dose (mean ± SD) of propofol than the P/O_2 group (255 ± 80 vs 344 ± 60 $\mu g \cdot kg^{-1} \cdot min^{-1}$) ($P = 0.0001$). The durations of surgery and anaesthesia and the stay in the PACU and DCU were similar among the three groups. The time from discontinuation of the anaesthetic to first oral intake was also similar. The P/N_2O group had a shorter time to extubation, recovery time, and time to first eye opening than the T/H and P/O_2 groups (Table II).

The number of patients who received morphine for analgesia was the same in each group. However, patients in the P/N_2O group received morphine earlier during the recovery period (Table IV).

Emesis in the hospital occurred in eight patients (32%) in the T/H group and in one patient in each of the propofol groups (4%). Patients who vomited in hospital continued to have further episodes after discharge. Additional patients in all of the groups vomited during the car ride home and, after discharge, nearly half of the patients vomited during the first 12 hr after discharge, with no difference among the three groups (Table III). When overall emesis in the groups during the 24 hr study period was compared, no differences in the incidence of emesis were found; T/H, 48%, P/O_2, 28%, and P/N_2O, 42% (Figure 2).

Metoclopramide, was administered to four patients in the T/H group but no patients in the propofol groups required any antiemetic while in hospital (Table III). No patient vomited more than twice while in the hospital.

Picture recall was tested in 48 patients and was positive and similar in all groups, T/H, 16/17 patients, (94%), P/O_2, 18/19 patients (95%), and P/N_2O, 11/12 patients (92%). No intraoperative awareness was reported.

TABLE III The incidence and time of postoperative emesis and antiemetic use

Time of postoperative emesis	*Thio/Hal*	*Propofol/O_2*	*Propofol/N_2O*	*P value*
In hospital†	8(32)	1(4)	1(4)	0.0017*
During transport home†	2(8)	4(16)	2(8)‡	0.71
Post-discharge, 0 to ≤12 hr†	9(36)	6(24)	8(33)‡	0.63
Post-discharge, >12 to 24 hr†	3(12)	1(4)	5(21)‡	1.0
Cumulative emesis†	12(48)	7(28)	10(42)‡	0.34
Metoclopramide received†	4(16)	0(0)	0(0)	0.11

Thio = thiopentone Hal = halothane.
*$P < 0.0166$, propofol/N_2O vs thio/hal and propofol/O_2 vs thio/hal.
†incidence (%).
‡$n = 24$.

TABLE IV Morphine administration after surgery

Morphine administration	*Thio/Hal*	*Propofol/O_2*	*Propofol/N_2O*	*P value*
# of patients given morphine‡	13(52)	17(68)	21(84)	0.053
# of morphine doses (1/2/3)‡	8/5/0	6/9/2	5/14/2	0.085
Time of 1st. dose (mins)†	42(19–93)	31(14–74)	19(12–52)	0.004*

Thio = thiopentone Hal = halothane.
*$P < 0.05$, propofol/N_2O vs thio/hal and propofol/N_2O vs prop/O_2.
†Median (range).
‡Count (%).

Post hoc analysis of the data showed that patients who vomited in hospital during the first 12 hr after discharge or who had vomited at any time had had longer mean anaesthetic times than patients who did not. Vomiting could not be correlated to narcotic use. Vomiting occurred in 56% of patients ≤3 yr and in 59% of patients ≤4 yr (NS).

Discussion

This study confirms that the use of propofol anaesthesia decreases the incidence and severity of early postoperative emesis in children after strabismus surgery. Propofol, regardless of whether nitrous oxide was part of the anaesthetic technique, reduced emesis in hospital to 4% compared with 32% when thiopentone, halothane and nitrous oxide were used. However, after discharge from hospital, 28–40% of all children vomited despite which anaesthetic was given. The highest incidence of vomiting occurred in the first 12 hr after discharge.

When propofol was used with nitrous oxide, a lower total dose of propofol was given. Extubation was achieved five minutes earlier and recovery occurred nine minutes sooner. All patients left the hospital within three hours. Morphine was given earlier to patients who had received propofol and nitrous oxide. Very few patients required antiemetics in hospital and these were confined to those who had received thiopentone and halothane.

These results are similar to those of Watcha[3] who found a 50% incidence of vomiting after 24 hr after halothane anaesthesia. This was reduced to 23% following propofol and air. When nitrous oxide was used with propofol, the incidence was 60%. Larsson, studying the same time period, documented a lower incidence of 27% after thiopentone and halothane and an incidence of 5% when propofol and nitrous oxide were used.[4]

A number of factors may have led to the wide variation in the reported incidence of postoperative emesis in these similar studies. Rectal midazolam premedication and intravenous fentanyl at induction were given in the Larsson study. Patients had compulsory gastric drainage intraoperatively and were allowed to refuse oral intake postoperatively.[4] Droperidol was used prophylactically in the halothane group in the Watcha study and patients underwent inhalational induction prior to receiving intravenous propofol. Morphine was also given at induction.[3] Patients in our study received no premedication and all underwent an intravenous induction. No narcotics or antiemetics were given until the postoperative period.

The mechanism of the antiemetic effect of propofol is speculative. These three studies show that, despite less postoperative sedation and the use of perioperative narcotics, the use of propofol decreases the incidence of emesis before discharge from hospital. This antiemetic effect does not protect against the factors that cause vomiting

after discharge, (e.g., ambulation, subsequent alimentation or pain). Propofol, after a single dose of 2.5 mg · kg^{-1} in children, has a three-compartment elimination profile, with a rapid clearance exceeding hepatic blood flow resulting in a $T_{1/2\beta}$ of 9 min and a $T_{1/2\gamma}$ of 215 min.[8] It may be that the drug is cleared so rapidly that the propofol is no longer present in a high enough concentration in antiemetic centres while emetic stimuli such as an oculovestibular reflex remain active. Whether propofol is still effective in reducing vomiting when used for induction alone and not for the maintenance of anaesthesia remains to be seen.

The doses of propofol used in this study for induction and maintenance are higher than those previously reported.[8-11] In two of these studies,[9,11] intravenous induction doses were determined using mask acceptance as an end-point and, after loss of consciousness, mask ventilation with halothane and nitrous oxide was commenced. In Borgeat's study,[10] propofol 3.0 mg · kg^{-1} was used for induction without the concurrent use of premedication, narcotics or potent inhalational agents and the incidence of "spontaneous movement" during induction was 75%. This was reduced to 14% in a subsequent study when propofol 5.0 mg · kg^{-1} was used.[12] After a pre-trial clinical assessment, we found that a lower induction dose of 3.5 mg · kg^{-1} despite the immediate commencement of a maintenance infusion of 300–400 μg · kg^{-1} · min^{-1} was inadequate to maintain suitable clinical conditions for mask ventilation, particularly when nitrous oxide was not used. We found no adverse effects with the use of propofol 5.0 mg · kg^{-1} for induction. The use of fentanyl or morphine at induction decreases the amount of propofol needed.[3,4]

The effect of nitrous oxide on vomiting remains controversial. After the first postoperative day, the incidence of vomiting in the propofol/oxygen versus the propofol/N_2O, group (28% and 42% respectively), was not different. Given the observed incidence of vomiting of 48% in the thiopentone/halothane group, the chance of Type II error in our study is 70%, which is higher than expected. Despite the use of nitrous oxide in Larsson's study,[4] the incidence of vomiting in the propofol group was only 5%. Watcha,[3] however, found a higher incidence of vomiting when nitrous oxide was used with propofol compared to propofol alone (60% and 23% respectively). These differences may be explained in part by the differences in study design. The disadvantages of the use of propofol alone are the use of a higher maintenance dose, 17% to 35%, a somewhat prolonged awakening time and the possibility of intraoperative awareness.[3,4,13]

Opioids, either fentanyl or morphine, were used in this and other cited studies.[3,4] The use of morphine postoperatively did not increase the incidence of vomiting immediately postoperatively or after discharge. It is uncertain why the recovery room nursing staff gave more morphine to patients who had received propofol and nitrous oxide. While the children may have been experiencing more pain than the other groups, no pain scoring system was used to substantiate this and it is possible that morphine was used to treat agitation, especially in the younger children where pain is more difficult to assess and the psychological effects of separation from parents are greater. Larsson's study also described more frequent agitation in the propofol-fentanyl group.[4]

The effect of lidocaine given at induction prior to strabismus surgery is controversial. Werner reported a decrease in the incidence of postoperative vomiting from 52% to 16% after lidocaine 1.0 mg · kg^{-1}, but Christensen reported an incidence of 50% after lidocaine 1.5 mg · kg^{-1}.[14,15] Lidocaine 0.2 mg · kg^{-1} combined with propofol 3.0 mg · kg^{-1} decreases the incidence of pain on injection in paediatric patients.[16] Because of a potential antiemetic effect of lidocaine, our study was designed so that patients in all groups received lidocaine. The incidence of pain on injection in this study using lidocaine, 0.3 mg · kg^{-1} mixed with propofol 5.0 mg · kg^{-1}, was 18%. When this higher dose of propofol is used, a higher dose of lidocaine may be required to prevent injection pain.

With respect to the effect of the surgical procedure on vomiting, the initial hypothesis was that recession causes more traction on eye muscle spindles than resection and may cause more postoperative pain and vomiting. In this study, 49% of the procedures were bilateral medial or lateral recession; only 8% of procedures were bilateral resections. The remaining operations were a variety of combinations of recessions, resections and myectomies so this relationship was not examined further.

In conclusion, the use of propofol for induction and maintenance of anaesthesia in paediatric patients undergoing strabismus surgery is effective as it almost eliminates postoperative vomiting in hospital. Whether propofol reduces vomiting after discharge requires further study with a larger number of patients.

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