Brief Reports

Perphenazine decreases vomiting by children after tonsillectomy

William M. Splinter MD FRCPC,
David J. Roberts MD FRCPC

Purpose: To test the hypothesis that perphenazine decreases the incidence of vomiting by children after tonsillectomy.

Methods: Healthy children (n = 260) aged 2–12 yr undergoing elective tonsillectomy on a day care surgical basis were studied in this randomised, stratified, blocked, double-blind investigation. General Anaesthesia was induced intravenously with propofol or by inhalation with halothane and N_2O. Perphenazine 70 $\mu g \cdot kg^{-1}$ up to 5 mg or placebo *iv* was administered before surgery. Management of perioperative fluids, emesis and pain were all standardised.

Results: The groups were similar with respect to demographic data. There was less vomiting after perphenazine during the first 24 hr after surgery 42% (95% CI = 34%–50%) *vs* 57% (95% CI = 48%–66%, placebo), $P < 0.01$. On the day of surgery, both in and out-of hospital emesis were decreased by perphenazine. The perphenazine treated patients required fewer rescue antiemetics than the control group, $P < 0.05$. Each episode of in-hospital vomiting delayed discharge by 20 ± 7 min (mean ± SD), $P = 0.007$.

Conclusion: The prophylactic administration of perphenazine decreases vomiting by children after tonsillectomy.

Objectif : Vérifier si la perphénazine diminue l'incidence des vomissements après une amygdalectomie chez l'enfant.

Méthodes : Des enfants bien portants (n = 260) âgés de deux à 12 ans soumis à une amygdalectomie en chirurgie réglée dans un centre de jour ont participé à cette investigation randomisée, stratifiée, avec blocs et en double aveugle. L'anesthésie générale était induite par la voie veineuse de propofol ou par inhalation d'halothane et de N_2O. Avant la chirurgie, on administrait *iv* de la perphénazine 70 $\mu g \cdot kg^{-1}$ jusqu'à 5 mg ou un placebo. La prise en charge des liquides périopératoires, des vomissements et de la douleur était uniformisée.

Résultats : Les groupes étaient comparables sous l'aspect démographique. Les vomissements survenaient moins souvent après la perphénazine pendant les premieres 24 h postchirurgicales, 42% (IC 95% = 34%–50%) *vs* 57% (IC 95% = 48%–66%), $P < 0,01$. Le jour de la chirurgie, les épisodes émétiques intra- et extrahospitaliers diminuaient sous perphénazine. Les patients traités à la perphénazine ont eu besoin de moins d'antiémétiques de sauvetage que le groupe contrôle, $P < 0,05$. Chaque épisode de vomissements intrahospitaliers a retardé le congé de 10 ± 7 min (moyenne ± ÉT), $P = 0,007$.

Conclusion : L'administration prophylactique de perphénazine diminue les vomissements après l'amygdalectomie chez l'enfant.

From the Department of Anaesthesia, Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa, Ontario, Canada K1H 8L1.
Address correspondence to: Dr. William M. Splinter, Department of Anaesthesia, Children's Hospital of Eastern Ontario, 401 Smyth Rd., Ottawa, Ontario, Canada K1H 8L1; E-mail: Splinter@cheo.on.ca
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MANY children vomit after tonsillectomy, so techniques that may minimise this problem are appealing to anaesthetists.[1] The most common technique is the administration of antiemetic agents. Perphenazine is a phenothiazine with moderate anticholinergic effects, weak to moderate sedative effects and strong antiemetic effects. Its antiemetic effects are comparable to those of ondansetron among adults after hysterectomy.[2] There have been no studies of the perioperative use of perphenazine in children. We hypothesised that perphenazine would decrease vomiting by children after tonsillectomy.

Methods and materials

Healthy children aged 2–12 yr undergoing elective tonsillectomy or adenotonsillectomy were enrolled in this double-blind, randomised, stratified, blocked study with the approval of our Research Ethics Committee and parental consent. Patients were excluded if they had an allergy to a study drug.

When indicated, the children were given 0.5 $mg \cdot kg^{-1}$ midazolam, 20–30 min before induction of Anaesthesia. General anaesthesia was induced by inhalation with N_2O & halothane or with 2.5–3.5 $mg \cdot kg^{-1}$ propofol *iv*. To equalise any effect of premedication and induction technique on vomiting, patients were stratified and blocked according to premedication and induction technique. Mivacurium, 0.25 $mg \cdot kg^{-1}$, was administered if a muscle relaxant was indicated to facilitate tracheal intubation. Patients were administered 50 $\mu g \cdot kg^{-1}$ midazolam (maximum dose 3 mg) *iv* if the child had not received premedication. Placebo or study drug, 70 $\mu g \cdot kg^{-1}$ perphenazine (maximal dose 5 mg) was administered in a double-blind fashion immediately after induction of anaesthesia which was maintained with N_2O and halothane. Patients received 1.5 $mg \cdot kg^{-1}$ codeine *im* before surgery began. Perioperative *iv* fluids were Ringer's lactate in a standardised fashion.

Patients were discharged from the PAR when they achieved an Aldrete recovery room score of 10.[3] Pain management included 50 $\mu g \cdot kg^{-1}$ morphine *im* in the PAR, while pain in the DCSU and at home was treated with acetaminophen and/or codeine *po*. If the patient vomited twice in-hospital, 1 $mg \cdot kg^{-1}$ dimenhydrinate *iv* was administered. Vomiting was defined as the forceful expulsion of liquid gastric contents. Nausea and retching were not considered vomiting. Nurses recorded in-hospital vomiting and parents recorded vomiting after discharge in a diary. Patients were encouraged to drink clear fluids in the DCSU before discharge. Patients were discharged after a minimal stay of four hours in the DCSU.

Normally-distributed data were compared with one-way ANOVA, non-parametric data were compared with Mann-Whitney U test, and nominal data were compared with chi square analysis. The relationship between the incidence of vomiting and the study intervention plus other potential confounders (such as age, weight, premedication, and induction technique) were evaluated with logistic regression analysis. Sample size was determined by assuming that an acceptable difference in vomiting was 15%. The acceptable alpha error was set at 0.05 (one-sided) and Type II error was set at 0.20.

Results

Two of the 260 patients enrolled in the study were excluded from data analysis because of protocol violations. The groups had similar demographic data and distribution of potential confounders (Table I). No patient received an anticholinesterase for reversal of muscle relaxation.

Patients vomited from 0–12 times. The incidence of vomiting was less in the perphenazine group, 42% (95% CI = 34%–50%) *vs* 57% (95% CI = 48%–66%). This antiemetic effect was detectable in the hospital and after discharge (Table I). Oral premedication did not alter the incidence of vomiting (44% premedicant *vs* 50% no premedicant, Table II). Induction technique also had no influence on the incidence of vomiting (48% intravenous induction *vs* 53% inhalation induction, Table II). Each episode of in-hospital vomiting delayed discharge by 20 ± 7 min (mean ± SD), $P = 0.007$.

Postoperative adverse events were similar among the groups studied, except more patients in the placebo group required rescue antiemetics while in-hospital (Table I). Five patients in the placebo group and two patients in the perphenazine group required medical attention for their vomiting after discharge. One patient in each group required readmission to hospital because of vomiting.

Discussion

Perphenazine reduced vomiting after tonsillectomy in children. This beneficial effect continued throughout the day of surgery, but did not persist to the day after surgery. The observed incidence of vomiting is similar to that noted in an ambulatory care setting where in-hospital vomiting rates after tonsillectomy are 10–30% and increases to 20–40% after discharge.[1,5,6]

There is only one published report of perioperative dystonia after perphenazine,[7] so it was not unexpected that there were no observed adverse effects attributable to perphenazine in the current study. Perphenazine is a phenothiazine and like other medications in its drug

TABLE I Demographic data, vomiting & rescue antiemetics

	Placebo	*Perphenazine*
n	128	130
Age (yr)	6.7 ± 2.7	6.81 ± 2.5
Weight (kg)	26 ± 12	28 ± 14
Intravenous induction	67	63
Premedication	18	18
Estimated intraoperative Blood loss (ml)	15 (0–150)	13 (0–200)
Anaesthesia time (min)	31 ± 9	32 ± 11
Mivacurium given (n)	94	97
PAR time (min)	43 ± 14	47 ± 24
DCSU time (min)	251 ± 30	259 ± 32
Vomiting		
PAR	9%	2%†
DCSU	34%	11%†
Day O	35%	23%*
Day 1	19%	24%
Overall	59%	42%†
Rescue antiemetics	15%	8%*

Values listed are n, mean ± SD or median(range).
PAR = Post anaesthetic recovery room,
DCSU = day care surgical unit.
*$P < 0.05$, †$P < 0.01$.

TABLE II 24-hour emesis rates by subgroup

	Placebo	*Perphenazine*	*Chi square P value*
Oral midazolam	11/18 (61%)	9/18 (50%)	0.450
No premedication	65/110 (59%)	46/112 (41%)	0.007
iv induction	36/67 (54%)	26/63 (41%)	0.155
Inhalation induction	40/61 (66%)	29/67 (43%)	0.012
All cases	76/128 (59%)	55/130 (42%)	0.01

class has a high therapeutic index and side effects are minor. The present results are congruous with Desilva *et al.*'s study of adults, in which only the patients who received perphenazine were free of adverse side effects.[2] The central nervous system dopaminergic activity of this drug which results in its antiemetic effect, may also produce extrapyramidal effects. These effects, which are easily treated with benzotropine, appear to be quite rare.

The dose of perphenazine to be utilised in children is not well-established. In the current study 70 μg·kg of perphenazine was administered, which is comparable to the recommended adult dosage of 5 mg. This dose appeared to be effective and without adverse effects in the small sample studied. Larger doses (8 mg) have been associated with drowsiness among oncology patients.[8] Dose finding studies with Kaplan-Meir survival curves still need to be performed in children with respect to antiemetic effect of perphenazine.

Costs and other non-surrogate end points were partially addressed in the current study. Perphenazine is an inexpensive agent ($0.81 CAN for treatment of 20 kg child), while a similar dose of ondansetron, 2 mg, costs $8.60 CAN. Non-drug costs, such as those associated with treatment of prolonged emesis, delayed discharge and unscheduled admissions to hospital were not assessed, although previous investigations have demonstrated decreased resource utilisation with reduced postoperative vomiting.[9] In the current investigation, vomiting increased resource utilisation by delaying discharge from hospital and increasing use of rescue antiemetics, especially in the placebo group.

In conclusion, perphenazine decreases vomiting by children after tonsillectomy in an ambulatory care setting. While perphenazine decreased emesis, the observed incidence of vomiting, 42%, may be considered unacceptably high and we believe the search for a better antiemetic technique should continue.

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