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Oral ondansetron decreases vomiting after tonsillectomy in children

Vomiting is a common, unpleasant aftermath of tonsillectomy in children. Intraoperative intravenous ondansetron (OND) reduces vomiting after this operation. Our double-blind, placebo-controlled, randomized investigation studied the effect of the oral form of OND on vomiting after outpatient tonsillectomy in children. We studied 233 healthy children age 2–14 yr undergoing elective tonsillectomy. Subjects were given placebo (PLAC) or OND 0.1 mg · kg⁻¹ rounded off to the nearest 2 mg one hr before surgery. Anaesthesia was induced with either propofol or halothane/N₂O. Vecuronium 0.1 mg · kg⁻¹ was administered at the discretion of the anaesthetist. Anaesthesia was maintained with halothane/N₂O, 50 µg · kg⁻¹ midazolam iv and 1–1.5 mg · kg⁻¹ codeine im. At the end of surgery, residual neuromuscular blockade was reversed with neostigmine and atropine. All episodes of in-hospital emesis were recorded by nursing staff. Rescue antiemetics in the hospital were 1 mg · kg⁻¹ dimenhydrinate iv for vomiting × 2 and 50 µg · kg⁻¹ droperidol iv for vomiting × 4. Parents kept a diary of emesis after discharge. Postoperative pain was treated with morphine, codeine and/or acetaminophen. The two groups were similar with respect to demographic data, induction technique and anaesthesia time. Oral OND (n = 109) reduced postoperative emesis from 54% to 39%, P < 0.05. This effect was most dramatic in-hospital, where 10% of the OND-patients and 30% of the PLAC-group vomited, P < 0.05. The OND-subjects required fewer rescue antiemetics, 7% vs 17%, P < 0.05. In conclusion, oral ondansetron decreased the incidence of vomiting after outpatient tonsillectomy in children.

Key words

ANAESTHESIA: paediatric, outpatient;
SURGERY: tonsillectomy;
VOMITING: postoperative, ondansetron.

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Chez l'enfant, les vomissements constituent un contre-coup désagréable de l'amygdalectomie. L'administration intraveineuse peropératoire d'ondansetron (OND) réduit l'incidence des vomissements après cette intervention. Notre recherche randomisée, à double aveugle et contrôlée avec placebo s'intéresse à l'influence de la forme orale d'OND sur les vomissements après une amygdalectomie en ambulatoire chez les enfants. Notre étude inclut 233 enfants bien portants âgés de 2 à 14 ans programmés pour amygdalectomie. Une heure avant la chirurgie, les sujets reçoivent soit un placebo (PLAC) soit de l'OND 0,1 mg · kg⁻¹ à la dose arrondie la plus proche de 2 mg. L'anesthésie est induite avec du propofol ou de l'halothane/N₂O. Du vécuronium 0,1 mg · kg⁻¹ est administré à la discrétion de l'anesthésiste. L'anesthésie est entretenue avec halothane/N₂O, midazolam 50 µg · kg⁻¹ iv et codéine 1–1,5 mg · kg⁻¹ im. À la fin de chirurgie, la curarisation est renversée avec de l'atropine et de la néostigmine. Tous les épisodes de vomissements sont compilés par le personnel infirmier. À l'hôpital, les antiémétiques de sauvetages sont le dimenhydrinate 1 mg · kg⁻¹ iv pour les vomissements × 2 et droperidol 50 µg · kg⁻¹ iv pour les vomissements × 4. Les parents notent les vomissements après le congé. Les deux groupes sont comparables au regard des données démographiques, de la technique d'induction et de la durée de l'anesthésie. L'OND oral diminue l'incidence des vomissements de 54% à 39%, P < 0,05. Cet effet est surtout dramatique à l'hôpital où 10% des patients du groupe OND vomissent comparativement à 30%, P < 0,05. Le groupe OND a moins besoin d'antiémétiques de sauvetage, 7% vs 17%, P < 0,05. En conclusion, l'ondansetron oral diminue l'incidence des vomissements postamygdalectomie en chirurgie ambulatoire chez l'enfant.

Vomiting is a frequent, unpleasant consequence of general anaesthesia in children.¹ Persistent vomiting may result in dehydration and metabolic derangements. Furthermore, it may raise costs to the Health Care System by delaying discharge from day care surgical units (DCSU) or unscheduled hospital admissions.

Pandit² reported a 75% incidence of vomiting after tonsillectomy in children. The aetiology of this vomiting is multifactorial and is probably controlled through the

chemoreceptor trigger zone (CRTZ) in the medulla. Effective antiemetic agents block neurotransmitters found within the CRTZ.³ Agents known to block dopamine (D_2), histamine (H_1), and muscarinic cholinergic receptors have antiemetic effects. Recently, antagonists of 5-hydroxytryptamine type 3 ($5-HT_3$) receptors have been noted to have antiemetic properties. The first commercially available drug of this class is ondansetron. Ondansetron given *iv* reduces vomiting after surgery.⁴⁻⁶ Unfortunately, the *iv* form of the drug is expensive. However, oral ondansetron is available at two-thirds of the price of the parenteral form and is effective in adults.⁷

The purpose of this double-blind, placebo-controlled, randomized study was to determine the effect of oral ondansetron on vomiting after outpatient paediatric tonsillectomy.

Methods

Following hospital ethics committee approval and written parental consent, we studied 233 healthy children age 2–14 yr scheduled to undergo elective tonsillectomy or adenotonsillectomy. Subjects were excluded if they had a study-drug allergy or they were unwilling to ingest the medication. Patients were given placebo or ondansetron $0.1 \text{ mg} \cdot \text{kg}^{-1}$ rounded off to the nearest 2 mg in a double-blind randomized fashion *po* one hr before surgery with a sip of water.

After placement of routine monitors, anaesthesia was induced with halothane/ N_2O or $2.5 \text{ mg} \cdot \text{kg}^{-1}$ propofol mixed with $0.5 \text{ mg} \cdot \text{kg}^{-1}$ lidocaine. Vecuronium $0.1 \text{ mg} \cdot \text{kg}^{-1}$ was administered to facilitate tracheal intubation at the discretion of the individual anaesthetist. Anaesthesia was maintained with halothane/ N_2O , $50 \mu\text{g} \cdot \text{kg}^{-1}$ midazolam *iv* and $1\text{--}1.5 \text{ mg} \cdot \text{kg}^{-1}$ codeine *im*. At the conclusion of surgery, residual neuromuscular blockade was reversed with $20 \mu\text{g} \cdot \text{kg}^{-1}$ atropine and $60 \mu\text{g} \cdot \text{kg}^{-1}$ neostigmine. Orogastric tubes were not used during this study. Postoperatively, patients were offered clear fluids in the DCSU only if the child requested a drink. All episodes of in-hospital emesis were recorded by nursing staff. Parents kept a diary of emesis after discharge. Post-discharge vomiting was double-checked on the day after surgery, when the parents were contacted by a research assistant and reminded to mail their diary. Rescue antiemetics in the hospital were $1 \text{ mg} \cdot \text{kg}^{-1}$ dimenhydrinate *iv* for vomiting $\times 2$ and droperidol $50 \mu\text{g} \cdot \text{kg}^{-1}$ for vomiting $\times 4$. Postoperative pain was treated with morphine, codeine and acetaminophen. Patients were discharged from our DCSU if after a minimal four-hour stay they were not nauseated, had little or no pain, were ambulatory and were not actively bleeding.

Data were compared with one-way ANOVA, Chi-square analysis and Fisher's Exact Test. For sample size

determination and significance testing, the accepted alpha and beta errors were 0.05 and 0.20, respectively. The predicted incidence of vomiting was 40% in the placebo group and 25% in the ondansetron groups.

Results

Six patients, three in each group, underwent adenoidec-tomy only. These patients were included in the analysis. The groups were similar with respect to demographic data, anaesthesia time and intraoperative blood loss (Table I). The study medication was administered $72 \pm 29 \text{ min}$, mean $\pm$ SD, before surgery. Sixty-eight patients underwent *iv* induction, of whom 32 received placebo and 36 ondansetron.

In-hospital pain management was almost identical. Fourteen patients in each group received morphine in the post-anaesthetic recovery room (PAR). Before discharge from hospital codeine $1 \text{ mg} \cdot \text{kg}^{-1}$ was given *po* or *im* to 79% of the patients in both groups.

Patients vomited from 0–14 times during the 24 hr after surgery (Figure) with a reduced incidence of emesis among the oral ondansetron patients (Table II). This was especially true in hospital, wherein only 10% of the ondansetron group vomited. Further, the placebo group had 12 and 53 more emetic spells in the PAR and DCSU, respectively, than did the ondansetron group, $P < 0.05$. Rescue antiemetics were required less often by the ondansetron-treated patients (Table II). Four patients, all in the placebo group, required a second rescue antiemetic, droperidol. One patient in each group was admitted after surgery because of vomiting. Also, one patient in each group returned to hospital the day after surgery because of emesis. The incidence of vomiting was not affected by induction technique with emesis rates of 45% and 51% in children whose anaesthesia was induced by *iv* and inhalation, respectively.

Discussion

The present study investigated a new therapeutic approach for the prevention of vomiting after paediatric tonsillectomy. A single, oral, preoperative dose of ondansetron decreased the incidence of vomiting during the first four hours after outpatient tonsillectomy in children, but there was no difference in the incidence of vomiting after discharge from hospital.

Other investigators have studied the effect of antiemetics on vomiting after tonsillectomy. The incidence of vomiting observed in this study is comparable with the 12–75% previously noted.^{2,8}

Could the 39% vomiting rate in the treatment group be improved? The dose of ondansetron is based on Dupuytron's⁷ adult study and a paediatric study in which the weight-normalized clearance and volume of distri-

TABLE I Patient characteristics

Group	n	Age (yr)	Weight (kg)	EBL (mL)	Anaes. time (min)	PAR time (min)	DCSU time (hr)
P	124	6.6 ± 2.9	26 ± 14	37 ± 25	36 ± 12	47 ± 11	4.0 ± 0.7
O	109	7.1 ± 2.7	27 ± 10	37 ± 25	37 ± 18	45 ± 10	3.9 ± 0.7

Mean ± SD, P = placebo, O = ondansetron, EBL = estimated intraoperative blood loss, PAR = post-anaesthetic recovery room, DCSU = day-care surgical unit.

TABLE II Vomiting incidence

Group	Vomit %	Vomit by location %				Rescue Meds. %
		PAR	DCSU	Day 1	Day 2	
P	54*	5*	29*	33	17	17*
O	39	nil	10	32	19	7

P = placebo, O = ondansetron, * $P < 0.05$, Chi-square or Fisher's Exact Test.

FIGURE The distribution of patients with 0-14 emetic episodes among the two groups.

bution of ondansetron in children aged 3-12 yr were similar to that in adults.⁹ Subsequently, Rust and Cohen⁹ observed a progressive decrease in postoperative vomiting among adults after an increase of a single oral dose of ondansetron from 0 to 4 to 8 to 16 mg (approximately 0-0.2 mg · kg⁻¹). Thus, an oral dose of 0.2 mg · kg⁻¹ of ondansetron should have a greater effect¹⁰ than the 0.1 mg · kg⁻¹ used in our study. Alternatively, Litman⁴ used ondansetron 0.15 mg · kg⁻¹ *iv* during paediatric tonsillectomy and noted a decrease in the frequency of vomiting from the control's 73% to 23%. Another option to extend the effect of ondansetron after discharge would be to repeat the oral dose immediately before release from hospital or by the use of a longer-acting 5-HT₃ antagonist.

Finally, an additional antiemetic may further decrease vomiting after tonsillectomy.

There were several problems with our study. Because the pharmacokinetic and pharmacodynamic behaviour of oral ondansetron have not been studied in the paediatric population, much of the study design was based on adult data. From a practical perspective, not all children will ingest oral medication, nor will they all arrive at least one hour before surgery to allow adequate absorption prior to anaesthesia. Finally, the study population included patients undergoing tonsillectomy and adenotonsillectomy (T&A). Theoretically, the T&A patients should bleed more postoperatively and have a greater incidence of emesis secondary to greater ingestion of blood in the postoperative period. There was not an observed increase in emesis in the T&A subgroup during the current study.

In summary, the current investigation demonstrated that a single dose of 0.1 mg · kg⁻¹ ondansetron gives *po* one hour before tonsillectomy in children decreased postoperative vomiting, particularly during the first four hours.

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