

PAEDIATRICS

Effect of intravenous fluid therapy on postoperative vomiting in children undergoing tonsillectomy

M. F. Elgueta¹, G. C. Echevarría^{1*}, N. De la Fuente¹, F. Cabrera¹, A. Valderrama¹, R. Cabezón², H. R. Muñoz¹ and L. I. Cortinez¹

¹ División de Anestesiología and ² Departamento de Otorrinolaringología, Escuela de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile

* Corresponding author. E-mail: gcechevarria@gmail.com

Editor's key points

- Postoperative vomiting (POV) is a frequent complication in children that leads to prolonged stay and readmission.
- The effects of intraoperative hydration with 10 or 30 ml kg⁻¹ h⁻¹ of lactated Ringer's on POV were compared in subjects aged 1–12 yr undergoing tonsillectomy.
- The higher volume hydration protocol significantly reduced POV, and is cost-effective in the absence of prophylactic antiemetic therapy.

Background. Postoperative vomiting (POV) is one of the most frequent complications of tonsillectomy in children. The aim of this study was to evaluate the antiemetic effect of super-hydration with lactated Ringer's solution in children undergoing elective otorhinolaryngological surgery.

Methods. One hundred ASA I–II children, aged 1–12 yr, undergoing elective tonsillectomy, with or without adenoidectomy, under general anaesthesia were studied. Induction and maintenance of anaesthesia were standardized with fentanyl, mivacurium, and sevoflurane in N₂O/O₂. Subjects were assigned to one of the two groups: 10 ml kg⁻¹ h⁻¹ lactated Ringer's solution or 30 ml kg⁻¹ h⁻¹ lactated Ringer's solution. A multivariable logistic regression was used for assessing the effects of super-hydration on POV (defined as the presence of retching, vomiting, or both). A value of *P*<0.05 was considered statistically significant.

Results. During the first 24 h postoperative, the incidence of POV decreased from 82% to 62% (relative reduction of 24%, *P*=0.026). In the adjusted logistic regression model, subjects in the 10 ml kg⁻¹ h⁻¹ group had an odds ratio of POV that was 2.92 (95% confidence interval: 1.14, 7.51) for POV compared with subjects in the 30 ml kg⁻¹ h⁻¹ group.

Conclusions. Intraoperative administration of 30 ml kg⁻¹ h⁻¹ lactated Ringer's solution significantly reduced the incidence of POV during the first 24 h postoperative. Our results support the use of super-hydration during tonsillectomy, as an alternative way to decrease the risk of POV in children.

Keywords: nausea, anaesthetic factors; paediatrics; PONV; vomiting, antiemetics

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Tonsillectomy, with or without adenoidectomy, is one of the most commonly performed surgical procedures in children throughout the world.¹ Postoperative vomiting (POV) is one of the most frequent complications of this surgery,^{2–3} and is the primary anaesthetic reason for readmission^{4–10} and prolonged stay in paediatric surgical patients.^{4–7 9 11 12} The reported incidence of POV is as high as 70% when no prophylactic antiemetic is given,^{13–14} such that prophylaxis is strongly suggested for this surgical procedure.

Pharmacological POV prophylaxis might not be cost-effective since many of the available antiemetics are expensive and cannot completely eliminate POV.^{15–17} In addition, the side-effects of some of these drugs such as agitation, bradycardia, dizziness, sedation, extrapyramidal symptoms, headache, or dry mouth are common.^{15–16}

The use of supplemental fluid therapy might be an inexpensive alternative to reduce POV.¹⁸ Studies assessing fluid administration and POV in adult patients, however, have shown controversial results.^{18–24} Fewer studies have been conducted in children. Goodarzi and colleagues²⁵ showed that in children undergoing strabismus surgery, intraoperative i.v. super-hydration with crystalloid solution more than halved the incidence of POV. Other studies have shown that the use of home i.v. hydration²⁶ or 24 h i.v. hydration²⁷ in paediatric patients after adenotonsillectomy does not reduce POV.

The aim of this study was to evaluate the antiemetic effect of intraoperative super-hydration with lactated Ringer's solution in children undergoing tonsillectomy with or without adenoidectomy. We hypothesized that administration of supplemental fluid would reduce the incidence of POV in this population.

Methods

After institutional ethics committee approval (School of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile) and written informed parental consent, 100 children, ASA physical status I or II, aged 1–12 yr, who were undergoing elective tonsillectomy or adenotonsillectomy under general anaesthesia, were prospectively studied between July 2010 and March 2012 (ClinicalTrials.gov Identifier: NCT01575600).

Exclusion criteria included a history of diabetes mellitus, mental retardation, obesity (BMI \geq 95th percentile for age and sex), intake of antiemetic or psychoactive medication within 24 h before surgery, or known gastro-oesophageal reflux.

All subjects were unpremedicated and fasted for at least 4 h. In the operating theatre, after routine monitoring, general anaesthesia was induced with sevoflurane in 100% oxygen by a face mask with spontaneous ventilation. After induction, i.v. access was established and subjects were randomly allocated using a table of computer-generated random numbers, to receive one of the two interventions during the intraoperative period. The control group (Group 1) received 10 ml $\text{kg}^{-1} \text{h}^{-1}$ lactated Ringer's solution, whereas the large volume infusion group (Group 2) received 30 ml $\text{kg}^{-1} \text{h}^{-1}$ lactated Ringer's solution. Subjects and their anaesthesiologist were blinded to group assignment.

Before tracheal intubation, all subjects received fentanyl 4 $\mu\text{g} \text{kg}^{-1}$ and mivacurium 0.16 mg kg^{-1} . Anaesthesia was maintained with oxygen/nitrous oxide (1:1 litre min^{-1}) and 2% sevoflurane. Supplemental bolus doses of fentanyl 1 $\mu\text{g} \text{kg}^{-1}$ were administered to maintain arterial pressure and heart rate within 20% of baseline. Lactated Ringer's solution was constantly infused using a pump with the screen and solution bag covered, to maintain blinding.

All tonsillectomies were performed in the same fashion, by dissection of the pericapsular plane using a cold steel technique. Haemostasis of the tonsillar fossa was achieved using gauze packing with bismuth subgallate and electrocautery to the remaining bleeding vessels. Adenoidectomy was performed with adenotome, and haemostasis obtained with gauze packing. At the end of surgery, gastric contents were suctioned via an orogastric tube before extubation.

During surgery, all subjects received rectal paracetamol, 40 mg kg^{-1} (maximum dose, 1 g). Monitoring of neuromuscular function performed with a peripheral nerve stimulator in all subjects and muscle relaxation was antagonized with a mixture of atropine 20 $\mu\text{g} \text{kg}^{-1}$ and neostigmine 50 $\mu\text{g} \text{kg}^{-1}$, as needed. After tracheal extubation, infusion of lactated Ringer's solution was stopped and children were transferred to the post-anaesthesia care unit (PACU) and 120 min later to the ward, where they stayed overnight. From the time of tracheal extubation, each episode of retching, vomiting, or both was recorded. Since nausea is difficult to assess in children, only retching and vomiting episodes were documented. At the first episode of retching, vomiting, or both, a rescue antiemetic consisting of i.v. ondansetron 0.15 mg kg^{-1} was

administered. If retching, vomiting, or both persisted for 20 min after the administration of ondansetron, a second rescue antiemetic consisting of i.v. droperidol 0.015 mg kg^{-1} was administered. Cardiac rhythm was monitored by electrocardiography during their PACU stay.

A visual analogue scale (VAS; 0, no pain; 10, worst possible pain) or the Children and Infants Postoperative Pain Scale (CHIPPS; 0–10 point) was used to assess pain in the recovery period, according to age and comprehension by the child. A nurse, blind to the subjects' allocation group, evaluated pain scores on arrival in the PACU and at 15, 30, 45, 60, 90, and 120 min. When reported CHIPPS or VAS was \geq 4, oral codeine (1 mg $\text{kg}^{-1} \text{dose}^{-1}$) was administered. If pain relief was considered inadequate, i.v. morphine (0.1 mg $\text{kg}^{-1} \text{dose}^{-1}$) was given, until pain score was $<$ 4. In the presence of vomiting, pain was managed with i.v. morphine. Opioid analgesics consumed were all converted to i.v. morphine milligram-equivalents.²⁸

In the PACU, subjects were allowed to drink liquids as soon as requested. No additional i.v. fluids were given during the postoperative period. On the ward, analgesia was with oral paracetamol (15 mg $\text{kg}^{-1} \text{dose}^{-1}$, every 8 h). Subjects were discharged home the day after surgery. Twenty-four hours after surgery, parents/guardians were asked via telephone whether their child experienced retching or vomiting, episode of fever above 100.4°F, or thirst since leaving the hospital. The highest pain score at 24 h follow-up was assessed using a scale of 0–10 (with 0 being no pain and 10 being worst pain). If the child was $<$ 6 yr old or unable to understand the pain scale, we used the CHIPPS scale, asking parents/guardians the information for each item (crying, facial expression, posture of the trunk, posture of the legs, and motor restlessness).

Subjects, parents/guardians, medical staff (nurse, anaesthesiologist, and surgeon), and investigators performing the postoperative assessments were blinded to group allocation during the entire study period.

Statistical analysis

Without prophylaxis, more than 70% of children undergoing tonsillectomy experience at least one episode of vomiting in the postoperative period.¹³ Based on this, 42 patients per group are needed to test a difference in proportions of 30% with a power of 80% and α -level of 0.05. We enrolled 50 subjects per arm to allow for possible dropouts.

We tested normality using the Shapiro–Wilk test and Q–Q plots. We used unpaired Student's *t*-test or the Wilcoxon rank-sum test for between-group comparisons, as appropriate. The χ^2 test and Fisher's exact test were used for inferences on proportions. Two-way repeated-measures analysis of variance (ANOVA) was used to analyse the postoperative VAS values.

The analysis of the primary outcome—presence of at least one episode of vomiting (defined as the forcible ejection of stomach contents through the mouth), retching (defined as unproductive effort to vomit) in the first 24 h postoperative

(POV), or both—was performed using logistic regression. The model building was done according to Hosmer and Lemeshow.²⁹ Variables identified as potential confounding factors in previous studies and those with a *P*-value of <0.25 in the univariable analysis were included in the multivariable logistic regression model. Using a backward elimination approach, the likelihood ratio test comparing the model including the variable with the nested model excluding it was used to assess whether the variable contributed significantly to the model (*P*<0.20). The Hosmer–Lemeshow goodness-of-fit test was used to assess calibration of the model.

Data are expressed as mean (standard deviation, *sd*), median (inter-quartile range, *IQR*), or odds ratio [95% confidence interval (*CI*)], unless otherwise stated. A two-sided *P*-value of <0.05 was considered significant. All analyses were performed with STATA/SE version 10.1 (StataCorp LP, College Station, TX, USA) according to the intention-to-treat principle.

Results

A total of 100 children were enrolled in this study. All received their assigned study treatment. One subject in each group developed a swollen uvula, receiving *i.v.* dexamethasone 0.1 mg kg⁻¹ before extubation. Five randomized subjects were lost to follow-up after they had left the hospital; since all five presented vomiting, retching, or both during the hospitalization, they were not excluded from the analysis (Fig. 1). Both groups were similar with respect to subject characteristics (Table 1), anaesthesia, and postoperative care data (Table 2). Most of the ASA II physical status patients had allergic rhinitis, asthma, or recurrent obstructive bronchial syndrome (63%, 18%, and 13%, respectively). Postoperative pain scores were also similar between the groups (*P*=0.891, Fig. 2). No prophylactic antiemetic drugs were used and no neuromuscular blocker reversal was required.

During the first 24 h postoperative, 41 of 50 patients in Group 1 (82%) and 31 of 50 patients in Group 2 (62%) experienced at least one episode of retching, vomiting, or both (incidence decreased by 24%, *P*=0.026).

The results of the univariable analysis using logistic regression for POV are shown in Table 3. The results of the multivariable logistic regression analysis are shown in Table 4.

For the POV model, we began with a model containing the variables group (10 vs 30 ml kg⁻¹ h⁻¹), morphine given in the PACU, gender, age,^{25 30} and weight. In the adjusted logistic regression model, subjects in Group 1 (10 ml kg⁻¹ h⁻¹) had an odds ratio of retching, vomiting, or both that was 2.92 (95% *CI*: 1.14, 7.51) times higher than that of patients in Group 2 (30 ml kg⁻¹ h⁻¹) (*P*=0.026).

Discussion

To our knowledge, this is the first randomized controlled trial studying the effectiveness of large intraoperative crystalloid

administration as prophylaxis of POV in children undergoing tonsillectomy or adenotonsillectomy. Using two different intraoperative regimens of fluid administration, a consistent decrease in the incidence of POV in the group receiving 30 ml kg⁻¹ h⁻¹ compared with 10 ml kg⁻¹ h⁻¹ lactated Ringer's solution was found, and this protective effect persisted after adjusting for potential confounders.

In the adult population, mainly patients undergoing laparoscopic cholecystectomy or gynaecological surgery, several studies have investigated the effect of different perioperative fluid administration schemes on POV, with variable results.^{18–24} The type of intraoperative fluid utilized has also been a controversial topic, with studies showing a positive effect of colloids compared with crystalloids in decreasing the incidence and severity of POV and the need of antiemetic drugs,^{31 32} and others reporting no extra benefit between the two solutions.^{33 34} Super-hydration has also been associated with a lower incidence of gut mucosal hypoperfusion and a decrease in the length of hospital stay in patients undergoing major surgery.³² Despite this benefit, several reports have shown a negative association between excessive fluid administration and perioperative morbidity.^{35–37} A meta-analysis on the efficacy of supplemental *i.v.* crystalloid for the prevention of POV suggested that this measure significantly reduced overall POV, but the effect was not statistically significant for early and late POV.³⁸

In paediatric patients, the use of home *i.v.* hydration²⁶ or 24 h *i.v.* hydration²⁷ after adenotonsillectomy have not been shown to offer an advantage on POV. In contrast, Goodarzi and colleagues²⁵ reported a decrease in the incidence of vomiting from 54% to 22% during the first 24 h post-strabismus surgery, when intraoperative 30 ml kg⁻¹ h⁻¹ Ringer's solution was given compared with 10 ml kg⁻¹ h⁻¹. In agreement with their results, in our study, the incidence of POV decreased from 82% to 62% (relative reduction of 24%). After adjusting for confounding variables, this represents an odds ratio of vomiting approximately three times higher in the low volume group. Contrasting these results with those found in adults, intraoperative fluid administration might be more effective in the paediatric population. This could be related to the fact that the baseline POV rate is higher than that reported in adults. Further differences in the amount and the type of fluid given, concomitant opioid administration, type of surgery, and anaesthetic technique could also explain these differences.

Considering that tonsillectomy is one of the most frequent surgeries performed in children and the incidence of POV in this procedure is extremely high, we should consider the cost of antiemetic prophylactic strategy.³⁹ Parents' willingness to pay for a reduction in the postoperative emesis experienced by children is around US\$80.⁴⁰ Our results support the use of fluid administration as an economic alternative in children.

The mechanism of supplemental fluid therapy in reducing POV is not clear. Maharaj and colleagues,²¹ studying patients undergoing elective gynaecological laparoscopy with general anaesthesia, reported a significant decrease in the incidence

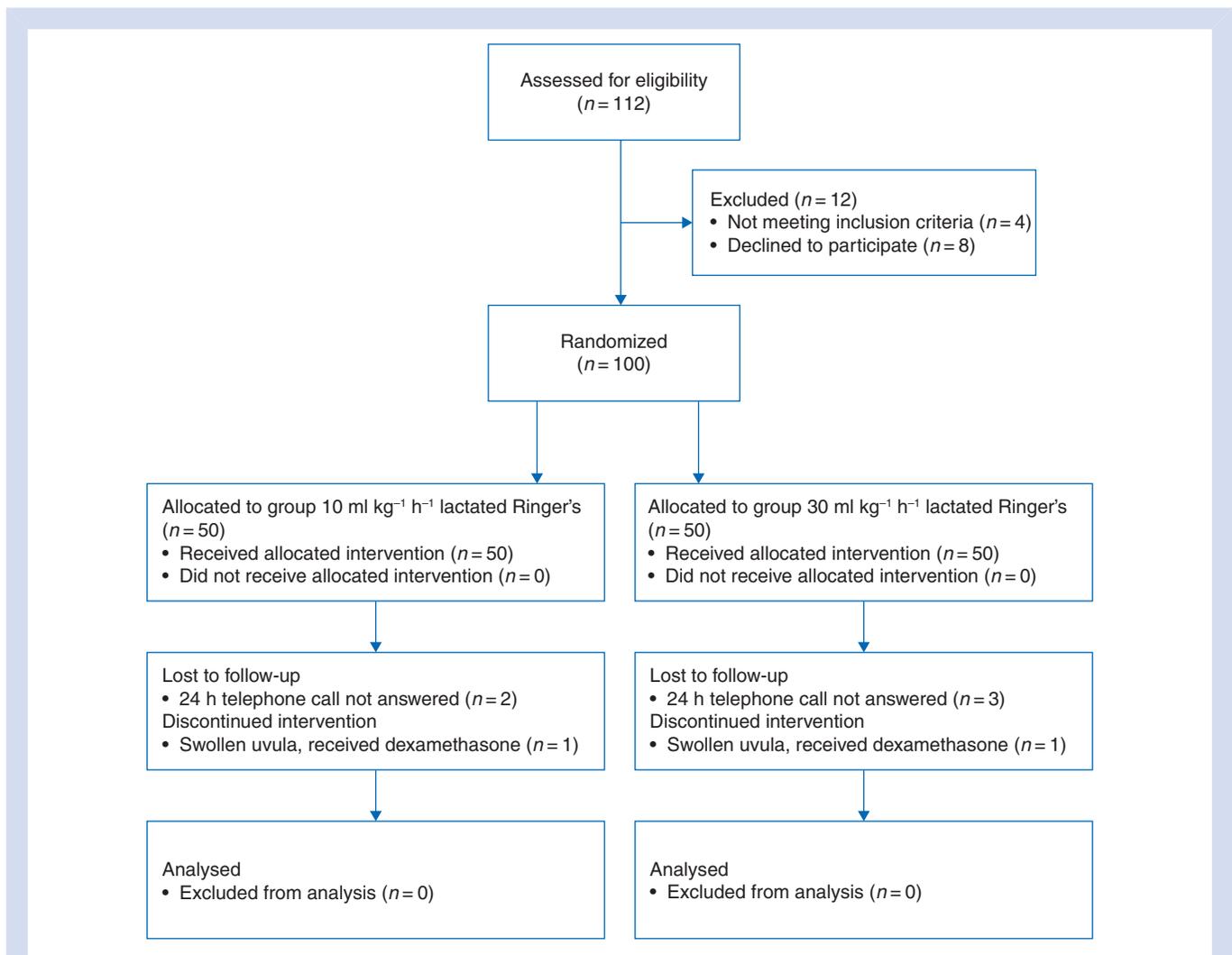


Fig 1 Flow diagram displaying the progress of all participants through the trial.

Table 1 Baseline subject characteristics. POV, postoperative vomiting. *Values are mean (range) for age, or mean (sd). †Number of patients (%)

	Group 1 (10 ml kg ⁻¹ h ⁻¹ ; n = 50)	Group 2 (30 ml kg ⁻¹ h ⁻¹ ; n = 50)	P-value
Male/female (n)	24/26	28/22	0.423
Age (yr)*	5.0 (1–12)	4.5 (2–9)	0.352
Weight (kg)*	23.3 (10.7)	20.4 (5.7)	0.093
Surgery (n): tonsillectomy/adenotonsillectomy	4/46	1/49	0.362
ASA I/II (n)	30/20	30/20	1.000
History of POV or motion sickness†	1 (2)	1 (2)	1.000

Table 2 Anaesthetic characteristics and postoperative care data. Rx, treatment; PACU, post-anaesthetic care unit. *Values are mean (sc). †Number of patients (%). ‡Values are median (IQR)

	Group 1 (10 ml kg ⁻¹ h ⁻¹ ; n = 50)	Group 2 (30 ml kg ⁻¹ h ⁻¹ ; n = 50)	P-value
Duration of anaesthesia (min)*	58.4 (14.4)	62.6 (19.8)	0.231
Duration of surgery (min)*	35.1 (14.2)	38.8 (17.2)	0.242
Fentanyl dose (µg kg ⁻¹)*	5.2 (1.6)	5.6 (1.7)	0.321
Antiemetic rescue Rx, more than 1 dose†	3 (6)	1 (2)	0.617
Morphine given in the PACU (mg)‡	3.5 (0–6)	3.5 (0–6)	0.831

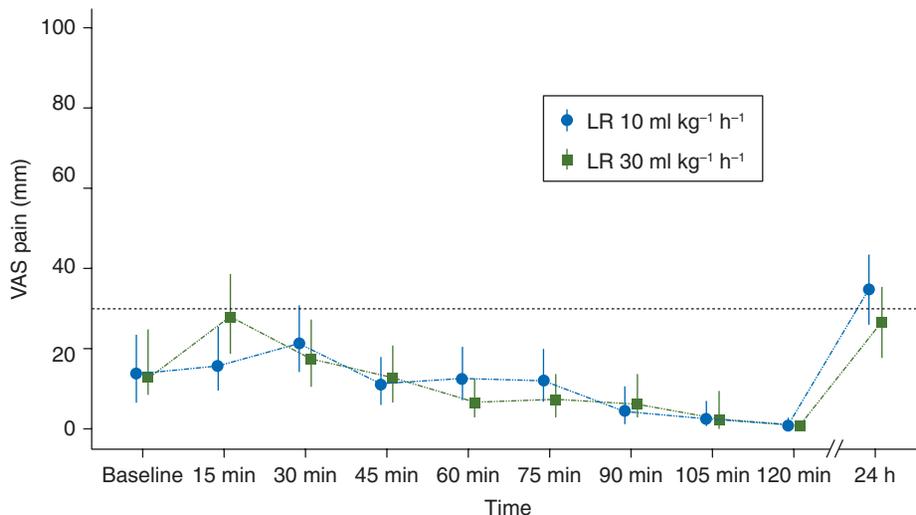


Fig 2 Postoperative VAS score. Values are presented as mean plus bootstrap 95% CI, based on 2000 replications with replacement and bias-corrected and accelerated. Two-way repeated measures ANOVA, $P=0.891$. LR, lactated Ringer's solution.

Table 3 Univariable analysis using logistic regression, composite outcome retching, vomiting, or both (0–24 h). OR, odds ratio; CI, confidence interval; PACU, post-anaesthetic care unit; POV, postoperative retching and/or vomiting. *Reference group is male. †Reference group is tonsillectomy. ‡Reference group is ASA I. †The variable was dropped because it predicts outcome perfectly

	POV (n=100)	
	OR (95% CI)	P-value
Gender female*	1.09 (0.46, 2.62)	0.845
Age (yr)	1.21 (0.97, 1.50)	0.091
Weight (kg)	1.04 (0.97, 1.10)	0.241
Adenotonsillectomy†	1.59 (0.17, 14.86)	0.685
ASA II‡	1.04 (0.43, 2.55)	0.928
Anaesthesia duration (1 min)	0.99 (0.97, 1.01)	0.402
Surgery duration (1 min)	0.99 (0.96, 1.01)	0.345
Fentanyl dose (1 $\mu\text{g kg}^{-1}$)	1.03 (0.78, 1.35)	0.835
Morphine given in the PACU (1 mg)	1.14 (0.99, 1.30)	0.061
History of POV or motion: sickness*	—	—
Fever (>100.4°F)	1.17 (0.12, 11.79)	0.892
Thirst (yes/no)	1.10 (0.42, 2.88)	0.846

and the severity of POV and also a decrease in pain with larger volume of i.v. fluids. Since opioids have a direct effect on the chemoreceptor trigger zone and super-hydration might decrease postoperative pain, one plausible explanation is that pain and secondary use of opioids mediate the effect between large volume i.v. fluid and POV. After adjusting for morphine use, we still were able to observe the protective effect of super-hydration on POV, suggesting that other pathways might also be involved. Fasting-related subclinical hypovolaemia leading to gut

ischaemia with subsequent increase in serotonin production is another plausible mechanism for POV.^{32 41 42} It is possible to speculate that the apparently greater antiemetic effect observed in the paediatric population is due to a higher risk of preoperative subclinical hypovolaemia, given the higher metabolic rate and greater body surface area/weight ratio compared with adults. Since we did not contemplate i.v. fluid administration during the postoperative period but only oral liquids, the possibility of a relatively low volume repletion in those subjects receiving 10 ml kg⁻¹ intraoperative infusion might also be considered. Unfortunately, we did not quantify the amount of oral liquids given in the PACU to clarify this possibility.

Several limitations in our study are worth noting. First, while outpatient tonsillectomy is a common practice in many institutions,^{43 44} all of our subjects stayed overnight. Nevertheless, many centres, such as our own, still consider tonsillectomy as an in-patient surgery and keep children hospitalized overnight after surgery.⁴⁵ This difference should be considered when generalizing the results, since POV is higher in outpatient care.^{46–48} Secondly, no child received prophylactic antiemetics in our study, in an attempt to reproduce Goodarzi and colleagues²⁵ protocol design in strabismus surgery. Withholding antiemetics in this type of surgery might raise ethical concerns. However, since our subjects were hospitalized overnight, we were able to effectively treat POV shortly after symptoms occurred. This strategy has been considered acceptable in terms of patient outcomes and satisfaction scores when compared with prophylactic treatment in adult patients.⁴⁹ Based on our results, however, we consider that for this type of surgery, super-hydration on its own is insufficient as a sole antiemetic prophylactic strategy. Our last limitation is that we did not administer steroids. Some evidence supports the use of dexamethasone for postoperative pain

Table 4 Multivariable logistic regression analysis, composite outcome retching, vomiting or both (0–24 h). OR, odds ratio; CI, confidence interval; PACU, post-anaesthetic care unit; POV, postoperative retching, vomiting or both. *Variables age, gender, and weight did not significantly improve the model fit. Hosmer and Lemeshow's goodness-of-fit test $P=0.53$. †Reference group is Group 2 (30 ml kg⁻¹)

	Unadjusted		Adjusted	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Model POV (n=100)*				
Group 1 (10 ml kg ⁻¹ h ⁻¹)†	2.79 (1.11, 7.01)	0.029	2.92 (1.14, 7.51)	0.026
Morphine given in the PACU (1 mg)			1.15 (1.00, 1.33)	0.056

relief^{50–52} and antiemetic prophylaxis^{50 52–55} in tonsillectomy patients. At the time of our study, dexamethasone was not routinely used in our institution because of the association between this drug and the increased risk of bleeding.³⁰ More recent studies have supported the routine use of dexamethasone in tonsillectomy,⁷ and it is now part of the standard-of-care in our institution.

In conclusion, the results of this study support the use of 30 ml kg⁻¹ h⁻¹ lactated Ringer's solution during tonsillectomy with or without adenoidectomy as an inexpensive alternative to decrease the risk of POV.

Declaration of interest

None declared.

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