Postoperative nausea and vomiting in pediatric anesthesia

Claudia Höhne

Purpose of review
Postoperative nausea and vomiting (PONV) has a high incidence in children and requires prophylactic and therapeutic strategies.

Recent findings
PONV can be reduced by the avoidance of nitrous oxide, volatile anesthetics, and the reduction of postoperative opioids. The use of dexamethasone, 5-HT_3 antagonists, or droperidol alone is potent, but combinations are even more effective to reduce PONV. Droperidol has a Food and Drug Administration warning. Hence, dexamethasone and 5-HT_3 antagonists should be preferred as prophylactic drugs. It is further reasonable to adapt PONV prophylaxis to different risk levels. Prolonged surgery time, inpatients, types of surgery (e.g. strabismus and ear–nose–throat surgery), and patients with PONV in history should be treated as high risk, whereas short procedures and outpatients are to be treated as low risk.

Summary
Concluding from the existing guidelines and data on the handling of PONV in children at least 3 years, the following recommendations are given: outpatients undergoing small procedures should receive a single prophylaxis, outpatients at high risk a double prophylaxis, inpatients with surgery time of more than 30 min and use of postoperative opioids should get double prophylaxis, and inpatients receiving a high-risk surgical procedure or with other risk factors a triple prophylaxis (two drugs and total intravenous anesthesia). Dimenhydrinate can be used as a second choice, whereas droperidol and metoclopramide can only be recommended as rescue therapy.

Keywords
5-HT_3 antagonist, children, complication, dexamethasone, PONV

INTRODUCTION

Although anesthetists are aware of postoperative nausea and vomiting (PONV/POV) as a common complication in pediatric anesthesia, its incidence in daily routine is still too high. During the last decade, different guidelines tried to standardize clinical practice, but failed to provide clear algorithms. Therefore, this review discusses the effectiveness, safety, adverse events, and economics of the currently available prophylaxis options and aims to give easy-to-use recommendations for everyday clinical practice.

INCIDENCE AND ASSESSMENT

The average incidence of PONV in childhood of between 33.2 and 82% can be twice as high compared with adults [1–5]. This high incidence warrants the use of antiemetic prophylaxis instead of therapy [2,6▪,7].

Eberhart *et al.* [8] identified four risk factors for PONV or POV in pediatric anesthesia: previous PONV or a positive family history, duration of anesthesia (>30 min), age (≥3 years), and strabismus surgery. The risk of POV was predicted as 9, 10, 30, 55, and 70%, respectively, depending on the presence of 0, 1, 2, 3, and 4 risk factors. Furthermore, excluding strabismus, the incidence of POV is 11.6% in the presence of only one risk factor, 28.2% POV with two risk factors, and up to 42.3% in the presence of three risk factors [9].

Department of Anesthesiology and Intensive Care Medicine, University of Leipzig, Leipzig, Germany

Correspondence to Claudia Höhne, MD, Professor, Department of Anesthesiology and Intensive Care Medicine, University of Leipzig, Liebigstrasse 20, D-04103, Leipzig, Germany. Tel: +49 341 97 19705; fax: +49 341 97 17709; e-mail: claudia.hoehne@medizin.uni-leipzig.de

Curr Opin Anesthesiol 2014, 27:303–308
DOI:10.1097/ACO.0000000000000073

KEY POINTS

- PONV has a higher incidence in children than in adults and warrants prophylactic strategies.
- Reduction of baseline risk factors is reasonable in all pediatric anesthesia cases.
- Dexamethasone, 5-HT3 antagonists, and TIVA are feasible pharmacologic strategies.
- Droperidol, dimenhydrinate, and metoclopramide can only be recommended as therapeutic rescue medication.
- Inpatients and outpatients have different PONV risk mainly because of variable anesthesia and surgery.

In addition, postdischarge nausea and vomiting (PDNV) describes nausea and vomiting even after discharge up to 7 days. In adults, the risk for PDNV is 10–80% depending on the number of risk factors such as female sex, age 50 years or less, or nausea in the postanesthesia care unit [10]. The incidence of PDNV in children highly depends on the type of surgery. After tonsillectomy, 20% of children experience PDNV on day 3 and still 8% on day 7 [11]. Davis *et al.* [12] were able to reduce this high risk from 32 to 14.5% treating the children with ondansetron-disintegrating tablets (two times daily for 3 days).

SPECIFIC EMETIC SURGICAL PROCEDURES IN CHILDREN

PONV has a multifactorial cause [13]. One important risk factor is the surgical procedure. Strabismus and ear–nose–throat surgery like tonsillectomy or adenoidectomy are associated with PONV incidences as high as 54 and 82%, respectively [1,14]. Even after prophylaxis, this incidence is still as high as 36 and 33%. Interestingly, new data show that appendectomy (42% nausea and 19.9% PONV) and combined small pediatric surgery (herniotomy and orchidopexy) are also associated with a very high risk for PONV (42.9% nausea and 28.6% PONV) [15]. Further, as outpatients have a lower PONV (10–29%) risk than inpatients (10–50%), the length of the procedure seems to be another influencing factor. As a result of this already lower PONV risk in very short procedures (surgery time of only about 19 min), it seems to be difficult to further reduce the incidence pharmacologically [16].

GENERAL ANTIEMETIC STRATEGIES DURING ANESTHESIA

Anesthetists are able to reduce the so-called baseline risk factors and can decrease the incidence of PONV with simple strategies [6▪]:

(1) avoidance of volatile anesthetics and preferential use of total intravenous anesthesia (TIVA) with propofol;
(2) preferential use of regional anesthesia or combined general and regional anesthesia to reduce postoperative opioids;
(3) multimodal postoperative pain therapy to reduce postoperative opioids;
(4) avoidance of nitrous oxide; and
(5) adequate hydration.

One part of a multimodal postoperative pain therapy to reduce opioid requirements is the use of nonsteroidal anti-inflammatory drugs (NSAIDs). However, there is still an ongoing debate about the potentially increased postoperative bleeding risk, especially after tonsillectomy. In a recent publication, Cardwell *et al.* [17▪] reviewed 12 trials evaluating the effect of NSAIDs on POV in 928 children. Apart from the expected decrease in emesis, Cardwell found no increase in bleeding events after the use of NSAIDs following tonsillectomy and adenoidectomy.

Another simple strategy to reduce emesis is super-hydration. Goodarzi *et al.* [14] and Elgueta *et al.* [1] showed that high-dose intravenous fluids (30 ml/kg/h) were associated with less emesis than the standard therapy (10 ml/kg/h) during strabismus repair (54 vs. 22% PONV) and tonsillectomy (82 vs. 62% PONV without any other prophylaxis).

The hypothesis that evacuation of gastric contents under anesthesia may reduce PONV could not be confirmed by two randomized controlled trials (RCTs) [18,19]. This maneuver, therefore, cannot be generally recommended as a nondrug PONV reduction strategy.

Further, Radke *et al.* [20] showed that prolonged postoperative fasting did not reduce the incidence of vomiting after general anesthesia in children when compared with a liberal regimen.

DRUGS FOR ANTIEMETIC STRATEGIES

Many drugs may reduce PONV. Dexamethasone, 5-HT3 antagonists, dimenhydrinate, droperidol, and metoclopramide will be discussed in detail.

Dexamethasone

Dexamethasone as glucocorticoid is one of the PONV prophylactic drugs. In adults, 4–5 mg of dexamethasone at the beginning of the procedure is effective to reduce PONV by 25% [21▪]. In children, there is no consent on the dose–response relationship. Kim *et al.* [22] could not show any difference in POV rate in children after adenotonsillectomy using dexamethasone 0.0625, 0.125, 0.25, 0.5, or 1 mg/kg (maximum dose 24 mg). In contrast, Czarnetzki *et al.* [23] found a dose-dependent reduction of POV, favoring higher

doses of up to 0.5 mg/kg dexamethasone. A recent Cochrane analysis concluded that 'appropriate dosing remains still unanswered and final recommendations must await randomized dose-control trials' [24]. Following these shortcomings, a prospective, randomized double-blind study by Hermans *et al.* [25▪] showed that 0.15 mg/kg dexamethasone was as effective as 0.5 mg/kg in reducing PONV incidence from 49% in placebo to 21 and 22%.

Side-effects of dexamethasone

One of the most severe complications of low-dose dexamethasone is the tumor lysis syndrome with consecutive hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia. These electrolyte and metabolic disturbances may progress very fast to clinical toxic effects, including renal insufficiency, cardiac arrhythmias, seizures, and death [26]. Clinical toxic effects have been reported in children with hematologic cancers who received intraoperative dexamethasone [27,28].

A second major concern is a potential increase in the bleeding incidences in children undergoing tonsillectomy. One randomized trial studying the dose–response of perioperative dexamethasone to PONV in children undergoing tonsillectomy was prematurely terminated because of a strong trend toward an increased risk for hemorrhagic events [23]. However, this effect was lost when primary hemorrhage cases, which are largely related to surgical technique, were excluded [29]. The following studies could not show an increased postoperative bleeding incidence comparing children receiving dexamethasone and placebo [30,31]. Subsequently, a clinical practice guideline from the American Academy of Otolaryngology-Head and Neck Surgery recommends the use of a single dose of dexamethasone in children undergoing tonsillectomy. Here, the benefits from dexamethasone such as decreased throat pain and POV incidence as well as earlier resumption of oral intake outweigh the risks [32].

The effect of dexamethasone on glucose metabolism and tolerance is another important issue. Dexamethasone may increase blood glucose concentration in adults undergoing bariatric surgery presenting with diabetes mellitus type II and high BMI [33]. In children, this increase in blood glucose could even be found independently of BMI [34].

5-HT3 antagonists

Ondansetron as one agent of the 5-HT_3 antagonist group is widely used for PONV prophylaxis and therapy [6▪]. Different reviews and meta-analysis give good evidence for this strategy [7,35,36]. Ondansetron may have a dose-dependent effect, but reduces PONV effectively with doses as low as 0.1–0.15 mg/kg intravenously [7]. Schnabel *et al.* [35] concluded in a systematic review that 5-HT_3 antagonists (ondansetron or granisetron) were more effective antiemetics than perphenazine in children. Further, Engelman *et al.* [36] did a Bayesian meta-analysis comparing six single antiemetics with five combination therapies, and concluded that single-drug prophylaxis with 5-HT_3 antagonists resulted in a relative risk reduction of 50%. However, Liechti *et al.* [37] found a further reduction in PONV incidence from 53% using tropisetron only to 24.4% by applying additional dexamethasone. In a RCT in 218 children undergoing orthopedic surgery, Park *et al.* [38▪] showed a clear advantage of ramosetron (8.3% PONV) vs. ondansetron (21.3%), especially concerning late PONV (6–24 h). There were no significant side-effects in both groups. Byon *et al.* [39] report a PONV incidence of 9% using ramosetron alone in a double-blind randomized trial in 405 children undergoing strabismus surgery.

Side-effects of 5-HT3 antagonists

In general, the 5-HT_3 receptor antagonists have a favorable side-effect profile and are considered equally well tolerated except palonosetron [6▪]. For chemotherapy-induced nausea and vomiting, the Food and Drug Administration (FDA) has recommended a dose of ondansetron not exceeding 16 mg in adults. The major concern regarding 5-HT_3 antagonists is the induction of cardiac dysrhythmias because of their QT interval lengthening effect. Mehta *et al.* [40] measured QT intervals and Tp-e intervals after the administration of droperidol or ondansetron in 108 children. Both drugs lengthened QT intervals by 10–17 ms and increased Tp-e intervals by 0–7 ms, with no intergroup differences. There were no instances of dysrhythmia. They concluded that droperidol and ondansetron, in therapeutic antiemetic doses, produce equivalent, clinically insignificant QT prolongation and negligible Tp-e prolongation, suggesting that neither is torsadogenic in healthy children at these doses, but clinicians have to be aware of this effect in children with long QT syndrome.

On the basis of the currently available data, dexamethasone 0.15 mg/kg (maximum 4–5 mg) and, for example, ondansetron 0.1 mg/kg (maximum 4 mg) can be recommended for prophylactic use in pediatric patients with risk for POV, unless there are contraindications. This is in accordance to the recommendation by the Association of Pediatric Anaesthetists of Great Britain, Ireland [41], and Germany [42].

Dimenhydrinate

Dimenhydrinate is an antihistamine drug with antiemetic effects. Kranke *et al.* [43] concluded in

a meta-analysis that dimenhydrinate is an inexpensive and clinically effective antiemetic. The reviewed placebo-controlled trials even suggest that its antiemetic efficacy may be similar to the 5-HT_3 receptor antagonists, dexamethasone, and droperidol. However, dimenhydrinate-treated patients tend to be more sedated and require significantly longer observation in the postanesthesia care unit (PACU) [44]. Further, optimal timing and dose–response have not yet been studied.

Droperidol

Droperidol has an antiemetic effect via dopaminergic receptors. As a result of its possible extrapyramidal symptoms, sedation, and QT prolongation leading to a FDA 'black box warning', the drug is currently recommended as rescue medication in therapy-refractory PONV only [45]. Schroeter *et al.* [46] showed in 144 children that a low dose of droperidol 10 μg/kg up to 1.25 mg was sufficient without neurological or cardiopulmonary side-effects. The risk of a prolonged QT syndrome is an absolute contraindication.

Metoclopramide

Metoclopramide is a dopaminergic antagonist with antiemetic properties. Bolton *et al.* [47] showed that in children undergoing tonsillectomy, prophylactic ondansetron was more effective in reducing PONV than metoclopramide with a dose of 0.5 mg/kg. A meta-analysis [7] of four studies investigating the effect of metoclopramide suggests that it is an effective agent, with no dose dependency. Thus, ondansetron 0.15 mg/kg is as effective as metoclopramide 0.5 mg/kg. The conclusion should be interpreted with caution because of the small amount of available data. Metoclopramide should not routinely be used as a prophylactic drug.

Concluding from all data, dimenhydrinate, droperidol, and metoclopramide seem to be effective drugs for rescue medication.

MULTIMODAL PROPHYLAXIS

In addition to reduction of general anesthesia-related baseline risk factors, pharmacologic prophylaxis with antiemetics should always be considered. Dose and time points are given in Table 1. Different combinations of drugs from different substance classes may be selected in order to optimize the effect. Meta-analyses showed that 5-HT_3 receptor antagonist combined with either dexamethasone [36,55] or droperidol [45,56] was more effective than monotherapy with any of the drugs. Further, droperidol alone was less effective than when combined with dexamethasone [57]. No differences were found between the efficiency of the following combinations: 5-HT_3 antagonist and dexamethasone, 5-HT_3 antagonist and droperidol, and dexamethasone and droperidol [56,57]. As a result of the 'black box warning' of the FDA because of the potential adverse events of droperidol, what remains as PONV prophylaxis in children is 5-HT_3 antagonist and dexamethasone.

ECONOMICS

PONV is the main cause of unplanned admission in all surgical specialties after day case surgery in 23.5% of children [58]. In 166 children after adenoidectomy and tonsillectomy, each episode of PONV increased the patient's length of stay in the PACU by 0.5 h [59].

RECOMMENDATION

Baseline risk reduction of PONV with avoidance of nitrous oxide and volatile anesthetics and preferential use of propofol instead, reduction of postoperative opioids with regional anesthesia and multimodal pain therapy, and adequate hydration are absolutely necessary in every pediatric anesthesia. The high incidence of PONV, existing not only in strabismus or ear–nose–throat surgery but also in general pediatric surgery, makes pharmacologic prophylaxis more than reasonable.

The following antiemetic interventions are feasible with a sensible risk–benefit ratio: TIVA, dexamethasone, and 5-HT_3 antagonist.

Concluding from all the reviewed data and guidelines, the author's recommendation for children at least 3 years are:

(1) outpatients (short anesthesia or surgery time less than 30 min, rare use of postoperative opioids):
   (a) small pediatric surgery: single prophylaxis;
   (b) strabismus or ear–nose–throat surgery or high-risk patients: double prophylaxis;
(2) inpatients (longer anesthesia or surgery time greater than 30 min, frequent use of postoperative opioids):
   (a) different pediatric surgical procedures: doubl prophylaxis;
   (b) strabismus or ear–nose–throat surgery or high risk: triple prophylaxis; and
(3) rescue therapy:
   (a) dimenhydrinate;

Table 1. Drugs for PONV prophylaxis, dose, time of application, and adverse events and contraindication

Drug	Substance group	Dose	Time of application	Adverse effects and contraindication
Dexamethasone [25▪,48]	Corticosteroids	0.1–0.15 mg/kg, maximum 4–5 mg	At induction	AE: potential increased BG
				CI: hematologic cancers, severe obesity and diabetes mellitus
Dolasetron [49]	Serotonin antagonist (5-HT_3 receptors)	0.35 mg/kg, maximum 12.5 mg	End of surgery	AE: headache and dizziness
				CI: QT prolongation
Granisetron [50,51]		0.02–0.04 mg/kg, maximum 0.6–1 mg		
Ondansetron [52]		0.1 mg/kg, maximum 4 mg		
Ramosetron [38▪,39]		0.006 mg/kg		
Tropisetron [53]		0.1 mg/kg, maximum 2 mg		
Droperidol [45]	Dopamine antagonist, butyrophenone (D2 receptors)	0.01–0.015 mg/kg, maximum, 1.25 mg	End of surgery	AE: extrapyramidal disturbance, sedation
				CI: QT prolongation
Metoclopramide [47,54]	Dopamine antagonist, benzamide (D2 receptors	0.15–0.5 mg/kg, maximum 25–50 mg	30 min prior to the end of surgery	AEs: extrapyramidal disturbance, hypotension (following fast injection)
Dimenhydrinate [43]	Histamine antagonists (H1 receptors)	0.5 mg/kg, maximum 25–62 mg	Intraoperatively	AE: sedation

These data are evidence based, though not all the drugs have an FDA or equal European institutional approval for PONV. PONV, postoperative nausea and vomiting. AE, adverse event; BG, blood glucose; CI, contraindication.

(b) droperidol; and
(c) metoclopramide.

These recommendations aim to avoid unnecessary risks for rare but well described side-effects of antiemetic drugs in low-risk patients, but to reduce the high PONV incidence in medium and high-risk patients.

The high incidence of PDNV in children can be reduced with ondansetron disintegrated tablets given until the third day after tonsillectomy and this makes continued prophylaxis with 5-HT_3 antagonists reasonable. Further RCTs are necessary to highlight this topic.

CONCLUSION

The incidence of PONV in children is still too high in outpatients and inpatients. There are simple strategies to reduce baseline risk. Additionally, prophylactic drugs should be used in adaption to the risk: inpatients and outpatients, surgical procedure, and individual risk.

Acknowledgements

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:
- ▪ of special interest
- ▪▪ of outstanding interest

1. Elgueta MF, Echevarria GC, De la Fuente N, *et al.* Effect of intravenous fluid therapy on postoperative vomiting in children undergoing tonsillectomy. Br J Anesth 2013; 110:607–614.
2. Apfel CC, Kranke P, Piper S, *et al.* Nausea and vomiting in the postoperative phase. Expert- and evidence-based recommendations for prophylaxis and therapy. Anaesthesist 2007; 56:1170–1180.
3. Eberhart LH, Morin AM, Guber D, *et al.* Applicability of risk scores for postoperative nausea and vomiting in adults to paediatric patients. Br J Anaesth 2004; 93:386–392.
4. Hamid SK, Selby IR, Sikich N, *et al.* Vomiting after adenotonsillectomy in children: a comparison of ondansetron, dimenhydrinate, and placebo. Anesth Analg 1998; 86:496–500.
5. Lerman J. Surgical and patient factors involved in postoperative nausea and vomiting. Br J Anaesth 1992; 69:24S–32S.
6. ▪ Gan TJ, Diemunsch P, Habib AS, *et al.* Consensus guidelines for management of postoperative nausea and vomiting. Anesth Analg 2014; 118:85–113.
These guidelines summarize the most recent data about PONV and prophylactic strategies in adults and children.
7. Bolton CM, Myles PS, Nolan T, *et al.* Prophylaxis of postoperative vomiting in children undergoing tonsillectomy: a systematic review and meta-analysis. Br J Anaesth 2006; 97:593–604.
8. Eberhart LH, Geldner G, Kranke P, *et al.* The development and validation of a risk score to predict the probability of postoperative vomiting in pediatric patients. Anesth Analg 2004; 99:1630–1637.

9. Kranke P, Eberhart LH, Toker H, *et al.* A prospective evaluation of the POVOC score for the prediction of postoperative vomiting in children. Anesth Analg 2007; 105:1592–1597.
10. Apfel CC, Philip BK, Cakmakkaya OS, *et al.* Who is at risk for postdischarge nausea and vomiting after ambulatory surgery? Anesthesiology 2012; 117:475–486.
11. Stanko D, Bergesio R, Davis K, *et al.* Postoperative nausea and vomiting following adeno-tonsillectomy – a long term follow up. Pediatr Anesth 2013; 23:690–696.
12. Davis PJ, Fertal KM, Boretsky KR, *et al.* The effects of oral ondansetron disintegrating tablets for prevention of at-home emesis in pediatric patients after ear–nose–throat surgery. Anesth Analg 2008; 106:1117–1124.
13. Kovac AL. Management of postoperative nausea and vomiting in children. Paediatr Drugs 2007; 9:47–69.
14. Goodarzi M, Matar MM, Shafa M, *et al.* A prospective randomized blinded study of the effect of intravenous fluid therapy on postoperative nausea and vomiting in children undergoing strabismus surgery. Paediatr Anaesth 2006; 16:49–53.
15. Balga I, Conrad C, Meissner W. Pediatric postoperative quality analysis. Pain and postoperative nausea and vomiting. Anaesthesist 2013; 62:707–719.
16. De Orange FA, Marques J, Flores M, *et al.* Dexamethasone versus ondansetron in combination with dexamethasone for the prophylaxis of postoperative vomiting in pediatric outpatients: a double-blind, randomized, placebo-controlled clinical trial. Pediatr Anesth 2012; 22:890–896.
17. ■ Cardwell ME, Siviter G, Smith AF. Nonsteroidal anti-inflammatory drugs and perioperative bleeding in paediatric tonsillectomy. Cochrane Database Syst Rev 2013; 7:CD003591.

The Cochrane analysis highlights the long-lasting discussion about the use of NSARs after the painful tonsillectomy and the potential risk of increased life-threatening bleeding events.

18. Chukudebelu O, Leonard DS, Healy A, *et al.* The effect of gastric decompression on postoperative nausea and emesis in pediatric, tonsillectomy patients. Int J Pediatr Otorhinolaryngol 2010; 74:674–676.
19. Jones JE, Tabaee A, Glasgold R, *et al.* Efficacy of gastric aspiration in reducing posttonsillectomy vomiting. Arch Otolaryngol Head Neck Surg 2001; 127:980–984.
20. Radke OC, Biedler A, Kolodzie K, *et al.* The effect of postoperative fasting on vomiting in children and their assessment of pain. Paediatr Anaesth 2009; 19:494–499.
21. ■ De Oliveira GS, Santana Castro-Alves LJ, Ahmad S, *et al.* Dexamethasone to prevent postoperative nausea and vomiting: an updated meta-analyses of randomized controlled trials. Anesth Analg 2013; 116:58–74.

This study gives the recent and useful data about the pros and cons of dexamethasone use for PONV prophylaxis.

22. Kim MS, Coté CJ, Cristoloveanu C, *et al.* There is no dose escalation response to dexamethasone (0.0625–10 mg/kg) in pediatric tonsillectomy or adenotonsillectomy patients for preventing vomiting, reducing pain, shortening time to first liquid intake, or the incidence of voice change. Anesth Analg 2007; 104:1052–1058.
23. Czarnetzki C, Elia N, Lysakowski C, *et al.* Dexamethasone and risk of nausea and vomiting and postoperative bleeding after tonsillectomy in children: a randomized trial. JAMA 2008; 300:2621–2630.
24. Steward DL, Grisel J, Meinzen-Derr J. Steroids for improving recovery following tonsillectomy in children. Cochrane Database Syst Rev 2011; CD003997.
25. ■ Hermans V, De Pooter F, De Groote F, *et al.* Effect of dexamethasone on nausea, vomiting, and pain in paediatric tonsillectomy. Br J Anesth 2012; 109:427–431.

An important RCT about the single use of dexamethasone for PONV prophylaxis.

26. Howard SC, Jones DP, Pui CH. The tumor lysis syndrome. N Engl J Med 2011; 364:1844–1854.
27. McDonnell C, Barlow R, Campisi P, *et al.* Fatal peri-operative acute tumour lysis syndrome precipitated by dexamethasone. Anaesthesia 2008; 63:652–655.
28. Osthaus WA, Linderkamp C, Bünte C, *et al.* Tumor lysis associated with dexamethasone use in a child with leukemia. Paediatr Anaesth 2008; 18:268–270.
29. Gunter JB, Willging JP, Myer CM 3rd. Dexamethasone and postoperative bleeding after tonsillectomy in children. JAMA 2009; 301:1764–1765.
30. Gallagher TQ, Hill C, Ojha S, *et al.* Perioperative dexamethasone administration and risk of bleeding following tonsillectomy in children. A randomized controlled trial. JAMA 2012; 308:1221–1224.
31. Plante J, Turgeon AF, Zarychanski R, *et al.* Effect of systemic steroids on posttonsillectomy bleeding and reinterventions: systematic review and meta-analysis of randomised controlled trials. BMJ 2012; 345:e5389.
32. Baugh RF, Archer SM, Mitchell RB, *et al.* American Academy of Otolaryngology-Head and Neck Surgery Foundation. Clinical practice guideline: tonsillectomy in children. Otolaryngol Head Neck Surg 2011; 144:S1–S30.
33. Hans P, Vanthuyne A, Dewandre PY, *et al.* Blood glucose concentration profile after 10 mg dexamethasone in nondiabetic and type 2 diabetic patients undergoing abdominal surgery. Br J Anaesth 2006; 97:164–170.
34. Gnatzy R, Hempel G, Hebestreit A, *et al.* The effect of intraoperative administration of dexamethasone for PONV prophylaxis on perioperative blood glucose level in obese and normal weight children. ESPA Meeting, Best Free Paper Session. Stresa, Italy; 2012.
35. Schnabel A, Eberhart LH, Muellenbach R, *et al.* Efficacy of perphenazine to prevent postoperative nausea and vomiting: a quantitative systematic review. Eur J Anaesthesiol 2010; 27:1044–1051.
36. Engelman E, Salengros JC, Barvais L. How much does pharmacologic prophylaxis reduce postoperative vomiting in children? Calculation of prophylaxis effectiveness and expected incidence of vomiting under treatment using Bayesian metaanalysis. Anesthesiology 2008; 109:1023–1035.
37. Liechti M, Feurer R, Gross D, *et al.* Prevention of postoperative nausea and vomiting in children following adenotonsillectomy, using tropisetron with or without low-dose dexamethasone. J Anesth 2007; 21:311–316.
38. ■ Park YV, Yang YE, Byon HJ, *et al.* Comparison of the efficacy of ramosetron and ondansetron in the prophylaxis of postoperative vomiting in children receiving fentanyl by patient-controlled analgesia after orthopedic surgery: a randomized controlled trial. Pediatr Anesth 2013; 23:360–364.

This RCT shows the higher efficacy of ramosteron than ondansetron in children.

39. Byon HJ, Lee SJ, Kim JT, *et al.* Comparison of the antiemetic effect of ramosetron and combined ramosetron and midazolam in children: a double-blind, randomised clinical trial. Eur J Anesthesiol 2012; 29:192–196.
40. Mehta D, Sanatani S, Whyte SD. The effects of droperidol and ondansetron on dispersion of myocardial repolarization in children. Paediatr Anaesth 2010; 20:905–912.
41. The Association of Paediatric Anaesthetists of Great Britain & Ireland. Guidelines on the prevention of postoperative vomiting in children. 2009. Available at http://www.google.com/url?sa=t&rct=j&q=&esrc=s&sou rce=web&cd=2&ved=0CDAQFjAB&url=http%3A%2F%2F Guidelines_on_the_Prevention_of_Postoperative_Vomiting_ in_Children.pdf&ei=il1PUP6FDaPj0QHIxICAAQ&usg=AFQ jCNEFPDwR2y-1n6-6TONmxwt18Y5BMg&sig2=9pzb3IQN517UzzFWE6Oktw&cad=rja. [Accessed 11 September 2012].
42. Becke K, Kranke P, Weiss M, *et al.* Guidelines for risk evaluation, prophylaxis and therapy of postoperative vomiting in children. Anästh Intensivmed 2007; 48:S95–S98.
43. Kranke P, Morin AM, Roewer N, *et al.* Dimenhydrinate for prophylaxis of postoperative nausea and vomiting: a metaanalysis of randomized controlled trials. Acta Anaesthesiol Scand 2002; 46:238–244.
44. Welters ID, Menges T, Graf M, *et al.* Reduction of postoperative nausea and vomiting by dimenhydrinate suppositories after strabismus surgery in children. Anesth Analg 2000; 90:311–314.
45. Henzi I, Sonderegger J, Tramèr MR. Efficacy dose–response and adverse effects of droperidol for prevention of postoperative nausea and vomiting. Can J Anaesth 2000; 47:537–551.
46. Schroeter E, Schmitz A, Haas T, *et al.* Low dose droperidol in children. Rescue therapy for persistent postoperative nausea and vomiting. Anaesthetist 2012; 61:30–34.
47. Bolton CM, Myles PS, Carlin JB, *et al.* Randomized, double-blind study comparing the efficacy of moderate-dose metoclopramide and ondansetron for the prophylactic control of postoperative vomiting in children after tonsillectomy. Br J Anaesth 2007; 99:699–703.
48. Madan R, Bhatia A, Chakithandy S, *et al.* Prophylactic dexamethasone for postoperative nausea and vomiting in pediatric strabismus surgery: a dose ranging and safety evaluation study. Anesth Analg 2005; 100:1622–1626.
49. Olutoye O, Jantzen EC, Alexis R, *et al.* A comparison of the costs and efficacy of ondansetron and dolasetron in the prophylaxis of postoperative vomiting in pediatric patients undergoing ambulatory surgery. Anesth Analg 2003; 97:390–396.
50. Rüsch D, Eberhardt LHJ, Wallenborn J, *et al.* Nausea and vomiting after surgery under general anesthesia. An evidence-based review concerning risk assessment, prevention, and treatment. Dtsch Arztebl Int 2010; 107:733–741.
51. Cieslak GD, Watcha MF, Phillips MB, *et al.* The dose response relation and cost-effectiveness of granisetron for the prophylaxis of pediatric postoperative emesis. Anesthesiology 1996; 85:1076–1085.
52. Khalil SN, Roth AG, Cohen IT, *et al.* A double-blind comparison of intravenous ondansetron and placebo for preventing postoperative emesis in 1- to 24-month-old pediatric patients after surgery under general anesthesia. Anesth Analg 2005; 101:356–361.
53. Kranke P, Eberhart LH, Apfel CC, *et al.* Tropisetron for prevention of postoperative nausea and vomiting: a quantitative systematic review. Anaesthesist 2002; 51:805–814.
54. Wallenborn J, Gelbrich G, Bulst D, *et al.* Prevention of postoperative nausea and vomiting by metoclopramide combined with dexamethasone: randomised double blind multicentre trial. BMJ 2006; 333:324–327.
55. Henzi I, Walder B, Tramer MR. Dexamethasone for the prevention of postoperative nausea and vomiting: a quantitative systematic review. Anesth Analg 2000; 90:186–194.
56. Habib AS, El-Moalem HE, Gan TJ. The efficacy of the 5-HT3 receptor antagonists combined with droperidol for PONV prophylaxis is similar to their combination with dexamethasone. A meta-analysis of randomized controlled trials. Can J Anaesth 2004; 51:311–319.
57. Apfel CC, Korttila K, Abdalla M, *et al.* A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. N Engl J Med 2004; 350:2441–2451.
58. Blacoe DA, Cunning E, Bell G. Paediatric day-case surgery: an audit of unplanned hospital admission Royal Hospital for Sick Children, Glasgow. Anesthesia 2008; 63:610–615.
59. Edler AA, Mariano ER, Goliano B. An analysis of factors influencing post-anesthesia recovery after pediatric ambulatory tonsillectomy and adenoidectomy. Anesth Analg 2007; 104:784–789.