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Postoperative Vomiting In Children

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Postoperative vomiting (POV) is approximately twice as frequent amongst children as adults with an incidence of 13-42% in all paediatric patients. [1,2] Severe POV can result in a range of complications including wound dehiscense, dehydration, electrolyte imbalance and pulmonary aspiration.[3] It is one of the leading causes of parental distress after surgery and is the leading cause of unanticipated hospital admission following ambulatory surgery resulting in increased health care costs.[4,5] Importantly, no research has focused on the children's perspective of postoperative vomiting , and whether they perceive this symptom with the same distress and loathing as adults.[6] Identifying children at high risk of POV is beneficial as prophylactic antiemetic therapy can then be targeted at this group. Indiscriminate prophylaxis is probably unnecessary as it is financially costly and may result in excessive adverse drug reactions.[7] Research into this important area is hampered by the difficulty in diagnosing nausea in younger children. Hence, vomiting and retching are used as the end points in most of the paediatric literature on this subject.[2]

I. Physiology of vomiting reflex

Vomiting is integrated by the vomiting centre, located in the dorsal part of the lateral reticular formation in the medulla oblongata. The vomiting centre contains predominately acetylcholine (ACh) receptors, with some histamine (H1) receptors. It receives input from the cerebral cortex, chemoreceptor trigger zone (CTZ), and the nucleus tractus solitarius (NTS). The cerebral cortex receives afferent CNS input from pathways mediating pain, smell, sight, emotion (fear/anxiety), and organic disturbances. The CTZ is functionally located outside the blood brain barrier on the floor of the fourth ventricle in the area postrema. It contains serotonin (5HT3) and dopamine receptors. It receives input from the vestibular apparatus, which contains H1 and ACh receptors. The NTS contains 5HT3 receptors, and receives input from the gastrointestinal tract stretch and chemoreceptors. The efferent pathways are carried by the vagus, hypoglossal, glossopharyngeal, trigeminal, and facial nerves to the stomach and via the spinal nerves to the diaphragm and abdominal muscles. The causes of POV are wide ranging. They include emotional, pharmacological and chemical stimuli, and also direct physical causes, such as the presence of blood in the gastrointestinal tract. The integrated pathway is complex, dynamic and multidimensional. Consequently, management must address several factors and there are both pharmacological and non-pharmacological options. Vomiting has two phases: 'pre-ejection' and 'ejection'. In the pre-ejection phase, the sympathetic nervous system causes the unpleasant symptoms of tachycardia, tachypnoea and sweating, whilst the parasympathetic system causes salivation, upper and lower oesophageal sphincter relaxation and retrograde contraction. This prepares the body for the ejection phase. In older children, the pre-ejection phase is experienced as nausea. The ejection phase starts with cessation of respiration in midinspiration; the hyoid and larynx elevate to open the crico-oesophageal sphincter, the glottis closes, the soft palate elevates to close off the nasopharynx, and contraction of the diaphragm occurs to increase intra-abdominal pressure. Finally, the gastro-oesophageal sphincter opens and the gastric contents are ejected.

II. CONSEQUENCES OF PONV

The consequences of POV are costly to the patient and family, the anaesthesiologist, and the institution. They also have the potential to impede recovery from surgery as POV results in adverse psychological, metabolic, and physiological events, including discomfort, hunger, dehydration, electrolyte imbalance and pulmonary aspiration. Pulmonary aspiration under anaesthesia has an incidence of 9.3 per 10,000 children.[8] There may be adverse surgical effects, such as wound dehiscence and reduced or delayed mobilisation. The cost to the institution results from delayed discharges or unanticipated hospital admissions of which 2% result from POV.[4,9] The institution must provide funding for the acquisition of drugs and strategies to prevent or treat

POV, but with a cost-effective strategy. Recently, the collection of data on patients' satisfaction, such as the 'NHS Friends and Family Test', is becoming more widespread and is likely to be influenced by events, such as POV. Injudicious use of antiemetic prophylaxis to every patient can lead to unnecessary and unjustified drug reactions, as demonstrated in the RCoA's Sixth National Audit Project, which examined perioperative anaphylaxis.[10] Furthermore, it has not been shown to improve outcome.[7] It is thereby imperative that all patients are risk stratified objectively and treated appropriately.

III. BASELINE ASSESSMENT OF THE RISK OF POV

Determining each patient's baseline risk allows the clinician to inform the patient and family, and to apply measures to reduce preventable factors and administer prophylaxis or treatment most appropriately (Table 1).

Table 1: Baseline assessment of the risk of POV

Steps for the clinician	Considerations amd options
Assess baseline risk factors	Age >3 years Surgery>30 minutes Strabismus and tonsillectomy Surgery
Inform patient and parent	Good communication
Decrease baseline risk	Regional anaesthesia Propofol Hydration
Treatment	Prophylaxis Treatment

Figure 1: Modified with permission from Morrison C, Wilmshurst S. Postoperative vomiting in children. BJA Educ. 2019 Oct;19(10):329-333.

RISK FACTOR ASSESSMENT

Children may have independent features which can be classified as low or high risk for developing POV, and should receive appropriate treatment (Table 2). The first step in determining who requires treatment is to determine a patient's baseline risk in terms of patient, anaesthesia or surgery-related factors.

Patient related

Nausea is difficult to recognise in very young children. This differs from the adult population, where the presence of symptoms of nausea allows for treatment before vomiting occurs. Children aged 3 yrs and above are at greater risk than those aged <3 yrs. In infancy, the rate of POV is around 5% compared to 20% in those of preschool age.[11] A large study demonstrated an incremental increase in POV incidence of 0.2 to 0.8% per year from the age of 3 yrs until adolescence.[12] Children with a prior history or direct family member history of POV, or those with a history of motion sickness are at an increased risk. Adult female patients are more at risk than males. In prepubertal children, there are no differences between boys and girls, but adolescent girls have two to four times the higher risk of POV than boys.[12,13] Management of anxiety in children is key to providing positive experience for patients in many areas of anaesthesia. There is low-level scientific but strong anecdotal evidence that anxiety increases the risk of POV, especially with air swallowing during a traumatic induction of anaesthesia.[14] The incidence of POV may be decreased by passive smoking; but this is not recommended as a preventative strategy.[3] There is weak evidence that higher BMI contributes to POV.

Table 2: Risk assessment for POV

Risk Category	Factors	Risk Factors	Treatment
No Risk	Patient	<3 years of age, no history of POV or motion sickness	No prophylaxis
	Anaesthetic	None	
	Surgical	<30 min duration	
Low Risk	Patient	>30 years of age, postpubertal female	Single prophylaxis
	Anaesthetic	Volatiles, opioids and anticholinesterases	
	Surgical	>30 min duration	
High Risk	Patient	Previous history of POV or motion sickness	Double prophylaxis; I consider TIVA usimg propofol as single agent
	Anaesthetic	Volatiles, N2O, Opioids and anticholinesterases	
	Surgical	Strabismus, tonsillectomy with or without adenoidectomy, middle ear surgery	

Figure 2: Modified with permission from Morrison C, Wilmshurst S. Postoperative vomiting in children. BJA Educ. 2019 Oct;19(10):329-333.

Anaesthesia related

The use of all inhalational anaesthetic agents, including nitrous oxide (N2O), contributes to the risk of POV. This risk is further amplified by the use of opioids and anticholinesterases. Total intravenous anaesthesia (TIVA) is as effective as a single-dose antiemetic, and therefore, its use may be considered in at risk patients of POV.[15] Maintaining adequate hydration decreases the risk of POV. The current recommendation for clear fluids for fasting in children is 1 h, but institutional guidelines should be followed.[16] Where possible, the use of opioid sparing regional anaesthesia should be considered.

Surgery related

Surgery lasting greater than 30 minutes in duration is an independent risk factor for POV, with an odds ratio of 3.25.[12,17] Procedures that are painful and have a high opioid requirement increase the risk. Tonsillectomy carries a high risk of POV.[18] This may be compounded by the administration of opioids. Certain procedures, such as middle ear and squint surgery, carry a higher risk, probably because of direct surgical stimulation of the vagus nerve and vestibular apparatus.

Risk scores for predicting POV

Two widely used risk scoring systems in children for POV are the postoperative vomiting in children score (POVOC) and the vomiting in the postoperative period score (VPOP). POVOC, developed by Eberhart and colleagues, identifies four independent variables, each scoring 1 point: strabismus surgery, age 3 yrs, duration of surgery >30 min and a history of PONV.[12] The VPOP scoring system provides the addition of multiple doses of opioids.[19]

Two other studies have identified four similar independent risk factors for POV in children: duration of surgery greater than 30 min, age >3 yrs, past or direct family member history of POV and strabismus surgery. Each study demonstrated an incremental increase in POV with each risk factor in an additive manner.[12,20] Children with independent risk factors should be considered for prophylactic antiemetic medication.

PHARMACOLOGIC TREATMENT OF POSTOPERATIVE VOMITING IN CHILDREN

Several guidelines on the management of POV in children have been published, including the most recent Association of Paediatric Anaesthetists of Great Britain and Ireland guidelines published in 2016.[13,17,21] The key features are to reduce modifiable risk factors and institute appropriate treatment. Children should be assessed using the risk scores to determine the pharmacological treatment.

IV. Anti-emetics for Prevention & Reduction of Postoperative Vomiting In Children

5HT3 Antagonists

5HT3 antagonists are effective anti-emetics in children. There are a large number of studies available examining the increasing number of these agents available as well as some of the other issues related to administration of 5HT3 antagonists. Ramosetron is a recent addition with new evidence to support its use in children.

ONDANSETRON

Ondansetron is licensed for use in the UK in children and young people (aged 2-18 years) for reducing post-operative vomiting and is commonly used. The product licence is for ondansetron 0.15mg/kg up to a maximum of 4mg.

TROPISETRON

Tropisetron is an effective anti-emetic for POV in children. It does not yet have a product license for use in children in the UK.

GRANISETRON

Three studies of the efficacy of granisetron in children undergoing tonsillectomy demonstrate an odds ratio for POV of 0.11 using a dose range of 10-80 mcg/kg. There is no clear dose related response as seen with ondansetron. [22] Furthermore a Cochrane meta-analysis suggests that the effect of granisetron on reducing POV may be overestimated by these papers.[23]

DOLASETRON

In a dose finding study in 204 children undergoing daycase surgery, dolasetron 350 mcg/kg was as effective at preventing POV as ondansetron 100 mcg/kg. [24] One study on 150 dexamethasone-pretreated children undergoing tonsillectomy showed an odds ratio of 0.25 for POV in children given dolasetron.[25]
Acute electrocardiographic changes in children and adolescents occur very commonly with dolasetron. There is evidence to suggest that acute changes in QTc interval are greater in children than in adults. Individual cases of sustained supraventricular and ventricular arrhythmias, cardiac arrestand myocardial infarction have been reported in children and adolescents. The use of dolasetron in children and adolescents under 18 years old is contraindicated.

RAMOSETRON

This recent addition to the 5-HT3 antagonists has a higher affinity and longer duration of action than ondansetron. A meta-analysis conducted without the fabricated literature of Fujii et al. compared Ramosetron with ondansetron or Placebo in adults.[26] The relative risk reduction in POV of 0.3mg of Ramosetron compared with Placebo was 0.48 (<6hr) and 0.5 (6-12 hours).
Ramosetron is not currently licensed for use in children. The pharmacokinetics need to be evaluated in children and dose ranging studies carried out. Further evidence of Ramosetron's use in paediatric POV is required before it can be recommended in preference to ondansetron.

DEXAMETHASONE

Dexamethasone has increasingly become recognised as an effective anti-emetic in children on its own and in combination with 5HT3 antagonists

METOCLOPRAMIDE

Metoclopramide in doses ranging from 0.15 mcg/kg to 0.25 mcg/kg has been shown to reduce POV in children in some studies only. [27-29] Overall, there is little support in the literature for the use of metoclopramide as an anti-emetic in children for the prophylaxis of post-operative vomiting in the doses tested (usually 0.25 mcg/kg). [30, 31, 32-36]

PROCHLORPERAZINE

The anti-emetic effect of prochlorperazine in children has not been determined. Side-effects have been reported when children have been given prochlorperazine .[37] These are predominantly neurological, independent of dose and disappeared spontaneously after discontinuation of the drug. Impaired consciousness, dyskinesia, pyramidal signs and hypertonus were the main neurological manifestations.

CYCLIZINE

Cyclizine is a piperazine antihistamine available over-the-counter and by prescription in the UK, Canada, US and Australia. In Canada the use of cyclizine for patients under 6 years old Is off-label. It has been reported as a drug with potential for abuse.[38]

DIMENHYDRINATE

Dimenhydrinate is the theoclate salt of diphenhydramine. Dimenhydrinate is available in Canada, the US and Australia both over-the counter and by prescription. It is not available In the UK. It can be given orally, intravenously and as a suppository. It was synthesized with the intention of antagonizing the moderately sedative effects of diphenhydramine with the mildly stimulant effects of theophylline. However sedation and dry mouth and other anti-muscarinic side effects do occur. Serious adverse reactions appear to be rare although it is a weakness of both published RCTs and meta-analyses that there is little documentation of side effects.

DROPERIDOL

This drug has been used as an antipsychotic and anti-emetic drug for several decades. It is a dopaminergic and GABA receptor antagonist. It has sedative effects, prolongs the Qt interval and is known to cause extra-pyramidal symptoms on occasion.

The use of droperidol is generally confined to rescue therapy, rather than Prophylaxis because of the concerns around sedation, extrapyramidal side effects (although they are infrequent and dose related), and the FDA warnings.

V. Anti-emetics for Treating Established Post-operative Vomiting in Children

There are few trials of efficacy of anti-emetics in controlling established POV in the recovery room in adults and even fewer in children, [3] compared to the multitude of trials on prophylaxis of POV. There is only one trial of a single dose of ondansetron (0.1 mg/kg) versus placebo for managing established POV in children who have not received prophylactic therapy [39]: children experiencing two emetic episodes within 2h of discontinuing anaesthesia were given IV ondansetron 0.1 mg/kg up to 4mg (n = 192) or placebo (n= 183). The proportion of children with no emetic episodes and no use of rescue medication was significantly greater (P <0.001) in the ondansetron group compared with placebo for both 2- and 24-h periods after study drug administration (78% of the ondansetron group and 34% of the placebo group for 2h; 53% of the ondansetron group and 17% of the placebo group for 24 h). Conclusions were a single dose of ondansetron (0.1 mg/kg up to 4 mg) is effective and well tolerated in the prevention of further episodes of postoperative emesis in children after outpatient surgery.

Table 3: Treatment of postoperative vomiting in children

Treatment Category	Classification	Drug	Dosage	Contraindications
Prevention/prophylaxis	5HT3 antagonists	Ondansetaron	0.15mg/kg, Maximum 4mg	Avoid in children with prolonged QT intervals
		Tropisetron	0.1 to 0.2 mg/kg. (Maximum 2 mg)	Not yet licensed for use in children
		Granisetron	10 to 80 mcg/kg (Maximum 3 mg	More evidence required
		Dolasetron	350 mcg/kg (Maximum 12.5 mg)	Contraindicated in children because of cardiac arrythmias
		Ramosetron	Undetermined	Further evaluation needed
	Steroids	Dexamethasone	0.0625 to 0.15 mg/kg (Maximum 8 mg)	Avoid in patients at risk of tumour lysis syndrome
	Antidopaminergics	Metoclopramide	0.25 mg/kg (Maximum of 10 mg)	Risk of extrapyramidal efffects, contraindicated in children <1 year of age
		Proclorperazine		Not recommended
		Droperidol	25 mcg/kg (Maximum	Second line to

			2.5 mg)	dexamethasone, long QT syndrome
	Antihistamines	Cyclizine		Not recommended
		Dimenhydrinate	0.5 mg/kg (Maximum 25 mg)	No clear evidence
	Combination therapy	Ondansetron and dexamethasone [40-42]	150 mcg/kg and 150 mcg/kg	
		Ondansetron and droperidol [43]	150 mcg/kg and 25 mcg/kg	
		Tropisetron and dexamethasone [37]	0.1 mg/kg and 0.5 mg/kg	
Treatment of established vomiting	5HT3 ANTAGONISTS	Ondansetron	0.1 mg/kg	
Novel approaches		Stimulation of P6 Accupuncture point		

Figure 3: Modified with permission from Morrison C, Wilmshurst S. Postoperative vomiting in children. BJA Educ. 2019 Oct;19(10):329-333.

NON-PHARMACOLOGICAL TREATMENT OF POST-OPERATIVE VOMITING IN CHILDREN

A variety of different non-pharmacological options have been described in order to prevent or treat PONV in children but the number of publications as well as patient numbers and study design are often insufficient to allow for a meta-analysis or structured review (i.e, type of bandaging following bat-ear surgery [44]). Thus, this section will only focus on the different types of stimulation of the P6 acupuncture point (acupuncture, acupressure, or electrical/laser stimulation) that has been reported in children.

Stimulation of the P6 Acupuncture Point

A meta-analysis in 1999 concluded various types of acustimulation in adults were equally effective compared to anti-emetic drugs in preventing vomiting after surgery and that such non- pharmacologic alternatives were more effective than placebo in preventing PONV in the early postoperative period.[45] No benefit was found within the paediatric population in this review.

VI. Conclusions

POV has detrimental effects for the patient, surgical recovery, the healthcare professional and the institution. Children should be risk stratified to receive appropriate management of risk factors and antiemetic therapy. Wherever possible, strategies to decrease exposure to emetogenic substances should be used. By decreasing baseline risk factors and correctly treating those at risk, we can provide better perioperative care to children.

Declaration of interest

The authors declare that they have no conflicts of interest.

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