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REVIEW ARTICLE

Postoperative Nausea and Vomiting in Pediatric Patients

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Abstract
Postoperative nausea and vomiting (PONV), postoperative vomiting (POV), post-discharge nausea and vomiting (PDNV), and opioid-induced nausea and vomiting (OINV) continue to be causes of pediatric morbidity, delay in discharge, and unplanned hospital admission. Research on the pathophysiology, risk assessment, and therapy for PDNV, OINV and pain therapy options in children has received increased attention. Multimodal pain management with the use of perioperative regional and opioid-sparing analgesia has helped decrease nausea and vomiting. Two common emetogenic surgical procedures in children are adenotonsillectomy and strabismus repair. Although PONV risk factors differ between adults and children, the approach to decrease baseline risk is similar. As PONV and POV are frequent in children, antiemetic prophylaxis should be considered for those at risk. A multimodal approach for antiemetic and pain therapy involves preoperative risk evaluation and stratification, antiemetic prophylaxis, and pain management with opioid-sparing medications and regional anesthesia. Useful antiemetics include dexamethasone and serotonin 5-hydroxytryptamine-3 (5-HT3) receptor antagonists such as ondansetron. Multimodal combination prophylactic therapy using two or three antiemetics from different drug classes and propofol total intravenous anesthesia should be considered for children at high PONV risk. "Enhanced recovery after surgery" protocols include a multimodal approach with preoperative preparation, adequate intravenous fluid hydration, opioid-sparing analgesia, and prophylactic antiemetics. PONV guidelines and management algorithms help provide effective postoperative care for pediatric patients.

1 Introduction

Nausea, vomiting, and retching continue to be common causes of unplanned admission of children following ambulatory surgery [1]. Nausea as a bad feeling in the stomach can occur alone or prior to retching or vomiting, which is the involuntary expulsion of stomach contents. Overall nausea and vomiting etiologies in children are listed in Table 1. While all the etiologies listed may be involved in some degree with postoperative nausea and vomiting (PONV) and postoperative vomiting (POV), opioids and pain-related causes are two of the more common causes of patient and/or family dissatisfaction that can delay postoperative discharge. PONV, POV, post-discharge nausea and vomiting (PDNV), and opioid-induced nausea and vomiting (OINV) continue to be problems in children undergoing anesthesia and surgery [2]. They are inter-related occurrences involved at overlapping perioperative time intervals extending from

Key Points

Postoperative nausea and vomiting (PONV), postoperative vomiting, post-discharge nausea and vomiting, and opioid-induced nausea and vomiting continue to be causes of pediatric morbidity, delay in discharge, and unplanned hospital admission.

A multimodal approach for antiemetic and pain therapy involves preoperative risk evaluation and stratification, antiemetic prophylaxis, and pain management including opioid-sparing medications and regional anesthesia.

Multimodal combination prophylactic therapy using two or three antiemetics from different drug classes and propofol total intravenous anesthesia should be considered for children at high PONV risk.

"Enhanced recovery after surgery" protocols include a multimodal approach with preoperative preparation, adequate intravenous fluid hydration, opioid-sparing analgesia, and prophylactic antiemetics.

PONV guidelines and management algorithms help provide effective postoperative care for pediatric patients.

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the preoperative period to operating room emergence, post-anesthesia care unit (PACU), and discharge to the hospital ward or home. PONV can occur in the PACU or during the first 24–48 h after surgery. PDNV occurs after discharge from the hospital or ambulatory surgery center (Fig. 1) [3].

2 Methodology

A review of PONV in children was previously published in 2007 [4]. The goal of this review is to summarize and update existing knowledge and new developments that have occurred in the last 13 years, especially in regards to tonsillectomy, strabismus surgery, newly available antiemetics and anesthetic techniques, and the recently updated 2020 PONV consensus guidelines [2]. A literature search involved the review of publications from December 2006 to July 2020 found in PubMed, Google Scholar, Ovid MEDLINE, and the Cochrane Database of Systematic Reviews. Specific keywords included postoperative nausea and vomiting, PONV, postoperative vomiting, POV, postoperative discharge nausea and vomiting, PDNV, opioid-induced nausea and vomiting, OINV, pediatrics, children, antiemetics, 5-HT3 antagonists, ondansetron, granisetron, tropisetron, palonosetron, ramosetron, dexamethasone, droperidol, systematic review, meta-analysis, tonsillectomy, adenotonsillectomy, and strabismus repair.

3 Pathophysiology and Incidence

Nausea and vomiting etiologies in children are listed in Table 1. Pathophysiology for nausea and vomiting stimuli in central and peripheral locations are illustrated in Fig. 2. Inter-related causes and connections exist between the central nervous system (CNS) and the peripheral nervous system. CNS neural pathways and physiological effects are listed in Table 2. PONV has been estimated to occur with an overall incidence of approximately 20–30% in the general surgical population and 70–80% in high-risk adult and pediatric surgical patients [2]. The incidence of POV is higher in children of school age and increases with age until puberty, with no difference observed between prepubertal children [5]. Children have about twice the POV incidence than adults, with an overall incidence ranging from about 8–42% [6–10]. Awad et al. [10] evaluated 10,772 pediatric patients having ambulatory surgery. The most common reasons for unplanned hospital admission were pain (16%), surgical complications (14%), late surgery (12%), and PONV (8%). PDNV as a newly evaluated area for postoperative

Table 1 Nausea and vomiting etiologies in children

Infections	Viral Bacterial
Gastrointestinal disease	Esophageal disease, achalasia Bowel obstruction, distension, gastroparesis Gastric and bowel irritants Inflammation: gastritis, hepatitis, pancreatitis, enteritis, cholecystitis
Intracranial disease	Malignant hypertension Increased intracranial pressure (brain cancer, tumors, hemorrhage) Migraines
Vascular, physiologic changes	
Vestibular and labyrinthine disorders	Labyrinthitis, vestibular neuritis Inner ear tumors Motion sickness
Metabolic diseases	Diabetic ketoacidosis Adrenal disease Thyroid disease, hyperthyroidism, parathyroid disease Uremia
Anxiety	
Pain	
Exposure to emetic substances	Opioids Anesthesia Addison's disease Diabetic ketoacidosis Poisons Radiation Chemotherapy

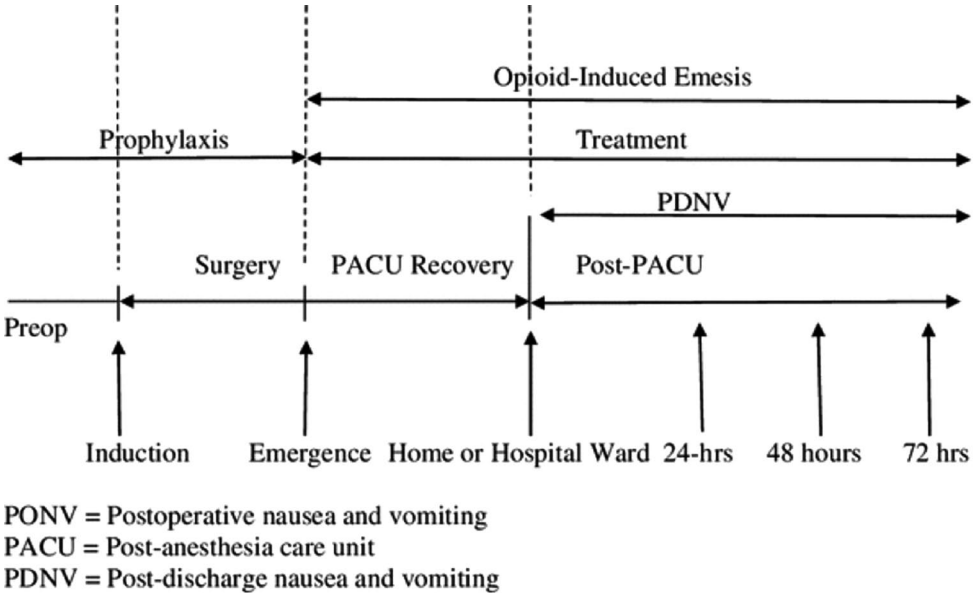

Fig. 1 Overlapping time intervals of postoperative nausea and vomiting (PONV), postoperative vomiting (POV), post-discharge nausea and vomiting (PDNV), and opioid-induced emesis. *PACU* post-anesthetia care unit. Reproduced with permission from Kovac [268]

investigation has an estimated risk of 14% in children [11]. Rowley and Brown [9] observed a lower POV incidence of 22–40% versus 42–51%, respectively, in children aged < 3 versus > 3 years. Khalil et al. [12] found an incidence of 27% and 28% in children aged 1–12 and 13–24 months, respectively.

Numerous PONV prevention studies have been performed in children. Two of the most common surgeries evaluated are adenotonsillectomy and strabismus repair. PONV treatment studies are uncommon. More pediatric antiemetic studies have evaluated POV rather than PONV as the feeling of nausea is subjective and more difficult for young children to understand and describe. Noll et al. [13] stated that self-reported postoperative subjective symptoms such as nausea are an important part of patient-reported outcomes. To help children describe their level of nausea, the Baxter Retching Faces (BARF) pictorial rating scale [14] was developed and validated in children aged 7–18 years, indicating that significant nausea occurred earlier than previously thought. Watcha et al. [15] further evaluated this visual scale, determining the effective use of the BARF score in both English- and Spanish-speaking children. The BARF scale had excellent performance in predicting patients' perceived need for antiemetics, with a maximum BARF score of 4 having 80.0% sensitivity and 85.6% specificity. Using the BARF score for English- and Spanish-speaking children improves the manner in which clinicians can help assess a subjective symptom such as nausea in children.

Specific surgeries in children that have a higher incidence of PONV and POV include strabismus repair, hernia surgery, orchiopexy, penile surgery, laparoscopy, brain surgery, adenotonsillectomy, otoplasty, ear (especially middle), and ear, nose, and throat (ENT) surgeries, with incidences ranging from about 15–80% [2, 16, 17]. ENT surgery accounts for approximately 30% of pediatric operative procedures, with PONV occurring in up to 30% of children [18]. For children aged 8–16 years, POV was the most common postoperative event (77%), especially under general endotracheal anesthesia for ENT surgery [19].

An estimated 7–15% of children have PONV in the PACU after adenotonsillectomy [16, 20]. In children undergoing strabismus surgery, an overall incidence of 37% for postoperative nausea (PON) and 32% for POV was reported [21]. The incidence of vomiting was 2.5-fold higher when surgery was performed on both eyes compared with one eye. In a study of children having outpatient dental surgery with oral sedation, 19.6% had nausea and 10.1% vomited [22]. The incidence of PONV in children having laparoscopic cholecystectomy was estimated to be 39% [23].

Over the last 30–40 years, the incidence of POV following strabismus and tonsillectomy surgeries has decreased. From a high of 85% [17], the incidence of POV following strabismus repair has decreased to a range of 32 [21] to 70% [24] and in adenotonsillectomy has decreased to an incidence of 7 [20] to 15.6% [16]. Increasing duration of surgery and anesthesia longer than 30 min increased POV incidence from 34 to 48% [9].

4 Adverse Side Effects

Postoperative adverse events due to severe nausea and vomiting have involved morbidity such as vision impairment following wound dehiscence [25–27] and hemorrhage post-tonsillectomy and adenotonsillectomy [28–31]. In addition, it has been hypothesized that off-label drug prescribing may

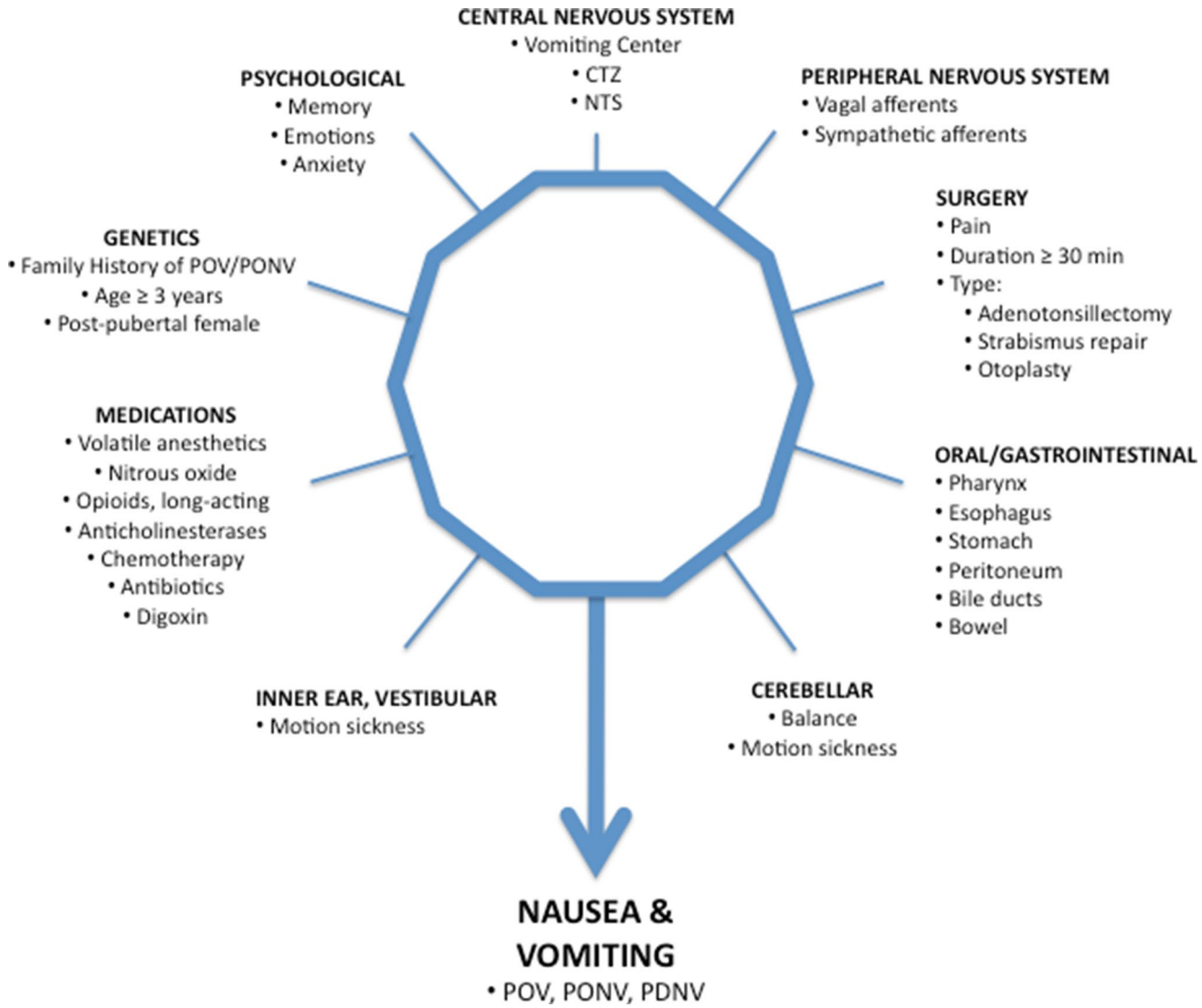

Fig. 2 Nausea and vomiting pathophysiology for stimuli in central and peripheral locations. *CTZ* chemoreceptor trigger zone, *NTS* nucleus tractus solitarius, *PDNV* post-discharge nausea and vomiting, *PONV* postoperative nausea and vomiting, *POV* postoperative vomiting

possibly be related to age-related development of adverse drug reactions [32, 33] and side effects [34]. This emphasizes the necessity of conducting PONV antiemetic research on medications for pediatric patients.

5 Risk Factors and Scoring Systems

Various factors in children contribute to PONV risk and incidence. Like in adults, PONV risk in children is related to surgery, patient, anesthesia, and medication factors [2]. However, adult risk scores cannot be directly applied to the pediatric population [35]. The effect of secondhand smoke as a risk factor for PONV in children is unknown. Pediatric POV risk assessments have been described by Eberhart and colleagues [35, 36], Kranke et al. [37], and Bourdaud et al. [38]. The Eberhart score (Fig. 3) includes the risk factors of surgery > 30 min in duration, age > 3 years, strabismus surgery, and history of POV or family history of PONV. Prior to puberty, female sex does not increase the risk of PONV. Kranke et al. [37] evaluated and validated the Postoperative Vomiting in Children (POVOC) score, which was essentially the Eberhart score with surgeries other than strabismus repair. Bourdaud et al. [38] developed and validated five factors contributing to POV in children: (1) age > 3 years, (2) duration of surgery, (3) type of surgery risk, (4) POV predisposition, and (5) multiple opioid doses. Inclusion of multiple opioid doses differs between the Bourdaud and Eberhart scores.

Table 2 Central nervous system (CNS) neural pathways and physiological effects

CNS pathways	Brain, cerebral Inner ear, vestibular system Vomiting center, area postrema, chemoreceptor trigger zone Abdominal vagal afferents Serotonin release from enterochromaffin cells of duodenum
CNS input and integration	Nucleus tractus solitarius Pons Cerebellar Ventral lateral medulla Salivary nuclei Dorsal motor nucleus Retrofacial nucleus Respiratory center
Physiological effects	Prodromal signs, symptoms, and effects Muscle sequence for retching Muscle sequence for vomiting

Yumura et al. [39] determined that the major PONV risk factors for mentally challenged patients undergoing outpatient general anesthesia for dental procedures were female sex, younger age, low weight, and not using propofol for anesthesia. Laufenberg-Feldmann et al. [40] suggested that PONV prophylaxis should be considered when "anxiety sensitivity" was high as a PONV predictive factor. When evaluating PDNV risk in children, Chandrakantan et al. [41] suggested that pain was an important contributing factor.

A retrospective study by Lee et al. [42] determined that children who underwent surgical atrial septal defect repair had a POV incidence of 37.5%. Independent predictors were age > 4 years and cardiopulmonary bypass time > 51 min. General anesthesia had a higher PONV incidence than regional anesthesia due to administration of volatile anesthetics [43]. This is felt to be because of a greater need for opioids to control postoperative pain after general anesthesia [44–46].

Canpolat et al. [47] found that hemogram parameters, such as platelet count (PLT), mean platelet volume (MPV), and the MPV/PLT ratio, may be useful in predicting the risk of POV in children after tooth extraction under deep sedation.

Corticosteroid antiemetic and anti-inflammatory mechanisms associated with PONV and inflammation have not been sufficiently investigated. Arpaci et al. [48] evaluated the association between neutrophil–lymphocyte ratio (NLR) and postoperative antiemetic administration to determine whether NLR could be a biomarker for PONV. They determined that NLR can be easily calculated with data obtained from the complete blood count and could be used to predict PONV. Patients undergoing ambulatory maxillofacial surgery with a NLR value > 2 had a higher incidence of PONV.

6 Genetics

Genetic predisposition and polymorphisms play a significant part in patient risk and drug response and effect by regulating the degree of high versus low drug metabolism [2]. Some genetic polymorphisms have been identified to affect PONV. Recent genetic research on antiemetic responsiveness has centered on a patient's family history, heritability, and genetic characteristics that help predict varying rates of PONV and medication effectiveness [2, 49–51]. A South African study [52] evaluating the effect of ethnicity on PONV in moderate- to high-risk patients undergoing general anesthesia found that PONV incidence in non-Africans was significantly higher than in Africans. Stern et al. [53] suggested that there may be a difference by race in vestibular hypersusceptibility and sensitivity to motion sickness when comparing Asian (Chinese) and non-Asian populations.

Other genetic examples support an association of serotonin polymorphism with PONV incidence. Stamer et al. [54] evaluated serotonin transporter polymorphism of the SS genotype (*5-HTTLPR, rs4795541*). In two independent cohorts, a polymorphism of *5-HTTLPR* in the serotonin transporter was independently associated with PONV in addition to known clinical factors. Evaluation of this biomarker could improve PONV risk prediction.

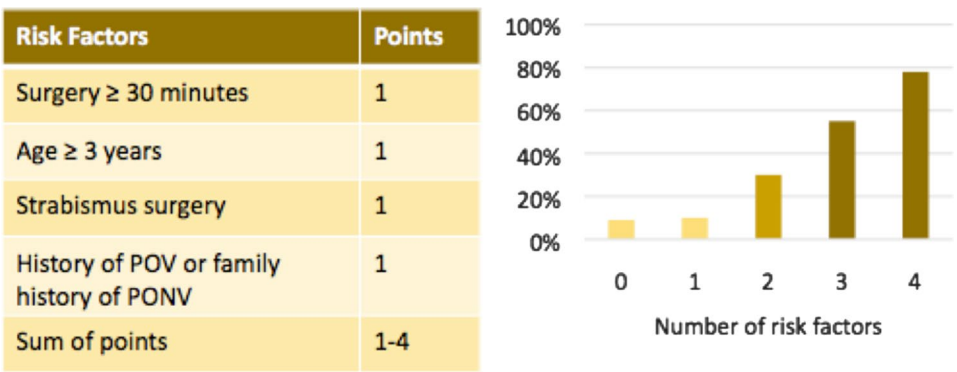

Fig. 3 Simplified risk score from Eberhart et al. [36] to predict the risk for postoperative vomiting in children. 0, 1, 2, 3, or 4 risk factors correspond to postoperative vomiting risks of approximately 10%, 10%, 30%, 50%, or 70%, respectively. Reproduced from Gan et al. [2] with permission from the American Society for Enhanced Recovery. *PONV* postoperative nausea and vomiting, *POV* postoperative vomiting

A genetic predisposition to PONV has been demonstrated with the muscarinic acetylcholine receptor *CHRM3 rs2165870* single nucleotide polymorphism (SNP) [55, 56]. Klenke et al. [55] retrospectively analyzed 472 patients undergoing elective surgery to determine how SNP contributes to PONV risk and how a genetic risk score might help summarize genetic PONV risk. A genetic risk score based on the *CHRM3 rs2165870* and the *KCNB2 rs349358* SNP was created and found to be associated with PONV independent from the Apfel score. A genetic predisposition with an SNP (rs2165870) for PONV was located upstream from the promoter region of the M3 muscarinic acetylcholine receptor *CHRM3* gene. They determined that *CHRM3* polymorphism and the Apfel score independently predicted PONV susceptibility.

The success or failure of antiemetics, such as ondansetron, has been shown to be influenced by polymorphism of the *5-HT3B* gene [57] and cytochrome P450 (CYP)-2D6 allele copy number [58]. Niewiński et al. [59] suggested that CYP2D6 basic genotyping may be a useful tool to improve ondansetron's antiemetic efficacy for PONV prophylaxis. This supports the findings of Klenke et al. [55], who determined that combined prophylaxis was found to be effective even though the *CHRM3 rs2165870* polymorphism was independently associated with PONV. In a study comparing ramosetron and palonosetron for preventing PONV after spinal surgery, ramosetron was felt to be superior to reduce PONV severity, especially in patients with the *ABCB1 3435TT* or *2677TT* genotype [60]. Thus, genetic research suggests that evaluation of genetic polymorphisms may be beneficial in determining PONV risk.

7 Post-Discharge Nausea and Vomiting (PDNV)

It has been estimated that 63% of surgeries in the USA are done on an outpatient basis, with more PONV occurring after discharge than in the PACU [61–63]. Of all patients having outpatient surgery, 30–50% may develop PDNV [64]. Minimal research has been completed on the incidence and causes of PDNV in the pediatric population. Efune et al. [11] determined that the PDNV incidence in children was 14%. Intraoperative and post-discharge opioids were found to increase the risk for PDNV. Children who did not receive intraoperative opioids had a lower incidence (8%) than those who received short-acting (14%) or long-acting opioids (24%). Chandrakantan et al. [41] determined that pain was an important contributing factor in PDNV in children with nausea and vomiting persisting into the post-discharge period.

8 Opioid-Induced Nausea and Vomiting (OINV)

Postoperative gastrointestinal tract dysfunction is common, complex, multifactorial, and associated with increased patient suffering and cost [65]. Opioids stimulate mu receptors centrally in the CNS and vestibular system and peripherally in the gastrointestinal tract, causing nausea and vomiting. OINV can be difficult to differentiate from other perioperative causes. After opioid administration, nausea may occur in approximately 40% and vomiting in 15–25% of patients [66]. The risk for OINV did not differ among different opioid analgesics compared with morphine, except for a lower incidence with fentanyl and higher incidence with buprenorphine [67]. Opioid analgesics administered for the perioperative treatment of pain are a major factor for nausea and vomiting in children at risk for PONV and PDNV [44, 68]. However, although postoperative opioids are a component of the adult Apfel PONV [44, 69] and PDNV [69] risk scores, they are not a factor in the pediatric POV risk scores of Eberhart et al. [36] and Kranke et al. [37] but are a factor for the Bourdaud et al. [38] score.

9 Antiemetic Approaches for Postoperative Nausea and Vomiting (PONV), Postoperative Vomiting (POV), PDNV and OINV

9.1 Multimodal Analgesia, Opioid-Free, and Nonopioid Analgesia

Nausea and vomiting are common side effects of medications used to treat pain during and after anesthesia, such as opioids and volatile anesthetic agents [43, 44, 66]. As postoperative opioids are a risk factor for PONV [45] and PDNV [69], the use of multimodal opioid-sparing analgesic medications and regional anesthesia techniques has received increased attention [2, 70, 71]. Randomized controlled trials, systematic reviews, and meta-analyses have shown that multimodal opioid-sparing methods combining the use of nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, ketamine, cyclooxygenase-2 inhibitors, β-blockers, local anesthetics, and regional anesthesia, when indicated, have dose-limiting opioid-sparing effects in the perioperative period [2, 71–75]. Acute pediatric pain management has evolved to include multidisciplinary and multimodal methods such as nonpharmacological therapies (e.g., acupuncture) and more advanced treatments (e.g., nerve blocks and infusions of centrally acting pain medications) [70, 76, 77].

9.2 Gabapentin

Gabapentin is a γ-aminobutyric acid analog that was originally used as an anticonvulsant and is now often used to treat neuropathic pain. Although gabapentin's antiemetic effect has been less frequently investigated, the PONV effect and mechanism appears to be related to a decrease in tachykinin neurotransmission. Gabapentin has been used to decrease emergence delirium in children following the use of inhalation anesthetics such as desflurane [78, 79]. In a study on the analgesic effects of gabapentin after scoliosis surgery in children, oral gabapentin 5 mg/kg did not result in a significant difference in opioid consumption or pain scores [80]. However, another study [79] determined that oral gabapentin 5 mg/kg reduced the incidence and severity of emergence agitation by 20%.

Rusy et al. [81] determined that perioperative oral gabapentin reduced the pain scores and amount of morphine used for postoperative pain after spinal fusion surgery but not overall opioid-related side effects. Perioperative use of gabapentin appeared to be an effective adjunct to improve pain control in the early stages of recovery in children and adolescents undergoing spinal fusion.

In a case study, Tsai et al. [82] reported gabapentin use for refractory vomiting after craniotomy in two children with medulloblastoma in the fourth ventricle [82]. The two patients (4-year-old boy and 11-year-old girl) underwent near-total excision of their tumor via craniotomy. Both children experienced refractory PONV treated with multiple traditional antiemetic drugs, but without relief. After gabapentin, their nausea and vomiting improved from one to two episodes per day to complete resolution of symptoms. The researchers suggested that gabapentin may be a novel antiemetic therapeutic intervention for patients with refractory nausea and vomiting after craniotomy. Gabapentin use for pediatric PONV deserves further investigation.

9.3 Lidocaine

Nonopioid analgesia intravenous medications have been used to provide good alternative analgesia. During tonsillectomy, children given an intravenous bolus of lidocaine 1.5 mg/kg, followed by an infusion of 2 mg/kg/h, had 62% less POV than a saline placebo control group [83]. For pediatric eye squint surgery [84], 2% lidocaine gel was compared with 0.5% proparacaine eyedrops applied to the operated eye. All patients received a rectal paracetamol suppository (30 mg/kg) and intravenous granisetron 40 mcg/kg after anesthesia induction. Lidocaine 2% gel provided better perioperative analgesia and less PONV than did multiple proparacaine 0.5% eye drops.

9.4 α-2 Agonists

Numerous systematic reviews and meta-analyses [85–88] have evaluated α-2 agonists such as clonidine and dexmedetomidine for their PONV effect because of their opioid-sparing effects and direct antiemetic properties. As a secondary outcome, PONV reduction was found in children who received intranasal dexmedetomidine for separation anxiety compared with intranasal or oral midazolam [86]. In another two studies [85, 89], children who received oral clonidine had fewer PONV episodes and lower need for rescue antiemetics. However, Gulhas et al. [90] determined that oral clonidine 4 mg/kg 1 h prior to surgery did not decrease POV. Use of an intravenous dexmedetomidine 0.5 mcg/kg bolus and 0.1–0.3 mcg/kg infusion reduced emergence agitation, opioid requirements, and PONV in children awakening from anesthesia [91–94]. To help decrease PONV risk, α-2 agonists deserve further evaluation, especially when used in combination with multimodal analgesia and recovery regimens.

9.5 Acetaminophen/Paracetamol

Acetaminophen/paracetamol, *N*-(4-hydroxyphenyl)acetamide, is an analgesic commonly used worldwide. Its analgesic mechanism of action is thought to interact synergistically at multiple CNS pathways and sites to include the serotonin, cyclooxygenase, opioid, vanilloid, and endocannabinoid systems [95, 96]. Perioperative pain in children can be effectively managed with systemic opioids, but the addition of acetaminophen or NSAIDs helps reduce opioid requirements, potentially improves analgesia, and reduces adverse effects. A systematic review by Wong et al. [97] supported the addition of NSAIDs and/or paracetamol to systemic opioids for a reduction of perioperative pain in children.

Aksoy et al. [98] studied 96 children undergoing strabismus surgery and determined that a paracetamol dose of 15 mg/kg decreased POV during the first 6 postoperative hours compared with placebo. Another study [99] in 90 children having strabismus surgery determined that intraoperative intravenous paracetamol decreased PONV incidence during the first 24 h.

9.6 Ketamine

Ketamine is a nonselective antagonist of the *N*-methyl-D-aspartate (NMDA) receptor that has been shown to have a morphine-sparing effect by inhibiting central sensitization, opioid-induced hyperalgesia, and acute opioid tolerance [100, 101]. The postoperative morphine-sparing analgesic effect of low-dose ketamine was studied using an

intraoperative and postoperative infusion. An intravenous ketamine bolus dose of 0.5 mg/kg and 2 mcg/kg/min infusion reduced morphine and antiemetic requirements without adverse effects for 48 h after posterior correction surgery for adolescent idiopathic scoliosis surgery [102].

Two studies [103, 104] that evaluated ketamine infiltration during tonsillectomy showed a decrease in postoperative pain, analgesic requirement, and PONV. Administering ketamine as an infiltration had no side effects. An updated meta-analysis by Tong et al. [103] evaluated ten studies using peritonsillar infiltration with ketamine 0.5 mg/kg. A short effective analgesia time was found, as postoperative pain scores were reduced at 30 and 60 min but not 120 min. A reduction in PONV, dysphagia, and postoperative pain scores was found when using preincision peritonsillar infiltration of 2 ml of ketamine 0.5 mg/kg combined with 2 ml of tramadol 2 mg/kg.

Ketofol is a 1:1 mixture of ketamine (10 mg/ml) and propofol (10 mg/ml) as a 20 ml combination. Ketofol has been studied for sedation in pediatric patients undergoing transcatheter pulmonary valve implantation [105]. Advantages over propofol were rapid onset of sedation, rapid recovery time, decreased PONV, and rapid PACU discharge.

Interest in combining ketamine and dexmedetomidine for sedation during diagnostic and surgical procedures has been increasing. Ketamine 2 mg/kg added to dexmedetomidine 1 mcg/kg produced effective anesthesia to perform a caudal block for lower abdominal or genital surgery in children [105].

9.7 Regional Anesthesia

Numerous studies have shown that regional anesthesia is a useful adjunctive method to decrease the amount of opioid use and PONV compared with general anesthesia. In ambulatory anesthesia, opioid-free regional anesthesia decreased PONV compared with general anesthesia [74]. An acute pain protocol with regional anesthesia for ambulatory pediatric circumcision surgery showed a reduction in opioid use and incidence of unplanned admissions [106]. For patients undergoing renal surgery, caudal anesthesia with bupivacaine 0.2% plus low-dose morphine provided a long duration of analgesia without significant side effects [107]. In ambulatory pediatric surgery for lower abdominal and perineal surgeries, caudal block with dexmedetomidine (0.5–1.5 mcg/kg) combined with 0.2% ropivacaine (0.75 mcg/kg) was effective for preventing postoperative pain [108]. Caudal and transversus abdominis plane (TAP) blocks were useful to decrease the amount of opioid use and incidence of PONV in children undergoing urologic robot-assisted laparoscopic surgery [109]. Ultrasound-guided TAP blocks with ropivacaine decreased pain scores in pediatric patients having laparoscopic appendectomy [110]. Sub-tenon blocks were effective as perioperative analgesia in infants having cataract [111] and strabismus surgery [112].

9.8 Total Intravenous Anesthesia

The antiemetic properties of propofol administered as an infusion during total intravenous anesthesia (TIVA) are well-documented [2, 113, 114]. Two systematic reviews and meta-analyses [115, 116] determined that TIVA was as effective as a single antiemetic prophylactic intervention to prevent POV in pediatric patients. In an inpatient study [115], PONV was less frequent after general anesthesia with TIVA than when using an inhalation agent alone. However, in an outpatient study [116], TIVA anesthesia with propofol during pediatric strabismus surgery increased the risk for bradycardia because of the oculocardiac reflex. The researchers felt that use of a single antiemetic intervention could compensate for the emetogenic effect of inhalation general anesthesia. Grundmann et al. [117] determined that TIVA with remifentanil and propofol was a well-tolerated anesthetic method in children with lower perioperative heart rate, postoperative agitation, and PONV (< 10%) compared with a desflurane-N_2O inhalation-based anesthetic. For children undergoing a surgery at high risk for PONV, Bailey [118] recommend a TIVA technique with propofol, no nitrous oxide, and combination antiemetic prophylaxis with dexamethasone plus a 5-hydroxytryptamine-3 (5-HT3) receptor antagonist such as ondansetron.

10 Pharmacologic Antiemetic Medications and Techniques

Antiemetic doses for POV prophylaxis are listed in Table 3. Pharmacologic combination therapy is listed in Table 4.

10.1 Dexamethasone

Dexamethasone's antiemetic action appears to occur in the area of the brain's vomiting center [119]. Dexamethasone's anti-inflammatory action [120] appears to be derived from a complex regulatory pathway triggered after binding to glucocorticoid receptors, thereby inhibiting synthesis of cytokine and anti-inflammatory mediators [121]. Previous controversy has centered around the risk of dexamethasone for post-tonsillectomy hemorrhage, but numerous studies [28, 31, 122] and reviews [30, 123] found no dose-related effects on bleeding.

Dexamethasone has shown effectiveness in decreasing the incidence of PONV in children [124–126]. In tonsillectomy patients, intravenous dexamethasone 0.1 mg/kg administered at induction of anesthesia was effective at reducing early and late PONV and pain on the second postoperative day. An

Table 3 Recommended antiemetic doses for children Reproduced with permission from Gan et al. [2]

Drug	Dose	References
Aprepitant	PO 3 mg/kg^{-1} up to 125 mg	[181]
Dexamethasone	IV 150 mcg/kg^{-1} up to 5 mg	[137]
Dimenhydrinate	IV 0.5 mg/kg^{-1} up to 25 mg	[254]
Droperidol[a]	IV 10–15 mcg/kg^{-1} up to 1.25 mg	[139]
Granisetron	IV 40 mcg/kg^{-1} up to 0.6 mg	[163]
Ondansetron[b]	IV 50–100 mcg/kg^{-1} up to 4 mg	[12]
Palonosetron	IV 0.5–1.5 mcg/kg^{-1}	[174, 175]
Tropisetron	IV 0.1 mg/kg^{-1} up to 2 mg	[255]

Recommendations are evidence based, and not all the drugs have an FDA indication for PONV

IV intravenous, *PO* oral administration, *PONV* postoperative nausea and vomiting, *POV* postoperative vomiting

[a]FDA black box warning: Recommended doses are 10–15 mcg/kg

[b]Approved for POV in pediatric patients aged ≥ 1 month

Table 4 Pharmacologic combination therapy for children

Ondansetron + dexamethasone [137, 138, 166, 256]
Ondansetron + droperidol [144]
Tropisetron + dexamethasone [257, 258]
Granisetron + dexamethasone [166, 259]
Propofol + dexamethasone [222]

Modified from Gan et al. [2]

intravenous dose of 0.15 mg/kg was as effective as 0.5 mg/kg [124]. During endoscopic adenoidectomy surgery under general anesthesia, intravenous dexamethasone 0.15 mg/kg reduced PONV without increasing bleeding risk [125].

Numerous studies [124, 127–135] have shown the effect of dexamethasone on post-tonsillectomy pain and PONV. Kaan et al. [131] determined that children who received preoperative intravenous dexamethasone 0.5 mg/kg had significantly decreased early post-tonsillectomy pain and improved oral intake and met discharge criteria without significant side effects. Giannoni et al. [136] determined that the combination of dexamethasone and preemptive analgesia of ropivacaine and clonidine had an additive decreased effect on pediatric tonsillectomy pain and PONV.

Numerous studies found that dexamethasone combined with another antiemetic was more effective than a single antiemetic alone. In a meta-analysis of children undergoing strabismus surgery, the combination of dexamethasone plus ondansetron was more effective than either dexamethasone or ondansetron alone [137]. However, in very low-risk surgeries, a multimodal combination antiemetic approach with dexamethasone in pediatric outpatients may have minimal effect. Dexamethasone 0.15 mg/kg plus ondansetron 0.1 mg/kg (to a maximum 4 mg) was compared with dexamethasone 0.15 mg/kg alone in children receiving surgery for inguinal hernia, umbilical hernia, cryptorchidism, or phimosis repair. All patients received a local anesthetic block (ilioinguinal, periumbilical, or penile) with 0.25% bupivacaine and the NSAID dipyrone 30 mg/kg. As the prophylactic antiemetics failed to reduce POV incidence in surgeries with low emetic potential, the researchers suggested that routine prophylaxis may not be necessary.

Studies evaluating the treatment of established PONV in children are less common than prophylactic studies. Ormel et al. [138] showed that, when used as treatment for PONV, dexamethasone has an additive effect combined with both ondansetron and droperidol.

An additional therapeutic effect under investigation, especially in tonsillectomy, is the anti-inflammatory effect of dexamethasone on postoperative pain. A tonsillectomy study comparing dexamethasone versus tramadol [133] found no difference in postoperative pain scores from 15 min to 2 h but did observe a difference at 6 and 24 h. However, another study [134] that included children who had dental rehabilitation surgery and received dexamethasone 0.3 mg/kg versus saline found a reduction in POV but not pain over 24 h. The dexamethasone dose in children is 150 mcg/kg, up to a dose of 5 mg [2].

10.2 Droperidol

Droperidol is a butyrophenone chemical compound and dopamine D_2 receptor antagonist originally developed in the 1950s as an antipsychotic medication and approved in the 1960s for use in anesthesia and PONV. Numerous researchers have described the effect of droperidol in single [113, 139–142] and combination [138, 140, 143, 144] dosing to decrease PONV.

Droperidol received a black box warning in 2001 from the US FDA because of the possibility of QT prolongation and torsades des pointes [145, 146]. However, this was controversial, as Mehta et al. [147] reported that therapeutic antiemetic doses of droperidol 20 mcg/kg and ondansetron 100 mcg/kg produced equivalent, clinically insignificant QT prolongation and negligible Tp-e prolongation, suggesting that neither drug has torsades-promoting effects at these doses in healthy children. Of particular interest was that the combination of droperidol and ondansetron had no QT or Tp-e effects [147].

To prevent PONV after tonsillectomy in children, Flubacher et al. [141] determined that the combination of dexamethasone 250 mcg/kg plus ondansetron 150 mcg/kg was more effective than dexamethasone 250 mcg/kg plus droperidol 10 mcg/kg. In a triple-agent combination study, Bourdaud et al. [143] evaluated the effect of adding droperidol to an intraoperative combination of ondansetron, dexamethasone, and oral hydroxyzine 1 mg/kg. In children

at high POV risk, adding droperidol did not decrease POV incidence below that obtained with the combination but increased the risk of drowsiness. In view of these findings, the combination of dexamethasone and ondansetron was recommended. The droperidol dose in children is 10–15 mcg/kg, up to a dose of 1.25 mg [2].

10.3 Transdermal Scopolamine

The transdermal route is a noninvasive and easy method of drug delivery in adults and children. Transdermal patches include fentanyl, buprenorphine, clonidine, scopolamine, methylphenidate, estrogens, nicotine, and tulobuterol. Some patches have labeling supported by pediatric clinical trials, whereas others are used off-label. An absence of approved transdermal formulations in children can lead to the risk of excessive drug administration because of an incompletely formed skin barrier [148].

Scopolamine is an anticholinergic medication used for its effect on sedation, motion sickness, nausea, and vomiting. Transdermal scopolamine crosses the blood–brain barrier and placenta. The transdermal patch delivery system contains scopolamine 1.5 mg delivered over 72 h. Absorbed percutaneously, scopolamine can be detected in the plasma within 2–4 h after skin application [149].

Horimoto et al. [150] evaluated a scopolamine patch for prevention of POV in 50 children undergoing strabismus surgery. Before operation, study subjects were randomly assigned to one of two treatment groups at either 0.75 or 0.375 mg or to a control group (no patch). The scopolamine patch doses used were less than the standard adult patch dose. Both the incidence and the frequency of POV in the scopolamine patch-treated group were lower than in the no patch group.

Use of a transdermal scopolamine patch does not have FDA approval for pediatric patients [148]. Caution should be exercised in children, as side effects can include dry mouth, diplopia, and delirium [151].

10.4 Serotonin 5-hydroxytryptamine-3 (5-HT3) Receptor Antagonists

The 5-HT3 receptor antagonists have a lower side effect profile than older traditional antiemetics. When the 5-HT3 receptor antagonists are used in combination with antiemetics of a different drug class, there is an improved prophylactic efficacy for patients at high risk for PONV [2].

10.4.1 Ondansetron

As a first generation 5-HT3 receptor antagonist introduced in the 1990s, ondansetron has been considered the "gold standard" and is one of the most commonly used antiemetics for PONV in adults and children [2]. Ondansetron has comparable antinausea and antivomiting effects when used as a single or combination antiemetic for prophylaxis or treatment [113, 152–154]. As a single agent, ondansetron has effectiveness equal to droperidol [113], haloperidol [155], dexamethasone [113], and propofol infusion [113]; less effectiveness than palonosetron [156, 157], ramosetron [157], granisetron [158], and aprepitant [159]; and greater effectiveness than dimenhydrinate [160], dexmedetomidine [161], and metoclopramide [162]. Ondansetron has shown therapeutic effectiveness when used as combination therapy with dexamethasone [137, 138]. The ondansetron dose in children is 50–100 mcg/kg, up to a dose of 4 mg [2].

10.4.2 Granisetron

Granisetron has been studied in children aged > 2 years [163, 164]. As its metabolism differs from other 5-HT3 antagonists, granisetron is less likely to adversely interact with other medications [164]. Granisetron has similar antiemetic effectiveness to the other first-generation 5-HT3 receptor antagonists and dexamethasone. However, a middle ear surgery study by Dua et al. [165] reported better effectiveness than ondansetron. Combination antiemetic therapy has usually been found to be more effective than single therapy alone [166, 167]. However, in a strabismus study [164] in 136 children, intravenous granisetron 40 mcg/kg combined with dexamethasone 150 mcg/kg did not decrease PONV compared with granisetron 40 mcg/kg alone. The granisetron dose in children is 40 mcg/kg, up to 0.6 mg [2].

10.4.3 Ramosetron

Ramosetron is a second-generation 5-HT3 receptor antagonist that is well-tolerated in adult and pediatric patients [168]. Yokoi et al. [169] determined that ramosetron was more effective in preventing late PON, late POV, and next-day PON than was ondansetron. The incidence of dizziness was lower with ramosetron than with ondansetron. A meta-analysis of 18 studies by Kim et al. [170] determined that ramosetron was effective and safe in children and adults in prevention of PONV without serious adverse effects. Park et al. [171] determined that, during the first 24-h period after surgery, ramosetron was more effective than ondansetron in children using fentanyl patient-controlled analgesia after general anesthesia. To decrease PONV in children after orthopedic surgery, intravenous ramosetron 6 mcg/kg was more effective than ondansetron 100 mcg/kg [171].

10.4.4 Palonosetron

Palonosetron is a second-generation 5-HT3 receptor antagonist that is distinctly different from the first-generation

5-HT3 receptor antagonists. This difference is shown in stronger receptor allosteric binding, longer duration of action, positive cooperativity, and receptor internalization resulting in a 40-h half-life [157, 172, 173]. In the last 10 years, more nausea and vomiting investigations have been performed with palonosetron in adult and pediatric patients [60, 174–178]. Palonosetron has been effective in decreasing chemotherapy-induced nausea and vomiting (CINV) [177] and PONV [175, 179, 180]. Palonosetron has FDA approval for the prevention but not the treatment of PONV in adults.

Yildirim and Cantekin [175] evaluated 286 children undergoing dental rehabilitation surgery regarding the safety and efficacy of three different intravenous doses of palonosetron (0.0025 mg, 0.0050 mg, and 0.0075 mg) or placebo administered immediately before induction of general anesthesia. The incidence of PONV was significantly lower in all palonosetron groups than in placebo groups, but no significant differences were found among the palonosetron groups. The lowest single dose of intravenous palonosetron 0.0025 mg was recommended for further evaluation.

Bicer et al. [174] conducted a dose–response study comparing palonosetron 0.5, 1.0, and 1.5 mcg/kg dose effectiveness during strabismus surgery. The percentage of children aged > 6 years with PON 0–48 h after anesthesia was 8.6%, 18.2%, and 15.4% with palonosetron 0.5, 1.0, and 1.5 mcg/kg, respectively. There was no significant difference between the three doses with respect to the number of children with POV during all time periods after anesthesia. Palonosetron doses of 0.5, 1.0, and 1.5 mcg/kg were recommended for further evaluation, as all were effective doses for PONV prevention.

While palonosetron does not presently have FDA approval for use in children, the palonosetron dose in children is 0.5–1.5 mcg/kg [2, 174].

10.4.5 Aprepitant

Aprepitant is an oral, selective neurokinin-1 receptor antagonist with a 40-h half-life approved for the prevention of PONV in adults and CINV in adults and pediatric patients from the age of 6 months [2, 159]. For PONV prophylaxis, aprepitant is given 1–2 h prior to surgery. Limited data are available regarding aprepitant use for PONV prevention in children. Salman et al. [181] evaluated the pharmacokinetics, pharmacodynamics, safety, and tolerability of aprepitant to identify dosing for PONV prevention in children and determined oral aprepitant 40 mg to be an appropriate dose. Kanaparthi et al. [182] retrospectively reviewed 31 patients (15 male, 16 female) aged 4–27 years (15.7 ± 7.4 years) and weight 14.4–175.7 kg (59.3 ± 30.2 kg). Most patients (30 of 31) received the 40 mg capsule; one received the liquid form. The average aprepitant dose was 0.9 ± 0.6 mg/kg. All patients had either a history of or risk factors for PONV. PONV occurred in one patient in the PACU and in three additional patients during the first 24 h postoperatively. No adverse events occurred. Future comparison studies in children with greater sample sizes are needed to demonstrate aprepitant's efficacy, especially compared with ondansetron.

11 Nonpharmacologic Methods and Techniques

11.1 Preoperative Carbohydrates and "Non Per Os" Fasting

Preoperative fasting can contribute to dehydration and is a major cause of perioperative discomfort. Evaluating the effect of preoperative carbohydrates and "non per os" fasting, various studies [183–185] have shown similar results regarding nausea and pain, but others [186] differ on vomiting. Tudor-Drobjewski et al. [183] showed that preoperative carbohydrates reduced gastric content and PON but not POV. Other studies [184, 185] found that a preoperative carbohydrate-rich drink minimized PON, POV, and pain in patients undergoing outpatient cholecystectomy. Shortening the preoperative fasting period prior to adenotonsillectomy helped facilitate the initiation of postoperative oral feeding but not PONV [186].

11.2 Fluid-Replacement Therapy

Preoperative fasting and bowel preparation can cause a degree of dehydration that can cause or exacerbate PONV [187, 188]. Numerous studies [187–189] have reported that intravenous crystalloid fluid administration decreases PONV by decreasing the level of dehydration and hypovolemia. Liberal intravenous fluid-replacement therapy of 30 ml/kg versus low fluid replacement of 10 ml/kg has been shown to be an effective method to decrease baseline PONV risk, especially in high-risk patients [190]. Liberal intraoperative intravenous fluid therapy was effective at reducing PONV in children undergoing lower abdominal surgery [191]. Using intraoperative hydration with 30 ml/kg lactated Ringers solution significantly reduced POV risk for 24 h postoperatively [192]. Sayed et al. [193] determined that combination therapy using intravenous dexamethasone 0.15 mg/kg given 1 min before induction and intraoperative hydration of an intravenous crystalloid solution 30 ml/kg helped reduce PONV and pain. The Face Legs Activity Cry Consolability (FLACC) score is an observational tool that has been verified and is used to quantify procedural pain behaviors in preverbal children [194–196]. Facial expression, leg movement, activity, cry, and consolability are each scored 0–2, for a total FLACC score of 0–10. FLACC measurements were done preanalgesia, at predicted onset of analgesia, and

at predicted peak analgesia. Following pediatric day case surgery, early postoperative oral fluid intake of apple juice 10 ml/kg in the PACU was associated with a reduction in opioid use and POV in children aged < 4 years who had a FLACC score ≥ 4 [185].

11.3 Honey

As an alternative adjunctive therapy, honey administered postoperatively has been found to enhance analgesia and decrease the amount of pain, required pain medications, and night awakening in children after tonsillectomy surgery [197–199].

11.4 Acupuncture

Application of intraoperative acupuncture at the P6 pressure point as a nonpharmacologic method has been evaluated regarding effectiveness on postoperative pain and PONV in adults and children [75, 200] and especially tonsillectomy patients [201–205]. A pediatric study [203] evaluated the effect of acupuncture used in combination with prophylactic antiemetics for tonsillectomy with or without adenoidectomy. A lower nausea risk occurred during phase I and II PACU recovery. Improved pain control was achieved with return to diet, but no PONV difference was observed on the first postoperative day. A meta-analysis and systematic review by Shin et al. [204] determined that PC6 (neiguan) acupuncture treatment was both effective and cost effective at preventing PONV after pediatric tonsillectomy. In 120 children aged 2–8 years undergoing tonsillectomy with or without adenoidectomy and with American Society of Anesthesiologists (ASA) scores of I–III, Moeen [206] compared the effect of intravenous dexamethasone 0.15 mg/kg plus sham acupuncture versus bilateral P6 acupuncture and CV13 on the incidence and severity of POV. Acupuncture at P6 bilaterally and CV13 provided a similar antiemetic effect to dexamethasone in children undergoing tonsillectomy.

Various researchers [75, 207–210] have reported the positive effects of acupuncture compared with placebo, or effectiveness equal to that of antiemetic medications, but controversy remains in the analysis of the effectiveness of acupuncture and acupoint PC6 stimulation in the prevention of PONV in adults and children. When controlling for possible placebo effects of standardized PC6 acupuncture needling during anesthesia without further stimulation of PC6, Liodden et al. [211] determined that acupuncture compared with standard care was not effective in reducing PONV in children after tonsillectomy with or without adenoidectomy.

Lee et al. [212] reported an update of a Cochrane review first published in 2004 and updated in 2009 and 2015. The purpose of the review was to determine the efficacy and safety of PC6 acupoint stimulation with or without antiemetic drug versus sham or antiemetic drug for prevention of PONV in patients undergoing surgery. The review included 59 randomized trials and involved 7667 participants. PC6 interventions included acupuncture, electroacupuncture, transcutaneous electrical acupoint stimulation, transcutaneous nerve stimulation, laser stimulation, capsicum plaster, an acu-stimulation device, and acupressure in people undergoing surgery. Primary outcomes were incidence of nausea and vomiting after surgery. Secondary outcomes were rescue antiemetic therapy and adverse effects. Compared with antiemetic drugs, the combination of PC6 acupoint stimulation and antiemetic therapy reduced the incidence of vomiting but not nausea. The quality of evidence was rated as very low because of substantial heterogeneity among trials, study limitations, and imprecision. The need for rescue antiemetics was lower in the combined PC6 acupoint stimulation and antiemetic group than in the antiemetic group. The researchers concluded that there was low-quality evidence supporting use of PC6 acupoint stimulation over sham. Comparing these conclusions with the last 2009 update, no further sham comparison trials are needed. To prevent PONV, there was moderate-quality evidence showing no difference between PC6 acupoint stimulation and antiemetic drugs. A new finding in the 2015 update was the recommendation that further trials were futile in showing a significant difference between PC6 acupoint stimulation and antiemetic drugs. There was inconclusive evidence supporting the use of a combined strategy of PC6 acupoint stimulation and antiemetic drug over drug prophylaxis. Further high-quality trials were recommended.

12 Specific Emetogenic Surgical Procedures in Children

12.1 Adenotonsillectomy

Tonsillectomy is the second most common pediatric ambulatory surgical procedure performed in the USA, following myringotomy with tube insertion [213]. Updated clinical practice guidelines for tonsillectomy in children by the American Academy of Otolaryngology, Head and Neck Surgery were published in 2019 [120]. Recommendations were for (1) perioperative pain counseling; (2) administration of a single intraoperative dose of intravenous dexamethasone; (3) administration of ibuprofen, acetaminophen, or both for postoperative pain control; (4) to not administer or prescribe codeine or any medication containing codeine after tonsillectomy in children aged < 12 years (codeine was felt to present a possible severe or life-threatening complication in children aged < 12 years who are ultra-rapid codeine metabolizers and might be first exposed to this medication after tonsillectomy); and (5) outcome assessment of postoperative

bleeding (follow-up with parents and/or caregivers after each tonsillectomy and for each surgeon to determine their rate of primary and secondary post-tonsillectomy bleeding at least annually). For pain control, codeine was excluded, as deaths due to respiratory depression from opioids (especially codeine) due to relative overdose and/or ultra-rapid CYP2D6 metabolizing converting codeine (prodrug) to morphine were reported [214]. Antiemetic medications and modalities for tonsillectomy surgery are listed in Table 5.

12.1.1 Dexamethasone

The effect of dexamethasone on bleeding in tonsillectomy patients has been of great interest and evaluated in numerous studies [28, 30, 31, 120, 215–219]. Czarnetzki et al. [216] concluded that, dexamethasone decreased PONV risk but there existed an associated increased risk of postoperative bleeding. However, other studies [28, 30, 31, 219] did not show a bleeding effect post-tonsillectomy. The 2019 ENT surgeon clinical practice guidelines also recommended administration of a single dose of dexamethasone [120].

In tonsillectomy patients, intravenous dexamethasone 0.1 mg/kg administered at induction of anesthesia was effective at reducing early and late PONV and pain on the 2nd postoperative day. An intravenous dose of 0.15 mg/kg was as effective as an intravenous dose of 0.5 mg/kg in reducing PONV [124]. In a meta-analysis evaluating 19 studies of steroid use during tonsillectomy, Steward et al. [220] found that children who received a single intraoperative intravenous dose of dexamethasone 0.15–1.0 mg/kg were half as likely to vomit in the first 24 h as children receiving placebo. They reported that a single intravenous dose of dexamethasone was an effective, safe, and inexpensive treatment for reducing morbidity and PONV from pediatric tonsillectomy.

Aouad et al. [221] determined that intravenous methylprednisolone 2.5 mg/kg was similar in efficacy to intravenous dexamethasone 0.5 mg/kg for the prevention of vomiting in children after tonsillectomy. Erdem et al. [222] determined that adding a subhypnotic infusion of propofol 20 mcg/kg/min to dexamethasone 0.15 mcg/kg improved antiemetic efficacy compared with dexamethasone alone.

Hermans et al. [124] evaluated 147 children, aged 2–8 years, who underwent elective tonsillectomy and received dexamethasone 0.15 mg/kg, 0.5 mg/kg, or placebo. The incidence of early PONV was lower in both dexamethasone groups than in the placebo group. The incidence of severe pain was reduced in the dexamethasone groups on the 2nd postoperative day. A single intravenous injection of dexamethasone at anesthesia induction was effective in reducing the incidence of early and late PONV and pain level on the 2nd postoperative day. Dexamethasone 0.15 mg/kg was as effective as 0.5 mg/kg in reducing PONV.

Steward et al. [220] conducted a systematic review of 19 studies (1756 children aged < 18 years) where a single intravenous dose of intraoperative dexamethasone 0.15–1.0 mg/kg was given for tonsillectomy or adenotonsillectomy. Compared with children receiving placebo, those receiving dexamethasone in the first 24 h were half as likely to vomit and more likely to advance to a soft/solid diet on post-tonsillectomy day 1 and have improvement in postoperative pain with no adverse events.

Moeen [206] compared the effect of intravenous dexamethasone 0.15 mg/kg versus P6 and CV13 acupuncture

Table 5 Antiemetic medications and modalities for adenotonsillectomy surgery

Study	Patients (*N*)	Age (years)	Antiemetic/modality	Conclusions
Aouad et al. [221]	160	2–12	IV DEX 0.5 mg/kg IV methylpred 2.5 mg/kg	PONV: DEX = methylpred
Hermans et al. [124]	147	2–8	IV DEX 0.15 mg/kg IV DEX 0.5 mg/kg PL	PONV: DEX 0.15 = DEX 0.5 > PL
Flubacher et al. [141]	300	2–10	IV DRO 10 mcg/kg IV OND 150 mcg/kg IV DEX 250 mcg/kg PL	PONV: OND + DEX > DRO + DEX
Moeen [206]	120	2–8	IV DEX 0.15 mg/kg + sham PL + P6 Acu	DEX + sham = PL + P6 Acu
Soliman and Alshehri [91]	150	4–14	SEV + PL SEV + DEXMED 0.5 mcg/kg + 0.1–0.3 mcg/kg/h	PONV: DEXMED + SEV > SEV
Izadi et al. [227]	102	5–15	Oxygen 80% Oxygen 30%	PONV: Oxygen 80% < 30%

DEX dexamethasone, *DEXMED* dexmedetomidine, *DRO* droperidol, *Methylpred* methylprednisolone, *OND* ondansetron, *P6 Acu* P6 acupuncture, *PL* placebo, *PONV* postoperative nausea and vomiting, *SEV* sevoflurane, *sham* sham acupuncture

bilaterally on POV incidence and severity in 120 children aged 2–8 years undergoing tonsillectomy with or without adenoidectomy. At induction of anesthesia, the dexamethasone group received dexamethasone plus sham acupuncture, and the acupuncture group received acupuncture at P6 bilaterally and CV13 plus 2 ml of normal saline intravenously. Between the acupuncture and dexamethasone groups, there was no difference in vomiting incidence at 0–6, 6–24, and 0–24 h postoperatively. The authors concluded that acupuncture provided antiemetic effectiveness similar to that of dexamethasone.

12.1.2 Ondansetron

Intravenous ondansetron has been found to be an effective prophylactic antiemetic for prevention of PONV following tonsillectomy when used alone [137, 152–154, 223, 224] or in combination with dexamethasone [137, 138]. Davis et al. [225] reported the effectiveness of ondansetron oral disintegrating tablet (ODT) for tonsillectomy in 221 children randomized for at-home administration of five doses of either ondansetron ODT or placebo and followed for 3 days after surgery. The researchers reported that at-home ondansetron ODT may prevent emesis in children during the first 3 days after tonsillectomy but that patients who required rescue after prophylactic treatment for PONV in the hospital may not respond to prophylactic ondansetron ODT at home.

Flubacher et al. [141] studied whether prophylactic droperidol 10 mcg/kg and ondansetron 150 mcg/kg in combination with dexamethasone 250 mcg/kg were equally effective in reducing nausea and vomiting after tonsillectomy as placebo control with dexamethasone in 300 children. Study patients received intravenous saline, droperidol, or ondansetron after induction of anesthesia and administration of intravenous dexamethasone. Ondansetron was more effective than placebo in preventing nausea or vomiting when given with dexamethasone, but droperidol was not.

12.1.3 Triple Antiemetic Therapy

Demidovich et al. [226] conducted a retrospective review evaluating the effect of using triple combination antiemetic therapy for PONV prevention in high-risk children (three or more risk factors) undergoing adenotonsillectomy. Study patients received either a scopolamine patch preoperatively (patients weighing > 40 kg) or diphenhydramine immediately post-extubation in addition to ondansetron and dexamethasone, which were given routinely. Postoperative antiemetic drug usage decreased during the first 60 min in the PACU for patients receiving diphenhydramine. Aggressive triple intraoperative antiemetic PONV management with diphenhydramine decreased PONV. However, a preoperative scopolamine patch did not improve PONV, which the researchers hypothesized was related to the drug's longer onset of action.

12.1.4 Dexmedetomidine

Soliman and Alshehri [91] evaluated the effect of dexmedetomidine on emergence agitation, time to extubation, and PONV in children receiving sevoflurane anesthesia for adenotonsillectomy. Dexmedetomidine decreased the incidence of agitation and was associated with shorter time to extubation, shorter PACU stays, and lower incidence of PONV.

12.1.5 Supplemental Oxygen

Izadi et al. [227] evaluated 102 children scheduled for adenotonsillectomy under general anesthesia, with two groups randomly divided to 30 versus 80% oxygen. The incidence of post-tonsillectomy nausea and vomiting after 2, 2–6, and 6–24 h was 13.72, 1.96, and 1.96% (30% group) and 3.92, 0, and 1.96% (80% group), respectively. The researchers reported that 80% oxygen was beneficial for reducing PONV in the first 2 h after surgery.

12.1.6 Acupuncture

Ozmert et al. [228] evaluated 70 children aged 2–14 years undergoing tonsillectomy and/or adenoidectomy under general anesthesia. In the study group, an acupuncture needle was intraoperatively applied to the P6 acupuncture point for 20 min. Antiemetics were not administered to either the study or the control group. There was no significant difference between groups with regard to age, sex, nature of the operation, duration of anesthesia or operation, surgical method, and ASA scores. A significant difference was found between the groups with respect to vomiting. As the acupuncture group presented 0.28 times fewer vomiting episodes than the control group, the researchers reported that acupuncture had an apparent antiemetic efficacy in POV.

12.2 Strabismus Surgery

Various researchers have evaluated the effect of ondansetron, dexamethasone [137], TIVA [229], granisetron [230], palonosetron [174], sub-Tenon's block [112], P6 acupressure [231], and dexmedetomidine [137, 232, 233] to decrease the incidence of PONV following strabismus surgery. Antiemetic medications and modalities for strabismus surgery are listed in Table 6.

Wolf et al. [229] evaluated the effectiveness of various antiemetics (ondansetron, dexamethasone) and methods (TIVA, inhalation) to reduce the frequency of PONV following strabismus surgery using an anesthetic technique specifically adapted to individual PONV risk according to

the POVOC score. Children with no, one, or two risk factors received balanced anesthesia, and those with three to four risk factors received TIVA with propofol. Dexamethasone 0.15 mg/kg and ondansetron 0.1 mg/kg were given for antiemetic prophylaxis. PONV incidence in low-risk pediatric patients receiving balanced anesthesia without prophylaxis was 38%. PONV incidence for pediatric patients at high risk receiving TIVA and multimodal antiemetics was 9%. The authors stressed the need to screen for PONV risk and individually adapt the type of anesthesia to PONV risk. In patients with high PONV risk, the combination of TIVA and antiemetics helped reduce PONV.

Shen et al. [137] conducted a systematic review and meta-analysis of 13 studies with 2006 children to evaluate the prophylactic effects of dexamethasone and ondansetron on PONV after strabismus surgery. The combination of dexamethasone and ondansetron was significantly more effective at reducing POV than either agent alone.

Sinha et al. [230] evaluated the efficacy of granisetron 40 mcg/kg versus a combination of granisetron 40 mcg/kg and dexamethasone 150 mcg/kg in 136 children aged 1–15 years for PONV prevention in strabismus surgery. There was no difference in incidence or severity of the oculocardiac reflex. Addition of dexamethasone did not increase the efficacy of granisetron.

Bicer et al. [174] evaluated three different palonosetron doses for PONV prevention in strabismus surgery: 0.5, 1.0, and 1.5 mcg/kg. All three doses were effective at decreasing PONV, but there was no significant difference between the three.

Tenon's capsule is a layer of connective tissue surrounding the eye. The sub-Tenon space is between the sclera and the capsule. Injection of local anesthesia into the sub-Tenon space diffuses posteriorly into the retro-orbital space causing analgesia and akinesia, blocking sensory and motor nerves of the eye. Tuzcu et al. [112] evaluated 40 children aged 5–16 years undergoing elective strabismus surgery who received either a sub-Tenon's or no sub-Tenon's block following intubation during general anesthesia. Sub-Tenon's block combined with general anesthesia was not effective in decreasing oculocardiac reflex and PONV. However, this method decreased post-operative pain and the need for additional analgesia.

Ebrahim Soltani et al. [231] compared the efficacy of P6 acupressure wristbands, intravenous ondansetron 0.15 mg/kg, metoclopramide 0.2 mg/kg, and placebo in 200 patients aged 10–60 years. The P6 wristbands were applied 30 min prior to anesthesia induction and removed 6 h after surgery. PONV incidence was not different between the acupressure, metoclopramide, and ondansetron groups.

Song et al. [232] studied 103 children aged 2–6 years undergoing strabismus surgery. Anesthesia was induced with sevoflurane and maintained with desflurane. Dexmedetomidine 0.25, 0.5, or 1 mcg/kg or saline was infused intravenously at the start of induction. The primary outcome was emergence agitation incidence. Secondary outcomes were the incidence of intraoperative oculocardiac reflex, POV, and desaturation events. POV and desaturation events were low in all groups. Dexmedetomidine 1 mcg/kg decreased the

Table 6 Antiemetic medications and modalities for strabismus surgery

Study	Patients (N)	Age (years)	Antiemetic/Modality	Conclusions
Sinha et al. [230]	136	1–15	IV GRA 40 mcg/kg GRA 40 mcg/kg + IV DEX 150 mcg/kg	GRA 40 = GRA 40 + IV DEX 150 mcg/kg PONV
Bicer et al. [174]	150	2–12	IV PALO 0.5 mcg IV PALO 1.0 mcg IV PALO 1.5 mcg	PALO 0.5 = PALO 1.0 = IV PALO 1.5 mcg PONV
Tuzcu et al. [112]	40	5–16	GA sub-Tenon's block + GA	Sub-Tenon's block had no effect on PONV or OCR
Ebrahim Soltani et al. [231]	200	10–60	OND 150 mcg/kg METO 200 mcg/kg P6 Acu PL	OND = METO = P6 Acu > PL PONV
Song et al. [92]	103	2–6	IV DEX 0.25 mcg/kg infusion IV DEX 0.5 mcg/kg infusion IV DEX 1.0 mcg/kg infusion	DEX 1.0 mcg/kg infusion decreased emergence agitation with no change in OCR
Chen et al. [233]	84	2–7	IV DEXMED 1 mcg/kg + 1 mcg/kg/h infusion IV KETA 1 mg/kg + 1 mg/kg/h infusion PL	POV: DEXMED > KETA > PL Emergence agitation: DEXMED = KETA > PL

DEX dexamethasone, *DEXMED* dexmedetomidine, *GA* general anesthetic, *GRA* granisetron, *IV* intravenous, *KETA* ketamine, *METO* metoclopramide, *OCR* oculocardiac reflex, *OND* ondansetron, *P6 Acu* P6 acupressure, *PALO* palonosetron, *PL* placebo, *PONV* postoperative nausea and vomiting, *POV* postoperative vomiting

incidence of emergence agitation without increasing intraoperative oculocardiac reflex.

Chen et al. [233] evaluated 84 children aged 2–7 years undergoing strabismus surgery under sevoflurane anesthesia and intraoperative dexmedetomidine 1 mcg/kg plus 1 mcg/kg/min infusion; ketamine 1 mg/kg plus 1 mg/kg/h infusion; or placebo for postoperative emergence agitation and POV. Dexmedetomidine and ketamine decreased postoperative agitation and pain. Dexmedetomidine also decreased POV. Times to resume mental orientation and PACU discharge were longer in the dexmedetomidine and ketamine groups than in the placebo group.

A review by Rodgers and Cox [234] recommended combination antiemetic therapy with dexamethasone and ondansetron in patients with high PONV risk. Metoclopramide has no additional benefit combined with other antiemetics. Droperidol was effective, but caution is required because of the black box warning for dysrhythmias. Opioids should be minimized because of the increased incidence of PONV. Effective analgesics include acetaminophen, NSAIDS, and peribulbar and sub-Tenon's block. Topical tetracaine drops have demonstrated mixed results, and topical nonsteroidal anti-inflammatory drops were not effective.

13 Approaches to Decrease or Prevent PONV and POV

13.1 Reduce Baseline Risk

Strategies to reduce baseline risk for PONV are listed in Table 7. Pediatric risk assessment has followed an approach similar to that for adult patients [2]. Baseline PONV risk should be decreased by the use of multimodal analgesia therapy protocols, minimal opioids, regional anesthesia, TIVA, and liberal fluid replacement [83, 85, 86, 98, 103, 115, 186, 190, 191, 200, 235]. Using minimal perioperative opioids with multimodal opioid-sparing analgesia is a main method to reduce baseline PONV risk [236]. A combination of general and regional anesthesia, especially using caudal blocks with or without intravenous dexamethasone has been shown to be an effective and safe way to reduce pain, need for opioids and decrease PONV incidence [237]. Other types of regional analgesia, such as TAP blocks, also help reduce opioid requirements during abdominal surgery [109, 110].

13.2 Pediatric Antiemetic Protocols

Figure 4 presents an algorithm for POV management in children as recommended by the 4th PONV consensus guidelines [2]. Analysis of risk factors allows for risk stratification and the choice of antiemetic prophylaxis. Definition of patients as low, medium, or high risk allows for the choice of one, two, or three antiemetic modalities, respectively. Rescue treatment should be a choice of an antiemetic from a class other than that of the prophylactic drug [2].

Drake et al. [238] demonstrated a decrease in PONV incidence using an antiemetic protocol. PONV was recorded in 272 children aged 1.5–15 years after inpatient surgery under general anesthesia. Before protocol introduction, PON and POV incidence was 36% and 34%, respectively. After introduction, moderate to severe nausea decreased (18 vs. 9%), but moderate to severe vomiting failed to reach significance (19 vs. 11%). The proportion of children with repeat nausea decreased after protocol introduction, but the proportion of those with repeated episodes of vomiting was unchanged. An increase in antiemetic protocol prescribing frequency led to a decreased incidence of moderate to severe PON and a reduction in the number of patients with repeated nausea.

13.3 Enhanced Recovery After Surgery (ERAS)

Implementation of standardized rapid recovery pathway algorithms have helped reduce pain and opioid consumption, decrease PONV, aid faster mobilization, lead to earlier discharge, and reduce the incidence of opioid-related side effects [239–241]. ERAS algorithms using multimodal pain and PONV medication protocols have been used for spine surgery operations [236, 239].

14 PONV Management and ERAS Pathways

ERAS pathways provide a framework and central principle for using multimodal pain protocols to help reduce reliance on opioid medications [240–244]. The 2016 ERAS consensus

Table 7 Strategies to reduce baseline risk for postoperative nausea and vomiting

Avoidance of general anesthesia by use of regional anesthesia [9, 260]
Use of propofol for induction and maintenance of anesthesia [261]
Avoidance of nitrous oxide in surgeries lasting over 1 h [262, 263]
Avoidance of volatile anesthetics [43, 113]
Minimization of intraoperative and postoperative opioids [43, 74, 264, 265]
Adequate hydration [266, 267]

Reproduced with permission from Gan et al. [2]

guidelines for gastrointestinal surgery [241] recommended the implementation of general multimodal prophylaxis with baseline risk reduction interventions. Use of dexmedetomidine, NSAIDs, and regional anesthesia in pediatric ambulatory surgery has been found to minimize the use of perioperative opioids [86, 112, 131, 200, 204, 245, 246]. An ERAS consensus document summarized algorithms and pathways that contained specific recommendations about interventions that reduce baseline PONV risk [240, 241]. These include the use of minimal preoperative fasting, carbohydrate loading, adequate intravenous fluid therapy hydration, PONV prophylaxis, propofol TIVA, and multimodal pain management with opioid-sparing analgesia. Opioid-sparing analgesia includes acetaminophen, NSAIDs, NMDA antagonists, α-2 agonists, glucocorticoids, central neuraxial techniques, surgical-site infiltration, and regional anesthesia [133–135, 242, 243]. ERAS pathways should include at least two antiemetic medication interventions for PONV prophylaxis with the addition of other antiemetic medications for high-risk patients [2]. PONV treatment should be administered as soon as possible. In ENT surgery, PONV prophylaxis with intravenous ondansetron 4 mg and dexamethasone 4 mg was effective when given 2 h prior to the end of surgery [244]. To optimize PONV management, the type and emetogenicity of surgery should be considered as well as the regional anesthesia and expected postoperative recovery [2]. When applied to appropriate pediatric surgical populations, the use of ERAS pathways with multimodal analgesic pain and antiemetic PONV prophylaxis can reduce the incidence of PONV, length of stay, and risk of readmission with no increase in complications [247, 248]. Short et al. [249] determined that implementation of a pediatric-specific enhanced recovery protocol in children undergoing colorectal surgery was feasible and safe and led to improved outcomes. Table 8 shows an example of pediatric-specific enhanced recovery protocol components organized by phase of care in colorectal surgery.

Minimal prospective ERAS management pathway data are available for orthopedic surgery in children [248]. For multilevel pediatric spinal surgery, implementation of multimodal analgesia and antiemetic management protocols reduced postoperative complications, including PONV [239]. Postoperative pain and weakness are some of the main reasons for delayed discharge [250]. In one prospective study using a perioperative multimodal approach, opioid-sparing analgesia and antiemetic prophylaxis decreased the amount of PONV on the 1st postoperative day [251]. The need for a multimodal approach was suggested in a prospective study using an ERAS pathway for cardiac surgery when intravenous ondansetron prophylaxis alone did not reduce POV during the first 48 h, only lowering nausea on the 3rd postoperative day [252]. PONV management strategies using ERAS recovery programs were similar in terms of their use and manner of PONV risk reduction, prophylaxis, and treatment [1].

Raval and Heiss [253] described the development of an ERAS protocol for children undergoing gastrointestinal surgery. Their center demonstrated an increase in the number of enhanced recovery protocol elements employed over time with a simultaneous median decrease in length of stays, time to regular diet, dose of intraoperative and postoperative opioids, and volume of intraoperative fluids. The researchers concluded that their protocol appeared feasible and safe and was associated with improved outcomes, including a decrease in complication rates and 30-day readmissions.

15 Clinical Guidelines for PONV and POV in Children

The updated 2020 PONV consensus guidelines [2] provide evidence-based clinical recommendations on the management of PONV and POV in children. Prevention of PONV and POV can be achieved through the use of strategies to reduce baseline risk with patient evaluation and risk assessment, baseline risk reduction, and use of preoperative antiemetic prophylaxis (Table 7). The benefits and risks of multimodal pain and PONV prophylaxis should be determined. The choice of medications is determined by availability, cost, patient factors, and hospital policy. No antiemetics or 5-HT3 antagonists are recommended for children at low risk (no or one risk factor). For medium risk (one to two risk factors), two antiemetic interventions are recommended with a 5-HT3 receptor antagonist, such as ondansetron plus dexamethasone. Children at high risk (three or more risk factors) are recommended to receive multimodal triple combination prophylaxis with a 5-HT3 receptor antagonist plus dexamethasone plus propofol TIVA. For optimal effect, antiemetic medications from different drug classes are recommended (Fig. 4) [2].

In patients for whom PONV prophylaxis fails, previously administered antiemetics should be reviewed. Effective rescue treatment involves the choice of antiemetics from a drug class other than that used for prophylaxis. If more than 6 h has passed since administration of a prior antiemetic medication, such as ondansetron, a repeat dose can be considered. The choice of medications for rescue treatment is limited, with minimal research on optimal effectiveness [2].

PONV management is a vital component of enhanced ERAS recovery algorithms and pathways. Multimodal PONV prophylaxis is recommended for surgical patients with multiple risk factors. PONV management protocols should consider cost effectiveness and what medications are available for prophylaxis. Antiemetics should be chosen from at least four different drug classes. Use of multimodal prophylaxis with at least two antiemetics and additional medications as needed in high-risk patients may be practical choices to optimize PONV prevention [2].

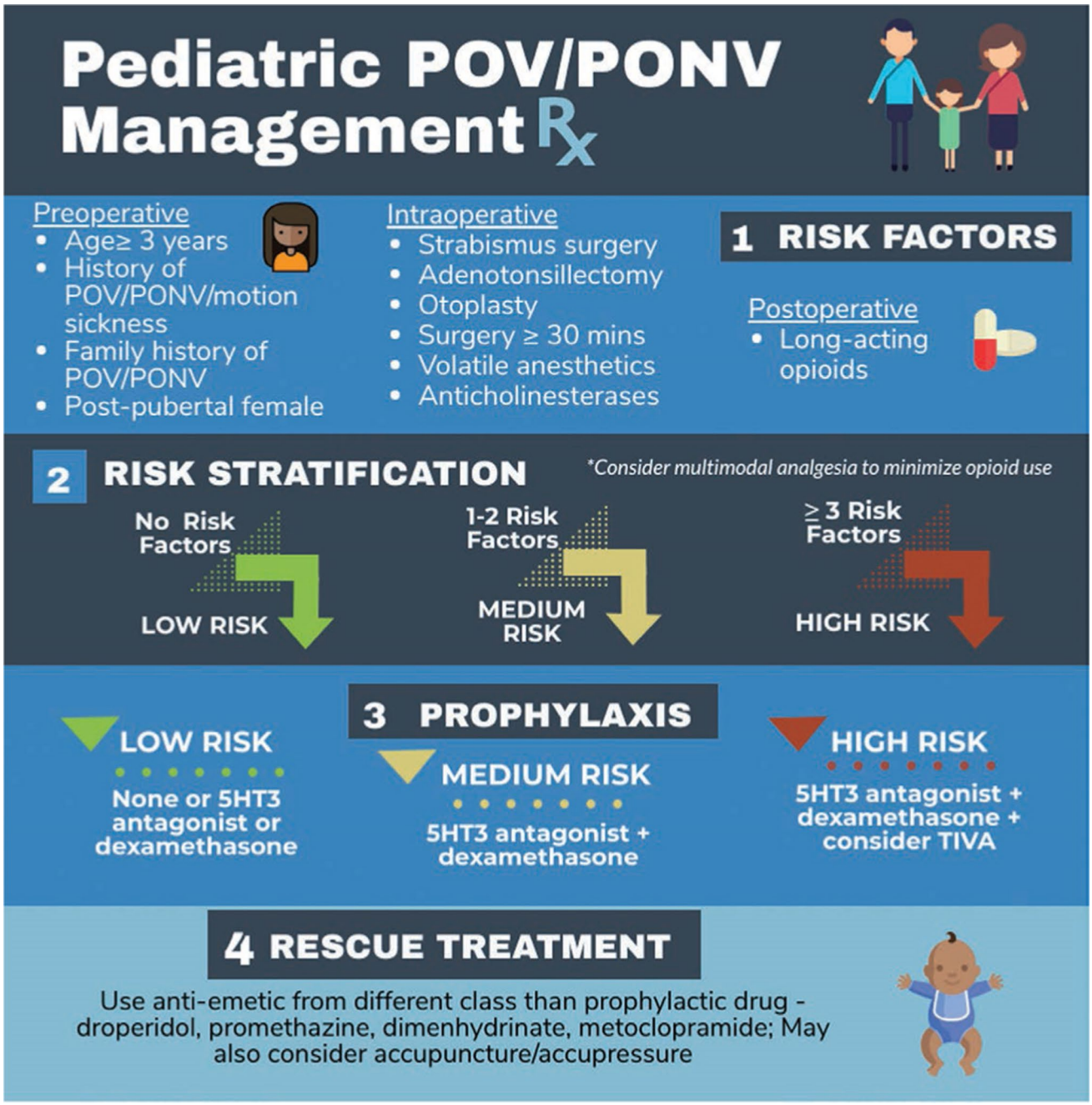

Fig. 4 Algorithm for management of postoperative vomiting in children, including risk identification, risk-stratified prophylaxis, and treatment of established postoperative vomiting. Reproduced from Gan et al. [2] with permission from the American Society for Enhanced Recovery. *PONV* postoperative nausea and vomiting, *POV* postoperative vomiting, *TIVA* total intravenous anesthesia, 5HT3 5-hydroxytryptamine-3

16 Summary

In the last 13 years, more studies have evaluated the efficacy and safety of various medications and techniques for the management of pain, nausea, and vomiting in children. The PONV consensus guidelines have also been updated. The inter-relationship between pain and pain therapy and nausea and vomiting has been further recognized and studied. This has stimulated interest in the development of combination multimodal pain and antiemetic management techniques, PONV protocols, and ERAS guidelines using perioperative opioid-sparing analgesia and regional anesthesia. Pediatric PONV risk factors differ from those of adults, with greater risk in children aged > 3 years, post-pubertal females, and

Table 8 Pediatric-specific enhanced recovery protocol components organized by phase of care in colorectal surgery

Preoperative clinic visit
Detailed counseling, including preset discharge criteria provided by surgical NP
Day before operation
Bowel preparation (antibiotics only): neomycin 10 mg/kg TID; metronidazole 250 or 500 mg
Day of operation, preoperative holding area
Clears allowed up until 2 h before operation
Preoperative carbohydrate loading: 20 oz. Gatorade or apple juice completed 2 h before operation
Loading dose of gabapentin 15 mg/kg 3 h before surgery
Placement of sequential compression devices (age > 12 years)
Intraoperative
Antibiotic prophylaxis, given < 1 h prior to incision
Laparoscopic technique
Avoidance of nasogastric tubes and perianastomotic drains
Regional anesthesia: TAP (ileocecectomy, colectomy, ileostomy reversal); epidural (J-pouch)
Minimization of opioids
Maintenance of normothermia
Maintenance of near zero fluid balance: limit crystalloids to 3–4 ml/kg/h
Postoperative, surgical ward
Early mobilization on postoperative day 0
Early oral intake starting with clears in the PACU and advancement to regular diet
Maintenance of near zero fluid balance: limit unnecessary boluses
Opioid-sparing pain regimen:
IV ketorolac (0.5 mg/kg up to 30 mg max dose) q6h × 72 h
PO gabapentin (10 mg/kg up to 600 mg max dose) q8h × 72 h
PO acetaminophen (10 mg/kg up to max 650 mg) q6h
IV morphine (0.05 mg/kg or 0.1 mg/kg) q4h PRN breakthrough pain
IV hydromorphone (0.005 mg/kg or 0.01 mg/kg) q4h PRN breakthrough pain
Prevention of nausea and vomiting
Ondansetron (0.1 mg/kg or 0.15 mg/kg) injection q8h
Aggressive pulmonary toilet: incentive spirometry on postoperative day 0

Reproduced with permission from Short et al. [249]

IV intravenous, *max* maximum, *NP* nurse practitioner, *PACU* post-anesthesia care unit, *PO* oral administration, *PRN* as needed, *qxh* every × hours, *TAP* transversus abdominis plane, *TID* three times daily

in procedures such as strabismus repair, adenotonsillectomy, and middle ear surgery. Procedures and children with high PONV risk can be managed by avoiding nitrous oxide and using combination antiemetic therapy with dexamethasone and ondansetron, opioid-sparing analgesia, and a propofol TIVA technique. The 5-HT3 receptor antagonists are more effective for prevention of vomiting than of nausea and are recommended as first-line antiemetics for PONV prophylaxis in children. As single and combination therapy, ondansetron and dexamethasone have been frequently studied and shown to be effective and well-tolerated. A multimodal approach for antiemetic and pain therapy involves preoperative evaluation, patient preparation, risk stratification, antiemetic prophylaxis, pain management, and choice of anesthesia to include opioid-sparing medications and regional anesthesia. Strategies to decrease pediatric baseline PONV risk are similar to those in adults. However, in some cases, antiemetic prophylaxis may not be needed for children at extremely low risk with surgeries lasting less than 30 min. For children at low risk (no to one risk factor), no prophylaxis or a 5-HT3 antagonist should be considered. With more than two risk factors, children at medium (one to two risk factors) or high risk (three or more risk factors) are recommended to receive double or triple antiemetic prophylaxis with propofol TIVA, respectively. Regional anesthesia should be considered if appropriate. Combination prophylactic therapy using two or three antiemetics from different drug classes should be considered and include the 5-HT3 receptor antagonists such as ondansetron, dexamethasone, and propofol TIVA. If prophylaxis fails, an antiemetic of a different drug class should be used for rescue treatment. ERAS protocols include a multimodal approach with preoperative preparation, adequate intravenous fluid hydration, opioid-sparing analgesia, and prophylactic antiemetics. PONV guidelines and management algorithms help provide effective postoperative care for pediatric patients.

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