Postdischarge nausea and vomiting (PDNV) in children: A review and observational study

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Postdischarge nausea and vomiting (PDNV) cause substantial pediatric morbidity with potentially serious postoperative complications. However, few studies have addressed PDNV prevention and treatment in pediatric patients. Here we searched the literature and processed it in a narrative review describing PDNV incidence, risk factors, and management in pediatric patients.. A successful strategy for reducing PDNV considers both the pharmacokinetics of the antiemetic agents and the principle of multimodal prophylaxis, utilizing agents of different pharmacologic classes. Since many highly effective antiemetic agents have relatively short half-lives, a different approach must be used to prevent PDNV. A combination of oral and intravenous medications with longer half-lives, such as palonosetron or aprepitant, can be used. In addition, we designed a prospective observational study with the primary objective of determining PDNV incidence. In our study group of 205 children, the overall PDNV incidence was 14.6% (30 of 205), including 21 children suffering from nausea and 9 suffering from vomiting.

Key words: postoperative nausea, postoperative vomiting, postdischarge nausea, postdischarge vomiting, antiemetics, setrons

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BACKGROUND

Postdischarge nausea and vomiting (PDNV) occur in patients after discharge from the hospital, most often after one-day surgery. PDNV can be a sequel to postoperative nausea and vomiting (PONV) or can newly develop after discharge, unrelated to PONV (ref.[1]). The occurrence of PDNV in children is a significant cause of distress for patients and their families. Moreover, severe vomiting in children can lead to dehydration and metabolic disorders, often leading to hospital readmission for treatment with antiemetics and intravenous rehydration[2].

The term "early PDNV" describes nausea and vomiting at home within 24 h after the patient undergoes a surgical procedure in an outpatient or inpatient setting and overlaps with PONV in some cases. The term "late PDNV" describes nausea and vomiting that occur over 24 h after surgery (Fig. 1) (ref.[3]). There is no strictly defined time limit of causality between surgery and PDNV. Most studies report PDNV during the first 48–72 h postdischarge; however, the available data indicate that PDNV may occur up to 7 days after surgery[1].

To date, few studies have addressed PDNV in pediatric patients. Therefore, we first searched the available literature for the present study and processed it as a narrative review. Next, we designed a prospective observational study to determine the incidence of late PDNV within the first three days after surgery.

MATERIAL AND METHODS

After Ethics Committee approval, we enrolled 205 children of both sexes, aged 3–7 years (median, 4 years), who underwent endoscopic adenoidectomy under general anesthesia. We obtained written consent from these children's parents. The study population comprised 98 males and 107 females. Table 1 presents the patients' demographic data. Our study included only patients with a medical condition corresponding to ASA I-II.

Preoperative preparation and management of anesthesia care were conducted according to the standard practice at the University Hospital of Ostrava. Briefly, premedication with orally administered midazolam at a dose of 0.5 mg/kg was initiated 60 min before the surgical procedure. Then, general anesthesia was induced by inhalation with sevoflurane, airway protection with a laryngeal mask airway, and intravenous administration of sufentanil at a dose of 0.2 μg/kg and paracetamol at a dose of 15 mg/kg. Patients were not routinely given antiemetic prophylaxis due to the low risk according to the POVOC score. A 2 h observation followed the surgical procedure in the post-anesthesia care unit (PACU).

Upon meeting the discharge criteria, the patients were transferred to the inpatient ward of the ENT department. Hospital discharge occurred on the morning of the 1st postoperative day. The parents were given careful instructions, and a telephone call obtained data on the

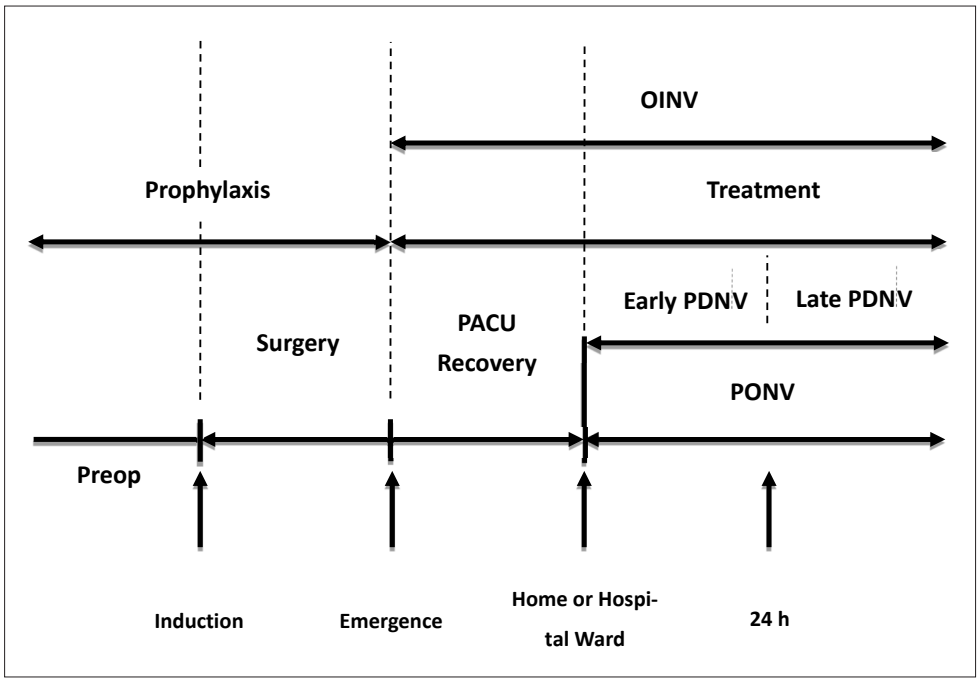

Fig. 1. Overlapping time intervals of postoperative nausea and vomiting (PONV), postdischarge nausea and vomiting (PDNV), and opioid-induced nausea and vomiting (OINV), modified according to Kovac[3].

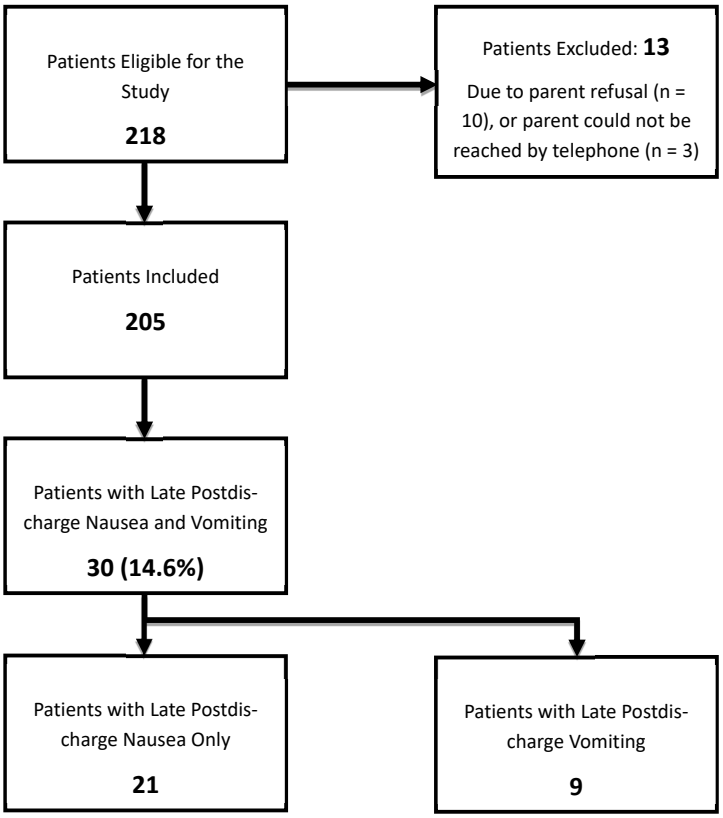

Fig. 2. Flowchart of the study.

4th postoperative day. The main question was intended to accurately determine the presence of nausea and vomiting and the postoperative day on which it occurred. The patient was automatically excluded from the study if the parent could not be reached by phone. The data obtained from the parents were verified using medical records from the patient's follow-up visit at the ENT clinic. Fig. 2 shows the flowchart of the study.

Incidence of PDNV

PDNV incidence in the adult population is between 37–57%. The considerable variability in PDNV incidence is a consequence of the different methodologies used in clinical trials and the unclear boundary between PONV and early PDNV. For example, nausea and vomiting occurring after the patient's discharge from the PACU to the ward may be evaluated as PONV, while nausea and vomiting occurring upon discharge to home care are assessed as PDNV (ref.[4-6]) .

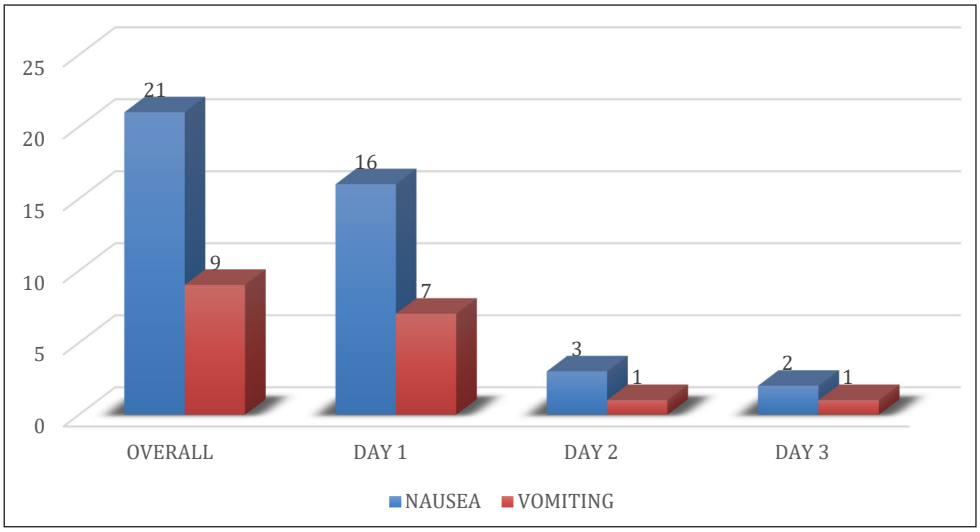

Fig. 3. The incidence of postdischarge nausea and vomiting (PDNV).

Little is known about PDNV incidence in children. A recent study indicated a 14% incidence of PDNV among 1013 pediatric patients who underwent tonsillectomy, strabismus repair, dental treatment, or other procedures[2]. In our study group of 205 children, the overall incidence of PDNV was 14.6% (30 of 205), including 21 children suffering from nausea and 9 from vomiting (Fig. 2). PDNV incidence was highest on the 1st postoperative day and gradually decreased until the 3rd postoperative day. No instances of PDNV occurred on the 4th postoperative day (Fig. 3). The presently observed PDNV incidence was similar to that reported in the earlier work of Efune[2] , which is much lower than that reported in the adult patient population.

There may be 2 principal reasons for this observation. First, the presence of nausea, as a purely subjective feeling of bodily discomfort, is challenging to detect in very young children; therefore, PDNV occurrence is likely underestimated in this group of patients[7]. One possible solution is the assessment of nausea using the Baxter Animated Retching Faces (BARF) score not only by medical professionals but also by parents. The BARF score has the highest discriminant validity between nausea and pain compared to other available nausea assessment systems (KIN index and PeNAT) (ref.[8]).

Another reason is that the studied population of children often undergo tonsillectomy with or without adenoidectomy, strabismus repair, or other surgical procedures, which do not usually involve the postoperative application of opioid analgesics. Opioid-induced nausea and vomiting (OINV) is another complication that partially overlaps with PONV and PDNV. OINV is caused by opioid-mediated activation of μ-receptors in the gastrointestinal tract and vestibular system. After opioid administration during the postoperative period, nausea occurs in 40% of patients and vomiting in 15–25% of patients[3].

Risk Factors and Prediction of PDNV

The essential prerequisites for successful PDNV management are risk stratification of patients and adequate prevention and treatment in indicated cases. However, comprehensive pharmacological prevention for all patients is not recommended, mainly due to the adverse effects of antiemetic administration in a low-risk patient population[9].

Among adult patients, there are five known independent risk factors for PDNV development, which together constitute the Apfel score: female sex, age under 50 years, history of PONV, opioid use during the postoperative period, and nausea before hospital discharge. The risk of PDNV development increases with the number of risk factors in a patient: 10% with 0 risk factors, 20% with 1, 30% with 2, 50% with 3, 60% with 4, and 80% with all 5 (ref.[6]). According to Odom-Forren, other risk factors include the administration of rescue antiemetic therapy in the PACU, operating room time, and postoperative pain[5].

It is complicated to determine the risk of PDNV development in children compared to adult patients since there is no specific risk scale. However, in many children, PDNV occurs due to persistent PONV. Therefore, the available scores for PONV can be used with an awareness of the possible inaccuracy of the estimated risk of developing PDNV.

The POVOC and VPOP scores are currently used to predict the risk of PONV in children. Eberhart's POVOC score includes four independent risk factors for PONV: surgery duration over 30 min, patient age over three years, history of PONV, and surgical repair of strabismus (Table 2). In the presence of 1, 2, 3, or 4 risk factors, the incidence of postoperative vomiting rises to 10%, 30%, 55%, or 75%, respectively[10]. The VPOP score includes the patient's age and the duration of the surgical procedure and considers both tonsillectomy and strabismus repair as high-risk surgical procedures (Table 3). Unlike the POVOC score, the VPOP score also includes opioid consumption as a significant risk factor[11]. Repeated administration of opioids during the postoperative period increases the risk of PONV and, according to recent studies, is associated with a higher incidence of PDNV (ref.[3]). Intraoperative administration of opioids is also likely to play an important role. PDNV incidence is reportedly lower among patients who received a short-acting opi-

Table 1. Demographic data of the study population.

	Median	Arithmetic mean	Minimum value	Maximum value
Height, cm	106.5	108.3	98	134
Weight, kg	17	18.9	11	42
Age, years	4	4.1	3	7

Table 2. POVOC score from Eberhart et al.[10].

Risk factors	Points
Surgery > 30 min	1
Age > 3 years	1
Strabismus repair surgery	1
History of PONV or family history of PONV	1
Sum of points	1–4

PONV, postoperative nausea and vomiting.

oid during surgery than children who received a long-acting opioid[2]. Severe pain and at-home use of opioids may also contribute to late PDNV. Accordingly, patients with severe pain experience a significantly greater degree of nausea and vomiting through the first five days post-discharge[6] .

Multiple studies have found that strabismus repair and tonsillectomy are associated with the highest incidence of PONV in children[2]. However, to date, only one study has evaluated these surgical procedures from the perspective of the risk of developing PDNV. Efune demonstrated that children who underwent tonsillectomy had a significantly higher risk of PDNV. In their study, the PDNV incidence was 27%, which is approximately double the incidence of PDNV we found in patients undergoing endoscopic adenoidectomy[2]. This difference may be explained by the fact that patients in the previous study underwent a more prolonged surgical procedure with higher postoperative pain and opioid consumption than endoscopic adenoidectomy. Additionally, Efune et al. did not identify strabismus repair as a significant risk factor for PDNV. They stated that due to the low number of patients (31 children), their study might have been underpowered to detect a significant risk for that surgical procedure[2].

The transport of a patient to their home from the hospital is a notable event during the postoperative period in the outpatient setting. Previous studies of adults have shown that a history of motion sickness increases the risk of PONV (ref.[2,12]). Similarly, it may be assumed that transport influences the incidence of PDNV in children. In 48% of children with PDNV, at least one episode of nausea and vomiting was induced by a previous car ride; however, the duration of transport does not significantly increase PDNV risk[2]. Accordingly, our study did not find that the car ride duration was associated with nausea and vomiting.

Based on the currently available knowledge, most children with a high risk of PONV are also at risk of developing early PDNV. Overall, PDNV incidence is highest among children undergoing tonsillectomy and those with severe postoperative pain requiring home administration of opioids and other analgesics. Table 4 presents an overview of proven risk factors associated with a higher risk of PDNV in children.

PDNV Management

Concerning PDNV management, the differentiation between early and late PDNV is essential. Fully developed PDNV that does not respond to home treatment is an indication for consultation at a medical facility or rehospitalization. Successful strategies for reducing PDNV consider both the pharmacokinetics of the antiemetic agents and the principle of multimodal prophylaxis, utilizing agents of different pharmacologic classes. Since many highly effective antiemetic agents have relatively short half-lives, a different approach must be used to prevent PDNV, combining oral and intravenous medications with longer half-lives (Table 5).

In many cases, early PDNV is a consequence of persistent PONV and thus occurs when the patient is in the PACU. According to recent guidelines, patients with nausea and vomiting are given one or two antiemetics, usually ondansetron, with or without dexamethasone. When PONV/PDNV develops in a patient who has received antiemetic prophylaxis (considered treatment failure), administering one or two antiemetics from another phar-

Table 3. VPOP score from Bourdaud et al.[11].

Risk factors	Point score		
	0	1	2
Age	< 3 years	3–6 years or > 13 years	between 6–13 years
Predisposition to PONV (previous PONV, motion sickness, family history)	No	Yes	–
Duration of anesthesia > 45 min	No	Yes	–
High-risk surgery (tonsillectomy, strabismus repair)	No	Yes	–
Multiple doses of opioids	No	Yes	–

PONV, postoperative nausea and vomiting.

Table 4. Proven risk factors for PDNV in children.

High-risk of PONV and developed PONV in PACU
Tonsillectomy (maybe strabismus repair surgery)
Severe pain and at-home administration of opioids

PDNV, postdischarge nausea and vomiting; PONV, postoperative nausea and vomiting.

Table 5. Antiemetic agents.

Antiemetic agent	Dose	Half-life
Palonosetron	0.5–1.5 μg/kg i.v.	40 h
Aprepitant	10–40 mg p.o.	9–12 h
Scopolamine patch	1.5 mg patch	9–12 h

macological group is indicated[9]. In a systematic review of 22 randomized clinical trials, Gupta et al.[13] demonstrated that adequate prevention of PONV yields a significant decrease in early PDNV among adult patients. However, among the available studies in children, none have shown that prophylactic administration of antiemetics leads to a statistically significant reduction of early PDNV. Ondansetron, the 5-HT_3 antagonist most commonly used in children, has little efficacy in preventing PDNV because of its short half-life of approximately 3 h (ref.[6]). In the randomized clinical trials by Efune[2] and De Orange[14], the PDNV incidence did not differ between children who received a placebo vs. dexamethasone alone vs. dexamethasone combined with ondansetron. Notably, Kearney even demonstrated a higher consumption of antiemetics during hospitalization among children who later developed PDNV. The authors concluded that the administration of antiemetics does not prevent PDNV development but only delays the onset of symptoms[15].

Other in-hospital strategies to reduce early PDNV are the same as those used to reduce and control PONV. Optimization of the patient's fluid status, use of opioid-sparing techniques (regional anesthesia), and total intravenous anesthesia (TIVA) are options that may contribute to PDNV risk mitigation[16-18] .

In children with multiple risk factors for PDNV, using at least one long-acting antiemetic agent is indicated. Palonosetron, a second-generation 5-HT_3 antagonist, can be administered intravenously at a dose of 0.5–1.5 μg/kg (ref.[19]). Palonosetron has higher efficacy than first-generation setrons due to higher receptor affinity and much longer half-life (approximately 40 h) (ref.[20-21]) . Another option is the oral administration of aprepitant at a dose of 10–40 mg 1–2 h before surgery. Compared with ondansetron, aprepitant is reportedly superior for the prevention of nausea and vomiting severity during the first 48 h, likely due to its superior antiemetic efficacy and significantly longer half-life of between 9–12 h (ref.[22]). Another available option is fosaprepitant, a preparation for intravenous use.

No single strategy has been published for treating delayed or late PDNV. The primary method is consistent treatment of postoperative pain, preferably with nonopioid analgesics, such as paracetamol, NSAIDs, or both. Nonopioid agents may be equivalent or superior to opioids for managing musculoskeletal pain and are associated with a lower incidence of PDNV (ref.[7]). In addition, it is necessary to prescribe antiemetics for home administration among high-risk and potentially high-risk patients. Since intravenous access is usually unavailable after hospital discharge, the antiemetic drugs must be administered orally, sublingually, or rectally, which are not always desirable or practical routes for PDNV treatment. Moreover, the need to obtain prescribed medication from a local pharmacy after discharge may result in a considerable delay in PDNV treatment[2,23] .

Another option for antiemetic prophylaxis, which is also suitable for home use, is the application of a scopolamine-containing patch. The transdermal route is a non-invasive and easy method of drug delivery in adults and children. Scopolamine is an anticholinergic agent used for its effects on nausea and vomiting. It has a significant advantage for PDNV management because the effect lasts up to 72 h after applying the patch[3] . Compared to a patch-free control group, Horimoto et al. demonstrated that scopolamine patches effectively reduced the incidence of postoperative vomiting among 50 children who underwent surgical correction of strabismus[24]. Possible side effects of the patch may include dry mouth, visual disturbances, and delirium[25]. However, transdermal scopolamine patches have not received FDA approval for use in pediatric patients[26].

The main issue associated with the home administration of antiemetic drugs after ambulatory surgery is the increased risk of cumulative possible adverse effects – particularly sedation, hypotension, extrapyramidal symptoms, and prolongation of the QT interval[1]. However, these risks may be minimized by management accounting for risk stratification, patient comorbidities, and chronic medication.

The latest evidence-based guidelines endorse the implementation of a PDNV management protocol in clinical settings[9] . However, observational studies show that many centers have not developed such protocols at all or that there is considerable heterogeneity regarding compliance with implemented institutional protocols[1]. A recent French study included 221 healthcare institutions and over 7000 patients and reported that only 12% of the participating centers had developed PDNV management guidelines and that antiemetic drugs were prescribed for home use in less than 2% of cases[27]. Despite the availability of validated evidence-based recommendations and effective pharmacological interventions, management gaps still exist, especially for pediatric patients. Due to the lack of risk stratification, we can still not predict any specific patient's level of risk for developing PDNV. Additionally, pharmacological prevention of PDNV is not applied to children, and local institutional protocols for PDNV management have not been set.

A commonly overlooked factor is the lack of parental education. When a child is discharged, the parents should be informed in detail about the risk of PDNV develop-

ment and treatment options. Feedback from parents is essential for assessing the efficacy of PDNV home treatment and revealing hidden obstacles[1] .

Future Implications

Very little research has specifically examined the occurrence of PDNV in pediatric patients. Although we know that PDNV can affect a child's recovery and resumption of regular activity, it remains unclear how nausea and vomiting impact recovery, the extent of the delay in recovery, and how these symptoms increase additional healthcare costs[28] . Additional charges may include expenses related to unplanned hospital admission, increased rescue medication, and delayed return to work for caregivers of the child[4] . Further clinical studies are needed to determine the exact incidence of PDNV, its risk factors, and how to implement these findings into clinical practice.

CONCLUSIONS

PDNV is a potentially severe postoperative complication in pediatric anesthesiology, with a significantly underestimated incidence, especially in young children. Since we do not yet know all risk factors, we cannot accurately determine a child's risk of PDNV development. For this reason, antiemetic prophylaxis is not administered to pediatric patients upon hospital discharge. In addition, PDNV threatens a child's recovery, especially when it leads to dehydration, and severe cases may require rehospitalization, with significantly increased financial costs.

Search strategy and selection criteria

To search the available literature, the PubMed/Medline database (https://www.ncbi.nlm.nih.gov/pubmed) was used to identify articles investigating PDNV, applying the following search algorithm: postdischarge nausea [Title/Abstract] AND vomiting [Title/Abstract]. As a result, we found 64 publications, 9 of which included pediatric patients aged 0–18 years. Two reviewers determined five of these nine articles be valid for the present study.

Author contributions: MFr: literature review, study conception and design, analyses and interpretation of data, writing-original draft, final adjustments of manuscript, visualization; VV, OJ: literature review, writing-review and editing; FB: writing-review and editing, data curation, visualization; MFo: resources, data curation, writing-review and editing; PS, VP: analyses and interpretation of data, final adjustments of manuscript, supervision.

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Ethics approval: The study was approved by The Ethics Committee of University Hospital Ostrava, Czech Republic, no. 566/2020.

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