Postoperative Nausea and Vomiting

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GRADUATE THESIS

Zagreb, 2024

This graduate thesis was made at the Department of Anesthesiology, Reanimatology and Intensive Care, University Hospital Centre, Zagreb School of Medicine, University of Zagreb, mentored by Professor Vilena Vrbanović Mijatović, MD, PhD. It was submitted for evaluation in the academic year of 2023/2024.

Abbreviations

5-HT3	Serotonin receptor
BBB	Blood-brain barrier
CNS	Central nervous system
CTZ	Chemoreceptor trigger zone
D2	Dopamine receptor
$GABA_A$	γ-Aminobutyric acid type A receptor
H1	Histamine receptor
IV	Intravenously
M1	Muscarinic receptor
NK 1	Neurokinin 1 receptor
NTS	Nucleus of the solitary tract
PNS	Peripheral nervous system
PO	"Per os" meaning by mouth
PONV	Postoperative Nausea and Vomiting
POVOC	Postoperative Vomiting in Children score
TIVA	Total Intravenous Anesthesia
VPOP	Vomiting in the Postoperative Period score

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Summary

Title: Postoperative Nausea and Vomiting

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Keywords: Postoperative nausea and Vomiting, PONV, surgery, anesthesia, risk factors, vomiting center, APFEL score

A comprehensive review of postoperative nausea and Vomiting (PONV) is presented, a widely recognized side effect occurring within the first 24 hours following a surgical procedure. This review aims to identify the factors influencing PONV, including patient-specific traits, anesthetic methods, and surgical interventions. It explains the neural pathways controlling vomiting and evaluates pharmacological and non-pharmacological approaches to managing PONV. Additionally, this thesis highlights the consequences associated with PONV and the importance of preventive measures tailored to individual risk profiles. It explores various methods in PONV management, including genetic investigations and nerve stimulation techniques, to improve patient outcomes and satisfaction. It emphasizes the complex nature of PONV, the significance of understanding contributing factors such as patient characteristics, anesthetic techniques, and surgical procedures, and the roles of pharmacological and non-pharmacological interventions in managing PONV.

Sažetak

Naslov: Postoperativna Mučnina i Povraćanje

Autor: Amanda Lynn LaBar

Ključne riječi: Postoperativna mučnina i povraćanje, PONV, operacija, anestezija, faktori rizika, centar za povraćanje, APFEL rezultat

Prikazan je opsežan pregled postoperativne mučnine i povraćanja (PONV), široko poznate nuspojave koja se javlja unutar prva 24 sata nakon kirurškog zahvata. Ovaj pregled ima za cilj identificirati čimbenike koji utječu na PONV, uključujući osobine specifične za pacijenta, metode anestezije i kirurške intervencije. Objašnjava neuralne putove koji kontroliraju povraćanje i procjenjuje farmakološke i nefarmakološke pristupe liječenju PONV-a. Dodatno, u radu se naglašavaju posljedice povezane s PONV-om i važnost preventivnih mjera prilagođenih individualnim profilima rizika. Istražuje različite metode zbrinjavanja PONV-a, uključujući genetske pretrage i tehnike stimulacije živaca, kako bi se poboljšali ishodi i zadovoljstvo pacijenata. Naglašava složenu prirodu PONV-a, važnost razumijevanja čimbenika koji doprinose kao što su karakteristike bolesnika, tehnike anestezije i kirurški postupci te ulogu farmakoloških i nefarmakoloških intervencija u liječenju PONV-a.

Introduction

Postoperative nausea and Vomiting (PONV) refers to nausea, retching, and vomiting within the first 24-48 postoperative hours (1). PONV is a widely recognized side effect during the postoperative recovery phase. Two of the most frequently encountered adverse events following surgery are nausea and vomiting. (2). In the general surgical population, it's estimated that around 30% experience this, though those with known risk factors may face significantly higher rates, potentially reaching up to 80%. (3, 4).

In modern healthcare settings, patient mortality due to PONV is low (5). Although patient mortality from PONV is low, PONV greatly influences patient well-being, impacting patient recovery duration and overall health outcomes (6). PONV can induce discomfort and distress, thereby impacting the overall surgical experience for patients (7). If not addressed, PONV may cause complications such as dehydration, electrolyte imbalances, and harm to surgical sites (8). Complications from PONV can result in prolonged recovery times, increased risk of further complications, and harm to the patient. Effective management of PONV is crucial for improving surgical outcomes, reducing hospital stays, and enhancing overall postoperative patient care quality. By implementing preventive strategies and tailoring anesthetic approaches to meet each patient's specific needs, anesthesiologists play a vital role in lowering the risk of PONV.

Risk Factors

PONV impacts approximately 30% of children and adults following anesthesia (9,10). However, incidence significantly differs among individuals, with rates soaring as high as 80% in high-risk populations (4,9,10) Certain factors contribute to the variability in the occurrence of PONV. For example, patient characteristics, anesthetic selection, and the complexity of the surgery contribute to the variability in the occurrence of PONV. (Table 1-2)

Table 1
General Risk factors for PONV (4)

Patient-specific risk factors:
Female gender
Nonsmoking status
History of PONV/motion sickness
Anesthetic risk factors:
Use of volatile anesthetics
Use of nitrous oxide
Use of intraoperative and postoperative opioids
Surgical risk factors:
Duration of surgery (each 30-min increase in duration increases PONV risk by 60%, so that a baseline risk of 10% is increased by 16% after 30 min)
Type of surgery

Table 2
Risk Factors for the Occurrence of PONV in Pediatric Patients (11)

Surgical	Duration greater than 30 minutes Ocular surgery ENT surgery (adenoidectomy, tonsillectomy)
Anesthetic	Use of volatile anesthetic Use of opioids Increased postoperative pain
Patients	Age of >3 years History or immediate family history Prolonged preoperative fast State of dehydration

Patient Risk Factors

In general, there are four patient-specific risk factors: 1) female gender, 2) smoking status, 3) age, and 4) history of PONV/motion sickness (4,12). The gender risk factor becomes significant after puberty, with females having a higher risk of experiencing PONV (4,13). In adults, being female is a strong predictor, with females being 2 to 4 times more likely to develop PONV (4,9,10,11,12). The authors found that the female gender was the strongest patient-specific

predictor, followed by the history of PONV and motion sickness (12). Nonsmokers are more prone to PONV compared to smokers (12). Children aged three years and older have a higher risk of PONV compared to those younger than 3 (11,14). Adults aged between 18 and 50 are considered a risk factor while increasing age has been shown to slightly decrease the risk of PONV (11,15). A personal history of PONV and motion sickness in adults and children has been identified as a risk factor (9,10,11). Children are more likely to experience symptoms if one of their family members has also experienced PONV (16). Often overlooked, preoperative anxiety is also a significant risk factor in children undergoing surgery, as the fear experienced before a procedure can trigger physiological responses contributing to PONV (11,17). Activation of the sympathetic nervous system due to anxiety results in elevated secretion of stress hormones, disturbs gastrointestinal motility, and delays gastric emptying (17).

Anesthetic Risk Factors

The choice of anesthetic also influences the risk of PONV (4,18). Different anesthetics have varying effects on the patient. (4,18). In contrast to general anesthesia, regional anesthesia has been found to reduce the risk of PONV in children and adults (19). Volatile anesthetics, such as sevoflurane, are associated with a higher risk of PONV as compared to total intravenous anesthesia using Propofol (20). A meta-analysis revealed a significant reduction in PONV in adults and children who received Propofol, showing a 5.7 decrease in adults and a 3.5 decrease in children (21). Nitrous oxide has also been shown to increase the risk of PONV in high-risk adults and children (9,10, 22, 23) The duration of anesthesia is also a contributing factor. Longer durations with volatile anesthetics correlate with higher risk, as more prolonged procedures require higher dosages, thereby increasing the risk to the patient (4,24). Furthermore, specific procedures known to be painful and require high doses of opioids can further elevate the risk of PONV (12).

Surgical Risk Factors

Many surgical procedures are known to increase the risk of PONV (4,11). For example, procedures on the upper airway, nose, throat, oral, pharyngeal, esophageal, and stomach in which blood is swallowed, or bleeding occurs within the GI tract are known to increase the risk of PONV (5). Procedures such as tonsillectomy, adenoidectomy, strabismus, and orchidopexy surgeries have been associated with a higher incidence of PONV in pediatric patients (11). As noted above, the length of the surgery also contributes to an increased risk, with studies showing a 60% rise in risk for every additional 30 minutes of operating time (9,10). In adults, specific procedures involving sensitive anatomical structures such as breast, gynecological, eye, and ear surgeries (due to vestibular system involvement) and neurosurgeries are also linked to heightened PONV risk (9). Moreover, procedures expected to cause significant postoperative pain also increase the risk of PONV (4,9).

PONV Risk Scores

Treatment and prevention of PONV requires accurate risk stratification (25). Numerous scoring systems have been developed to predict a patient's risk of experiencing PONV (28,29,26). Some of the more notable scoring systems are the Apfel, Koivuranta, and Palazzo & Evans (27,28,29). The PONV scoring systems were developed using logistic regression modeling (27). In general, the PONV scoring systems consider various factors, including, but not limited to, patient characteristics, anesthetic choices, and surgical procedures (10).

Risk Scores for Adults

Initially proposed by Apfel and colleagues in 1999, the APFEL scoring system is commonly used in predicting the risk of PONV in adult patients (25, 28, 29, 30). The formula and original scoring system were developed using a multivariable logistic regression analysis (29). The scoring system was further simplified to a four-factor risk score, determined by the number of predictors present (29). The APFEL scoring system is simple, feasible, and the most adequate tool for assessing a patient's risk of PONV (29,31). Numerous groups have already implemented the APFEL scoring system in their daily practice (26,29). In a 2023 study, the authors indicated that the overall cost of prevention and treatment for PONV was less when the APFEL scoring system was used (32). In a 2015 prospective study, the authors concluded that the APFEL scoring system is a simple and reliable test to identify patients at high risk and can thus be used for preventative treatment strategies (29).

The APFEL scoring system defines PONV as at least one episode of nausea and Vomiting within the first 24 hours after surgery (29). The APFEL scoring system assigns a single point for each of the four risk factors: female sex, non-smoking status, personal history of PONV and motion sickness, and opioid use either intraoperatively or postoperatively (Table 3). The total score, ranging from 0 to 4, correlates with the predicted risk of PONV (28,29). Each APFEL risk factor is supposed to elevate the incidence of PONV by about 20% (28,29).

Table 3
Simplified APFEL Risk Scoring System (29)

Risk factors	**Points**
Female gender	1
Nonsmoker	1
History of PONV	1
Postoperative opioids	1
Total Points	0-4

APFEL scores of 0-1 are generally considered low risk, while those of 3-4 denote high risk, often prompting the use of multiple antiemetic agents (28,29). As seen below, Table 4 illustrates the APFEL point values followed by their corresponding levels of risk.

Table 4
APFEL Levels of Risk (28)

Points	*Level of Risk*
0-1	Low risk for PONV
2	Moderate risk for PONV
3-4	High risk for PONV

Risk Scores for Children

In the pediatric population, there are two risk-scoring systems commonly used by healthcare providers to assess the risk of PONV. (34,36) The first system used to predict the risk of PONV in children is known as the Postoperative Vomiting in Children score (POVOC). The second system to predict PONV in children is the vomiting in the Postoperative Period score (VPOP). (34,36) Leopold H. Eberhart developed the POVOC score, which consists of four variables, each assigned a score of 1 (34). Eberhart's variables include undergoing strabismus surgery, being three years of age, having a duration of surgery longer than 30 minutes, and having a history of PONV (35). On the other hand, the VPOP score also considers the administration of multiple doses of opioids (36).

Pathogenesis

The regulation of vomiting is controlled by the vomiting center, located in a region of the brainstem called the medulla oblongata (37). This center receives inputs from various parts of the body, including higher brain centers, the vestibular system, the chemoreceptor trigger zone, and the nucleus tractus solitarii (NTS) (38). The four primary pathways transmit signals to the vomiting

center, triggering nausea and vomiting. Five primary neurotransmitter receptors are involved in the mediation of nausea and vomiting: muscarinic (M1), dopamine (D2), histamine (H1), serotonin (5-HT3), and neurokinin 1 (NK1) receptors associated with substance P. Every receptor serves as a prospective target for the prevention and treatment of PONV (10).

Chemoreceptor Trigger Zone

The chemoreceptor trigger zone (CTZ) is within the brainstem, specifically in the medulla, known as the area postrema, located at the base of the fourth ventricle (8). This region lies outside the blood-brain barrier (BBB) and features fenestrated capillaries (10). Fenestrated capillaries allow the sampling of particles in the peripheral blood by the CTZ. The CTZ contains a variety of receptors, including opioids, NK1, M1, 5-HT3, D2, and H1 receptors (10). The receptors exhibit sensitivity to neurotransmitters and substances, thereby contributing to the CTZ's ability to detect stimuli and coordinate the initiation of nausea and vomiting.

Higher Cortical Areas

The cortex processes information from various sources, including thoughts, sights, smells, pain, memory, and fear (39). The cortex then transmits the signals to higher brain centers, eventually reaching the vomiting center (40). A recent systematic review on reducing pain after breast surgery found conclusive evidence that loco-regional blocks (specifically paravertebral and pectoralis blocks) and glucocorticoids led to a significant relative reduction in the incidence of PONV by 70% (41) This 70% reduction in PONV incidence contributes to improved postoperative outcomes for breast surgery patients (41).

Vestibular Input

Vestibular input, including motion sickness, is transmitted through cranial nerve eight, the vestibulocochlear nerve, conveying information that undergoes processing in the cerebellum (8,

42). The processed signal then travels to the vomiting center, which triggers the vomiting reflex. This pathway involves the H1 and M1 receptors.

Vagal Inputs

Direct stimulation of the gastric mucosa triggers the release of substance P and serotonin from enterochromaffin cells in the stomach (43). The cells activate the vagus nerve and 5-HT3 splanchnic nerves, transmitting signals to the NTS and relaying the signals to the vomiting center (8). A 2021 study examined whether the gut-vagus-brain reflex mediates PONV (44). Among the 3,223 patients undergoing vagus nerve trunk resection or non-vagotomy surgery in the study, PONV occurred less in vagotomy patients (11.9%) than in non-vagotomy patients (28.7%) (44). This finding suggests that vagus nerve-dependent gut-brain signaling may primarily contribute to PONV (44).

Response

Stimulation of the vomiting center triggers a series of responses, including the contraction of the smooth muscle lining the digestive tract and the abdominal muscles, relaxation of the esophageal sphincter, and stimulation of the salivary glands (8). This series of responses leads to the involuntary and forceful expulsion of stomach contents from the mouth.

Pharmacological Treatment

The pharmacological management of PONV entails administering medications to relieve or prevent symptoms of nausea and vomiting by targeting specific receptors (13). Treatment selection depends on multiple factors, such as the patient's risk profile, the surgical procedure, and current medical conditions. Combination therapy involving medications from different classes is frequently employed to manage PONV effectively.

Antiemetics

A variety of antiemetics employ diverse mechanisms to prevent and alleviate PONV. Studies indicate that antiemetics can decrease the risk of PONV by 25% (28). Tailored to each patient, healthcare providers select antiemetics based on individual patient risk factors and any potential side effects. Higher-risk patients who receive antiemetics generally experience more excellent symptom relief than lower-risk patients (28). However, all antiemetics carry potential side effects. If an antiemetic was administered prophylactically, rescue treatment should involve an antiemetic from a different drug class (45).

Serotonin receptor antagonists

The 5-HT3 receptor antagonists selectively block serotonin 5-HT3 receptors, including first-generation serotonin antagonists such as ondansetron, granisetron, and dolasetron, which are commonly used for both the prevention and treatment of PONV (46). Ondansetron, a 5-HT3 receptor antagonist, blocks serotonin receptors in the gastrointestinal tract, CTZ, and NTS (47). In adults, ondansetron is typically administered at a dose of 4 mg intravenously or 8 mg orally before surgery (4, 28, 48, 49, 50). In children, the dose is 0.1 mg/kg intravenously, with a maximum dose of 4 mg (51). Ondansetron may cause well-tolerated side effects, such as headaches, constipation, serotonin syndrome, and flushing (47). On rare occasions, ondansetron may result in prolonged QT syndrome (47).

For granisetron, the recommended dose for adults is 1 mg intravenously (52), and for children, it is 40 mcg/kg intravenously, with a maximum dose of 0.6 mg (53). Common side effects from granisetron include headaches (10-15% incidence), constipation, somnolence, diarrhea, and minor transient changes in blood pressure (54). Dolasetron is typically administered at a dose of 12.5 mg intravenously in adults (4,55), and in children, the dose is 0.35 mg/kg intravenously, with

a maximum dose of 12.5 mg. Common side effects of dolasetron include headaches, dizziness, and diarrhea (56). Antiemetics can prolong the QT interval and should be avoided in at-risk patients (4).

Second-generation serotonin antagonist, palonosetron, is administered intravenously at a dose of 0.075 mg in adults and 0.5 to 1.5 mcg/kg in children at the induction of anesthesia (57). Palonosetron exhibits higher receptor binding affinity and has a longer half-life of 40 hours without affecting the QT interval. (58,59). Common side effects of palonosetron include headaches and dizziness. Palonosetron is particularly effective in preventing early PONV and vomiting after laparoscopic surgery (60).

Glucocorticoids

Dexamethasone is commonly used for the reduction of PONV. Dexamethasone is known to have a slow onset but is more effective when administered after induction. In adults, dexamethasone is typically administered at a dose of 4 mg intravenously after induction (61), while in children, the dose is 0.25 mg/kg with a maximum of 4 mg (62). Dexamethasone, a corticosteroid, exerts its antiemetic effects through its anti-inflammatory properties (9,63). Dexamethasone is often used as an adjunct to other antiemetics for prophylaxis and is typically administered intravenously at the induction of anesthesia. Side effects of dexamethasone may include hyperglycemia, perineal pain with rapid IV bolus administration, and mental disturbances (64).

According to a recent analysis of 38 studies, dexamethasone is not likely to increase the risk of postoperative infection. However, due to imprecise trial results, its effect on delayed wound healing still needs to be determined (65). Dexamethasone may cause a mild increase in glucose levels, especially in patients without diabetes, with limited evidence suggesting a more pronounced increase in diabetic patients (65).

Anticholinergics

Scopolamine, an anticholinergic medication, is commonly applied as a 1.5 mg transdermal patch for PONV prophylaxis. This long-acting patch should be applied at least 2 hours before anesthesia (66, 2). Side effects are generally mild and may include dry mouth and blurry vision (4,66, 67). However, in older adults, confusion or agitation may occur (41, 68), and acute angle-closure glaucoma is a potential side effect (44). Therefore, it is contraindicated in patients with angle-closure glaucoma (69).

Antidopaminergics

Dopamine receptor antagonists like Droperidol block dopamine receptors in the CTZ (9). Droperidol is typically administered at a dose of 0.625-1.25 mg intravenously. At the same time, haloperidol is given at a dose of 1 mg intravenously, orally, or intramuscularly, and amisulpride at a dose of 5 mg intravenously at the induction of anesthesia (4, 70). Haloperidol and droperidol are given as single IV doses at the end of surgery, with haloperidol having the option of oral or intramuscular administration. However, haloperidol and droperidol are not used for PONV prophylaxis in children. Droperidol, used for treatment, can cause sedation, prolonged QT, and lactation.

Additionally, since droperidol does not readily cross the BBB, it is thus suitable for patients with Parkinson's disease due to droperidol’s reduced risk of extrapyramidal symptoms. Patients receiving droperidol should be monitored with ECG for arrhythmias (71). Amisulpride is a newer drug associated with a mild elevation in serum prolactin, hypokalemia, chills, hypotension during injection, and pain at the injection site (72). Amisulpride should be avoided in patients with congenital long QT syndrome.

Neurokinin 1 receptor antagonists

Long-acting antiemetics such as fosaprepitant and oral/IV aprepitant have a half-life of 40 hours (73). Aprepitant blocks substance P, a neurotransmitter involved in the vomiting reflex, and is frequently used in combination with a 5-HT3 antagonist like ondansetron to enhance the prevention of PONV (4,6,9). In adults, oral aprepitant is administered at a dose of 40 mg preoperatively (74, 75), while fosaprepitant is given at a dose of 150 mg IV preoperatively (76).

Antihistamines

Antihistamines such as cyclizine, diphenhydramine, and dimenhydrinate function by blocking histamine receptors, offering antiemetic effects for preventing and treating PONV (10). When administered at a dose of 50 mg orally or intravenously, cyclizine, which also exhibits some anticholinergic activity, may lead to antimuscarinic effects such as tachycardia, dry eyes, dry mouth, blurred vision, and sedation (13).

Diphenhydramine can be administered via intramuscular, oral, or rectal routes. The recommended dose for diphenhydramine is 1 mg/kg intravenously in adults and 0.5 mg/kg with a maximum of 25 mg in children (77). Common side effects include sedation, dry mouth, dizziness, and urinary retention (78).

Phenothiazines

Promethazine is administered intravenously at a dose ranging from 6.25 to 12.5 mg at the induction of anesthesia (79, 80, 81). It acts like an anticholinergic and antihistamine. Side effects include sedation, delirium, confusion, vision changes, seizures, fast or difficulty breathing, and fast or irregular pulse (4, 82).

Sedatives

When administered at the doses required for Total Intravenous Anesthesia (TIVA), certain sedatives like Propofol possess antiemetic properties (83, 84). For patients under 55 years old with

mild systemic disease, an initial intravenous dose of 40 mg should be administered every 10 seconds until the onset of action is achieved. However, if patients are not premedicated with oral benzodiazepines or intramuscular opioids, the initial dose should be adjusted to 2-2.5 mg/kg intravenously. For patients over 55 years old, debilitated, or with a severe systemic disease that is not life-threatening, a lower initial intravenous dose of 20 mg should be given every 10 seconds until the onset of action is reached. Rapid bolus administration should be avoided to reduce the risk of adverse cardiorespiratory effects such as hypotension, apnea, airway obstruction, and oxygen desaturation.

In a 2015 double-blinded study, patients were randomized into four groups and received either Propofol 20 mg, Propofol 30 mg, Metoclopramide 10 mg, or a placebo (85). The prevalence of PONV within 0-6 hours after anesthesia was significantly lower in the Propofol groups compared to the placebo group (85). The study indicated that a subhypnotic dose of Propofol (30 mg) was as effective as Metoclopramide (10 mg) in reducing the incidence and severity of PONV in the study patients (85).

Combination therapy

To achieve PONV prophylaxis, combining at least two antiemetics from different drug classes (73, 86). This combination approach is more effective in preventing PONV in children and adults (4, 87).

Non-pharmacological Treatment

Non-pharmacological treatments include a variety of interventions that do not involve medication. Non-pharmacological treatments can be used alone or alongside pharmacological treatments.

Acupressure

One such intervention is acupressure, which involves applying pressure to specific acupuncture points on the body (28). As illustrated in Figure 1 below, stimulating the P6 point, located three finger-widths away from the inner wrist, has been found to help alleviate motion sickness (28, 88). In a 2015 review, 40 trials were analyzed, showing that the stimulation of the P6 acupoint effectively reduced PONV, with only minor side effects. This intervention was considered comparable to the efficacy and safety of antiemetic drugs (69). Another study assessed the impact of acupressure on PONV in laparoscopic surgery. Analyzing 11 randomized controlled trials involving 941 patients, acupressure significantly decreased the incidence of nausea, vomiting, and the need for antiemetic drugs in the early and extended postoperative phases (70). The findings suggest that acupressure is an effective non-pharmacological intervention for managing PONV in laparoscopic procedures (70).

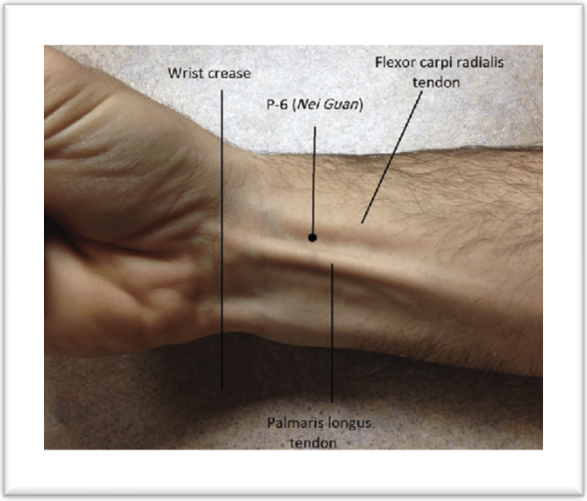

Figure 1
Illustration of the P6 Point (88)

Acupuncture

Acupuncture involves the insertion of thin needles into specific points on the body to achieve therapeutic effects (46, 50). A 2021 meta-analysis examined the effectiveness and safety of acupuncture therapy for PONV following gynecologic surgery. The 2021 meta-analysis included nine randomized controlled trials and one prospective cohort study covering 1,075 participants (72). Results showed that acupuncture therapy significantly reduced the risk of PONV by 48% and 42% for nausea and vomiting, respectively (72). There were no significant differences in side effects between groups, and acupuncture therapy was associated with lower rescue antiemetic usage and higher postoperative recovery satisfaction. The study suggests that acupuncture is an effective and safe therapy for preventing PONV in gynecologic surgery patients (72).

Ginger

Ginger, known for its natural antiemetic properties, can be consumed in different forms, including ginger tea or capsules (48,49). In a 2021 study, the authors aimed to assess the preventive efficacy of ginger on PONV through a systematic review and meta-analysis. Fourteen studies involving 1417 participants were included. Compared to placebo, the ginger group showed significantly lower nausea severity, reduced rescue antiemetic use, and lower incidence of nausea and vomiting over 6 hours post-operation (75). Compared to prophylactic antiemetics, ginger significantly reduced the incidence of nausea but showed no significant difference in vomiting or rescue antiemetic use. The findings suggest ginger could be an effective alternative for preventing PONV, although more research is needed to compare its efficacy with traditional antiemetics (75).

Hydration

Proper hydration before and after surgery has been shown to help alleviate PONV symptoms and adhere to dietary modifications. Patients should adhere to fasting guidelines before surgery and include light, easily digestible meals after surgery (28). In a 2007 study, the authors investigated the impact of preoperative and intraoperative hydration on PONV in patients undergoing laparoscopic cholecystectomy. In the study, 210 patients were randomly assigned to receive either preoperative or intraoperative volume replacement. Results showed a significant reduction in PONV in the preoperative replacement group compared to the intraoperative group. The study results suggest that replacing fluid deficits preoperatively can effectively reduce PONV (74).

Aromatherapy

Deep breathing and relaxation techniques, including aromatherapy, have been demonstrated to reduce stress and anxiety and alleviate nausea (51). In a 2018 systematic review, the authors assessed the impact of aromatherapy on PONV in adult surgical patients. The review included five randomized controlled trials and found that aromatherapy positively affected reducing PONV. Therefore, the author's findings suggest aromatherapy could be considered as a complementary therapy or adjunct to antiemetic medications for managing PONV. However, more research is needed to support the use of aromatherapy in this context further, and future studies could focus on standardizing nausea assessment scales to improve the reliability and validity of research findings on PONV (76).

Complications

Postoperative nausea and vomiting can lead to various complications that significantly impact the patient's overall well-being and recovery process (11,20). Complications due to PONV

have the potential to prolong the patient's recovery period after surgery, causing significant discomfort and distress for the patient during the postoperative period.

Dehydration

Continuous vomiting can result in fluid loss, potentially leading to dehydration (89).

Electrolyte Disturbances

Vomiting can disrupt patients' electrolyte levels, impacting vital bodily functions, including potassium and sodium (90). Sodium is critical in maintaining extracellular fluid volume and regulating cell membrane potential. Common electrolyte disorders associated with sodium include hyponatremia and hypernatremia (81). Potassium, primarily located intracellularly, contributes to maintaining cell membrane potential and is regulated through various mechanisms. Imbalances in potassium levels, such as hypokalemia and hyperkalemia, can potentially induce cardiac arrhythmias (81).

Alkalosis

Prolonged vomiting may even lead to metabolic alkalosis, which involves the loss of hydrogen (acidic component) and chloride (91). Metabolic alkalosis is a common acid-base imbalance seen particularly in hospitalized patients, characterized by elevated serum bicarbonate and arterial pH, often accompanied by increased Pco2 due to compensatory hypoventilation. It can result from acid loss or bicarbonate accumulation in the body, often through gastrointestinal or renal mechanisms (80).

Aspiration

Severe vomiting poses an elevated risk of aspiration, where the stomach contents may enter the respiratory system, potentially leading to pneumonia and other respiratory complications (21).

Wound Damage

Dehiscence is the partial or complete separation of previously approximated wound edges, typically manifesting 5 to 8 days after surgery. Factors contributing to this complication include ischemia, infection, elevated abdominal pressure, diabetes, malnutrition, smoking, and obesity (84). Excessive abdominal contractions during vomiting may exacerbate the risk of wound dehiscence in patients who have undergone abdominal surgery (22).

Prevention

Prevention of PONV involves addressing various risk factors that contribute to its development. The prevention of PONV is critical due to its distressing nature for patients and the potential to delay recovery. Several preventative measures can help minimize the risk, including identifying high-risk patients based on factors such as history of PONV, motion sickness, gender, smoking status, and type of surgery, utilizing tools like the APFEL scoring system. (4,11,28,29,92) Prophylactic measures for PONV should be tailored to individual patient risk factors to reduce the incidence of PONV effectively.

The Society of Ambulatory Anesthesia (SAMBA) presents a straightforward risk evaluation method, incorporating point-based assessments for distinct risk factors and practical guidelines for managing at-risk patients. As seen below, Figure 2 lays out SAMBA's guidelines to reduce the risk of PONV.

1. Identify patients at risk for PONV.
2. Employ management strategies to reduce PONV risk.
3. Employ one to two prophylactic measures in adults at moderate PONV risk.
4. Use multiple interventions in patients at high PONV risk.
5. Administer prophylactic antiemetic therapy to children at high risk using combination therapy.
6. Provide antiemetic therapy to patients with PONV who did not receive prophylactic therapy or in whom prophylaxis failed. Therapy should be with a drug from a different class than that which failed to provide prophylaxis.

Figure 2
SAMBA Guidelines to Reduce the Risk of PONV (4,92)

Prevention in Adults

PONV prophylaxis is recommended for adults, with standard prophylaxis consisting of two antiemetics, such as dexamethasone with a 5-HT3 receptor antagonist. (Figure 2) High-risk patients may require additional antiemetics with different mechanisms of action. (Figure 2) Combination therapy is generally more effective than single agents (83). Additionally, they are educating patients about the importance of promptly reporting any symptoms of nausea or vomiting to healthcare providers (11).

Antiemetics in adults

Administering antiemetic medications before surgery to high-risk patients has been shown to help prevent PONV (11,12). Commonly used options include 5-HT3 antagonists, D2 receptor antagonists, and corticosteroids.

In adult patients without preoperative risk factors but are undergoing inhalation anesthesia or total intravenous anesthesia (TIVA) with opioids, standard practice typically involves administering dexamethasone 4 to 8 mg intravenously after anesthesia induction and ondansetron 4 mg after surgery (93). A study indicated that the combination of ondansetron and dexamethasone resulted in lower nausea scores at 0, 2, and 24 hours postoperatively compared to ondansetron alone (73). Additionally, vomiting was significantly lower in the combination group than the ondansetron-alone group (73).

A multimodal approach to antiemetic administration is recommended. Just 2 hours prior to anesthesia induction, patients can apply a scopolamine patch, which should be removed 24 hours after surgery. Following anesthesia induction, intravenous dexamethasone (4-8 mg) is typically administered. After surgery, intravenous ondansetron (4 mg) is commonly given. In the event of PONV occurrence in the post-anesthesia care unit, an antiemetic from a different class may be warranted. Options include intravenous prochlorperazine (5-10 mg) or droperidol (0.625 mg) (23).

Prevention in Children

PONV prophylaxis is recommended for children, with standard prophylaxis consisting of two antiemetics, such as dexamethasone with a 5-HT3 receptor antagonist. (Figure 2) For high-risk children with more than three risk factors, regional anesthesia with sedation is preferred for older children (94). If the surgery requires general anesthesia, then total intravenous anesthesia (TIVA) with Propofol is used for high-risk patients (94). Children with one or two risk factors are

managed similarly to high-risk patients, except not using TIVA. The choice for children without risk factors is based on doctor and patient preference.

Antiemetics in children

Dexamethasone is given at 0.25 mg/kg intravenously, while ondansetron is administered at 0.1 mg/kg intravenously (62,95). In cases where rescue antiemetics are needed, dimenhydrinate or diphenhydramine can be administered intravenously at a dosage of 0.5 mg/kg, with a maximum of 25 mg (62,95). If a repeat dose of ondansetron is required, it should be given intravenously at 0.1 mg/kg, with a maximum dose of 4 mg (62,95).

Avoidance of Volatile anesthetics

Modifiable risk factors can also be addressed to effectively reduce the risk of postoperative complications. These include abstaining from the use of nitrous oxide, which has been linked to heightened risks, and opting for regional or local anesthesia over volatile agents whenever suitable for the patient (30).

Minimizing Opioids

Minimizing opioid usage has also been shown to yield benefits. Recent studies suggested that opioid-free anesthesia may reduce the incidence and severity of PONV as well as decrease opioid consumption after surgery (63,96,97). If not contraindicated, patients can be administered nonsteroidal anti-inflammatory drugs and acetaminophen for pain relief.

Hydration

Adequate hydration is crucial for preventing dehydration and optimizing postoperative pain management (25,28). Studies have demonstrated that administering intravenous (IV)

crystalloid solutions in adults reduces the risk of PONV (67). In pediatric patients, IV fluid administration has been linked to decreased PONV (68).

A study focused on preoperative IV fluid supplementation, comparing crystalloids and colloids in female patients undergoing elective open cholecystectomy. The study, involving 60 participants, randomized the participants into three groups: 1 control group receiving Ringer lactate IV and two experimental groups receiving varying volumes of Ringer lactate or hydroxyethyl starch. (77). The results indicated that both crystalloids and colloids significantly reduced the incidence of PONV compared to the control group, with no significant difference observed between the two fluid types (77).

Future Directions

The future of PONV entails advancements in comprehending its underlying mechanisms and devising more efficient prevention and management strategies. As research advances in these domains, the goal is to enhance existing approaches and elevate the overall quality of care and patient experience during and after surgical procedures.

Genetics

Ongoing research explores the genetic factors that influence an individual's susceptibility to PONV. At the University of Miami, a study was conducted to explore the role of genetics in the management of PONV (52). The authors discussed various genetic polymorphisms related to serotonin, dopamine, and muscarinic receptors, as well as the involvement of pharmacogenomics in the pathophysiology of PONV. The authors highlighted the potential for personalized medicine in the future, where genetic testing could help identify individual patient risks and responses (52).

Investigations into metabolic pathways, including CYP450 2D6 isoform (CYP2D6), have also been conducted due to their involvement in metabolizing antiemetics (98).

In a separate study, the researchers focused on identifying patients at risk of PONV by characterizing genetic risk factors. The researchers genotyped 601 patients who were followed for PONV symptoms during the first 24 hours after surgery without antiemetic prophylaxis (99). The authors examined the impact of selected single nucleotide polymorphisms around 13 different genes and the predicted activity of 6 liver drug-metabolizing enzymes from the cytochrome P450 family on the occurrence and recurrence of PONV (99). The study confirmed the significance of genetic variations in the type 3B serotonin receptor in the occurrence of PONV and suggested that integrating the rs3782025 genotype into preoperative risk assessments may improve the targeting of antiemetic prophylaxis for patients at risk of PONV (99).

Nerve Stimulation

Advancements in non-invasive neurostimulation methods, such as transcutaneous electrical nerve stimulation, promise to mitigate PONV by modulating neural pathways (55, 57). In a study from 2000, the authors explored the efficacy of transcutaneous impulse stimulation in averting PONV following gynecological surgery. Seventy women undergoing elective procedures were randomly assigned to an activated (stimulation group) or inactive (non-stimulation group) impulse stimulation. The stimulator, placed over the mastoid processes and nuchal region, delivered adjustable electrical pulses. Results indicated reduced postoperative nausea scores, diminished vomiting incidence, and decreased postoperative dizziness in the stimulation group. Moreover, less antiemetic medication was needed in the stimulation group compared to the non-

stimulation group. The findings suggest that electrical vestibular system stimulation may hold promise in PONV prevention (100).

Conclusion

PONV is a multifactorial challenge that impacts a significant portion of patients undergoing anesthesia and surgery. Understanding the various contributing factors, including patient characteristics, anesthetic techniques, and surgical procedures, is essential for effective PONV prevention and management. Patient-specific factors, such as gender, age, smoking status, and history of PONV or motion sickness, along with preoperative anxiety, play significant roles in determining an individual's PONV risk. Anesthetic factors like the choice of anesthesia and specific drugs used can also influence the likelihood of PONV, with regional anesthesia and certain medications like Propofol associated with lower rates.

The regulation of vomiting involves complex neural pathways and neurotransmitter systems, offering potential targets for pharmacological interventions. Antiemetic medications targeting serotonin, dopamine, histamine, and other receptors are commonly used to enhance efficacy. Non-pharmacological interventions such as acupressure, acupuncture, ginger supplementation, hydration, and aromatherapy provide alternative approaches to managing PONV. Non-pharmacological interventions can also complement pharmacotherapy.

Complications of PONV, including dehydration, electrolyte disturbances, aspiration, and wound complications, underscore the importance of prevention. Identifying high-risk patients, employing prophylactic measures such as combination therapy, and addressing modifiable risk factors are critical strategies in PONV prevention. The future of PONV management holds promise

with ongoing research into genetic factors, nerve stimulation techniques, and refined risk stratification models.

Acknowledgments

First, I thank Dr. Vilena Vrbanović Mijatović from the Department of Anesthesiology, Reanimatology, and Intensive Care at the University Hospital Centre Zagreb. I would not have been able to complete this thesis without the invaluable support of my mentor, Dr. Vilena Vrbanović Mijatović. Dr. Vilena Vrbanović Mijatović played a vital role in developing my thesis by providing guidance, corrections, insightful comments, and feedback. I would also like to thank the University of Zagreb School of Medicine's Final Exams Committee for evaluating this graduate thesis. Finally, I would like to thank my parents and brother for their years of unwavering support and encouragement. This achievement would not have been possible without them.

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Biography

Amanda Lynn LaBar was born in Tualatin, Oregon, on March 22, 1995. Amanda was raised in Wilsonville, Oregon, where she graduated from Wilsonville High School in 2013. Graduating with Cum Laude honors, Amanda received a Bachelor of Science degree in Health Sciences from Boise State University in 2017. After receiving her Bachelor of Science from Boise State University, Amanda attended the University of Zagreb School of Medicine in Zagreb, Croatia. Amanda is now in her final year of studies, nearing the completion of her medical studies at the University of Zagreb School of Medicine. Throughout her life, Amanda has actively engaged in volunteer work with various hospitals in Idaho and Oregon. Amanda's involvement within rural areas has provided her with hands-on experience, aligning with her aspirations to practice in rural medicine.