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TO STUDY THE OCCURRENCE OF POSTOPERATIVE NAUSEA AND VOMITING IN PATIENTS AFTER ANAESTHESIA

Anaesthesiology

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ABSTRACT

Background-Postoperative nausea and vomiting (PONV) is one of the most common postoperative complications we sought to determine the incidence of ponv and complex and significant problems in anesthesia practice, with growing trend toward ambulatory and day care surgeries. This review focuses on pharmacological prophylaxis, and rescue therapy for PONV. PONV is influenced by multiple factors which are related to the patient, surgery, and pre, intra, and postoperative anesthesia factors. The risk of PONV can be assessed using a scoring system. which is based on four independent risk predict , PONV prophylaxis is administered to patients with medium and high risks based on this scoring system. Newer drugs such as neurokinin1 receptor antagonist are used along with serotonin 5hydroxytryptamine subtype 3 receptor antagonist, corticosteroids, anticholinergics, antihistaminics, and butyrophenones for PONV prophylaxis. Combination of drugs from different classes with different mechanism of action are administered for optimized efficacy in adults with moderate risk for PONV. Multimodal approach with combination of pharmacological and nonpharmacological prophylaxis along with interventions that reduce baseline risk is employed in patients with high PONV .
Conclusion- A planned multimodal approach starting from preoperative period most likely ensures success in the Management of ponv.

KEYWORDS

Nausea,and vomiting, postoperative nausea and vomiting,

INTRODUCTION

Postoperative nausea and vomiting (PONV) is the phenomenon of nausea and vomiting or retching experienced by a patients in the posanesthesia care unit[PACU] or within 24hours following a surgical procedure, it is an unpleasant complication that affects about 10% of the population undergoing general anaesthesia each year.And second common complaint with pain being the most common postoperative nausea and vomiting, PONV, nausea-vomiting, PONV prophylaxis, and rescue. The review shows that the incidence of PONV is still unacceptably high despite a number of studies on PONV.

over decades, due to complex mechanism of PONV pathogenesis as well as relative lack of concern regarding this issue. PONV remains a significant problem in modern anesthetic practice because of the adverse consequences such as delayed recovery, unexpected hospital admission, delayed return to work of ambulatory patients, pulmonary aspiration, wound dehiscence, and dehydration. Considering increasing demand for ambulatory surgery, a holistic approach should be attempted before and during surgery to prevent PONV. The goal of PONV prophylaxis is therefore to decrease the incidence of PONV and thus patient-related distress and reduce health care costs.

Nausea

unpleasant sensation referred to a desire to vomit not associated with expulsive muscular movement.

Vomiting

forceful expulsion of even a small amount of upper gastrointestinal contents through the mouth.

PHYSIOLOGY OF POSTOPERATIVE NAUSEA AND VOMITING

The pathophysiology of PONV is complex [Figure 1]; it involves various pathways and receptors.

There are five primary afferent pathways involved in stimulating vomiting as follows:

1. The chemoreceptor trigger zone (CTZ)
2. The vagal mucosal pathway in the gastrointestinal system
3. Neuronal pathways from vestibular system
4. Reflex afferent pathways from the cerebral cortex
5. Midbrain afferents.

Stimulation of one of these afferent pathways can activate the sensation of vomiting via cholinergic (muscarinic), dopaminergic, histaminergic, or serotonergic receptors

The neuroanatomical site controlling nausea and vomiting is an ill-defined region called “vomiting center” within reticular formation in the brainstem. It receives afferent inputs from above-mentioned pathways. Further interactions occur with nucleus tractus solitarius.

Neurokinin-1 (NK-1) receptors are located in area postrema and are thought to play an important role in emesis.

CTZ is outside blood–brain barrier and is in contact with cerebrospinal fluid (CSF). CTZ enables substances in blood and CSF to interact. Adsorbed toxins or drugs circulating in the blood can cause nausea and vomiting by stimulation of CTZ. Its stimulation can send emetogenic triggers to the brainstem's vomiting center to activate the vomiting reflex.

Vomiting center can also be stimulated by disturbance of the gut or oropharynx, movement, pain, hypoxemia, and hypotension.

There is coordinated contraction of abdominal muscles against a closed glottis which raises intra-abdominal and intrathoracic pressures. The pyloric sphincter contracts and the esophageal sphincter relaxes, and there is active antiperistalsis within the esophagus which forcibly expels the gastric contents. This is associated with marked vagal and sympathetic activity leading to sweating, pallor, and bradycardia.

PONV is generally influenced by multiple factors that are related to the patient, surgery, and anesthesia and

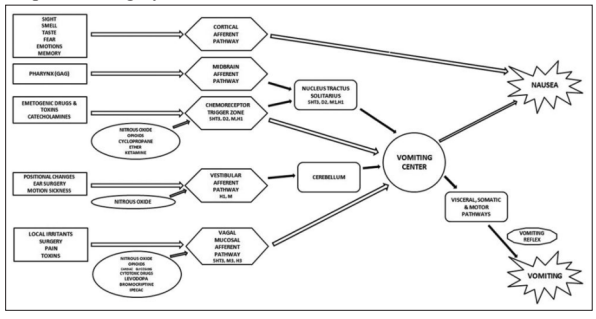

Figure 1: Physiological and pharmacological mechanism of nausea and vomiting. 5HT3 serotonin, H1, H3 histamine, M, M1, M3 muscarinic, D2 dopamine. 5HT3 = 5hydroxytryptamine subtype 3

which requires release of 5-hydroxytryptamine (5-HT) in a cascade of neuronal events involving both the central nervous and gastrointestinal tract. The 5-HT subtype 3 receptor (5-HT_3) participates selectively in the emetic response.

FACTORS INFLUENCING POSTOPERATIVE NAUSEA AND VOMITING

The etiology of emesis is multifactorial. The factors influencing the PONV are as follows:

I. Patient factors
II. Preoperative factors
III. Intraoperative factors:

a. Surgical factors
b. Anesthesia factors

IV. Postoperative factors

Patient factors

a. Sex: Women are more likely to experience PONV compared to men. It is the strongest patient-specific predictor
b. Motion sickness: Patients with history of motion sickness or vomiting after previous surgery are at increased risk for PONV
c. Smoking: Nonsmokers are more prone for PONV. In smokers, gradual desensitization of CTZ occurs
d. Age: Age <50 years is a significant risk factor for PONV
e. Obesity: Recent data suggest that body mass index is not correlated with an increased risk for development of PONV
f. Delayed gastric emptying: Patients with abdominal pathology, diabetes mellitus, hypothyroidism, pregnancy, increased intracranial tension, history of swallowing blood, and with full stomach are at increased risk of PONV.

Preoperative factors

a. Perioperative fasting: It is uncertain as risk factor
b. Anxiety: Clinically not relevant for PONV prediction.

Intraoperative factors

a. Surgical factors:

- Type of surgery: Cholecystectomy and gynecological and laparoscopic surgeries are associated with high incidence of PONV
- Duration of surgery: Longer duration surgeries are associated with increased incidence of PONV. Increasing operative duration by 30 min may increase the risk of PONV by 60%.

b. Anesthesia factors:

- **General anesthesia:**
- Nitrous oxide: Significant decrease in postoperative emesis was noted if nitrous oxide was avoided in patients undergoing laparoscopic procedures. Two meta-analyses have demonstrated that avoiding nitrous oxide reduced PONV risk Three mechanisms have been suggested as contributing factors to the increase in postoperative emesis associated with nitrous oxide

1. Stimulation of sympathetic nervous system with catecholamine release
2. Middle ear pressure changes resulting in traction of the membrane of round window and consequent stimulation of the vestibular system
3. Increased abdominal distension resulting from exchange of nitrous oxide and nitrogen in gas introduced into gastrointestinal tract during mask ventilation

- Inhalational agents: Ether and cyclopropane cause a higher incidence of PONV due to increase in endogenous catecholamines. Sevoflurane, enflurane, desflurane, and halothane are associated with lesser degree of PONV. Effect of volatile anesthetics on PONV is dose-dependent and prominent in the first 2–6 h after surgery.Volatile anesthetics were the primary cause of early PONV (0–2 h after surgery); they did not have an impact on delayed PONV (2–24 h after surgery)
- Etomidate: Continuous etomidate infusion as a part of balanced anesthetic technique markedly increases the incidence of postoperative emesis
- Ketamine: Studies have shown that ketamine used for induction resulted in delayed discharge, vivid dreams, hallucinations, and higher incidence of PONV compared to a patient receiving barbiturates with nitrous oxide. Emetic effect is secondary to endogenous catecholamine release
- Propofol: It is popular for outpatient anesthesia due to its favorable recovery characteristics including rapid emergence and reduced PONV
- Balanced anesthesia: Compared to inhalational or total intravenous (IV) technique, the use of nitrous oxide-opioid-relaxant technique is associated with higher incidence of postoperative emesis. Emesis with balanced anesthesia has been attributed to use of an opioid-nitrous oxide combination, directly stimulating CTZ
- Opioids: It causes emesis through stimulation of opioid receptors located in CTZ. The contribution of intraoperative opioids is weak; there is no difference among different opioids
- Neuromuscular reversal agents: Incidence of PONV is uncertain.
- **Regional anesthesia:** Risk for PONV was 9 times less among patients receiving regional anesthesia than those receiving general anesthesia. The incidence of postoperative emesis following regional nerve block procedures is usually lower than with general anesthesia. Emesis with central neuraxial block is greater than that with peripheral nerve block because of associated sympathetic nervous system blockade, which contributes to postural hypotension induced nausea and vomiting. The incidence of nausea after epidural opioid may be lower with more lipid soluble opioids such as fentanyl and sufentanil, which have less rostral spread from lumbar epidural injection site to CTZ and vomiting center, than the less lipid soluble opioids such as morphine.

POSTOPERATIVE FACTORS

a. Pain: Visceral or pelvic pain is a common cause of postoperative emesis
b. Ambulation: Sudden motion, changes in position, transport from the postanesthetic recovery unit to the postsurgical ward can precipitate nausea and vomiting in patients who have received opioid compounds
c. Opioids: Postoperative opioids increase risk for PONV in a dose-dependent manner;this effect appears to last for as long as opioids are used for pain control in the postoperative period. Irrespective of route of administration, the incidence of nausea and vomiting appears to be similar. Nonsteroidal anti-inflammatory agents can be used in perioperative period to reduce opioid requirement
d. Supplemental oxygen is no longer recommended for PONV prevention.

In addition, other clinically relevant aspects should be taken into consideration, such as whether vomiting

ANTIEMETIC DRUGS

Various drugs are used for the management of PONV. They can be classified based on their action over various receptors [Table 1]. would pose a significant medical risk, for example, in patients with wired jaws, increased intracranial pressure, and after gastric, or esophageal surgery.

5hydroxytryptamine subtype 3 receptor antagonists

These peripherally block gut vagal afferents and act centrally in area postrema. Side effects are headache, mild sedation, dizziness prolongation of QT interval.

Ondansetron

Recommended dose is 4 mg IV at the end of surgery. the Food and Drug Administration (FDA) had recommended that single dose should not exceed 16 mg due to the risk of QT prolongation. The effect of 8 mg oral disintegrating tablet is equivalent to 4 mg IV dose.It is less effective than aprepitantfor reducing emesis and palonosetron for the incidence of PONV.

Dolasetron

Dose is 12.5 mg IV at the end of surgery. the FDA banned the use of dolasetron for chemotherapy-induced nausea and vomiting in adults and children because of concerns of QT c prolongation and torsades de pointes.

Granisetron

Dose 3 mg IV in combination with dexamethasone 8 mg IV is more effective than either drug alone.

Tropisetron

Dose is 2 mg IV at the end of surgery.

Table no.1 Classification of antiemetic drug

Receptor antagonism	Antemetic drug examples
Serotonin (5hydroxytryptamine subtype 3) antagonist	Ondansetron, granisetron, dolasetron, ramosetron, palonosetron, tropisetron, corticosteroids
Anticholinergics/ antimuscarinics (M)	Scopolamine
Histamine (H_1) antagonist	Promethazine, perphenazine, dimenhydrinate, diphenhydramine, meclizine, chlorpromazine
Dopamine (D_2) antagonist	Domperidone, chlorpromazine, metoclopramide, droperidol, haloperidol
Neurokinin1 antagonist	Aprepitant, cospitant, rolapitant

Ramosetron
Dose 0.3 mg IV is most effective to prevent vomiting and decrease nausea for patients receiving fentanyl patient-controlled analgesia (PCA).

Palonosetron
It is the second generation 5-HT_3 receptor antagonist with a longer half-life of 40 h. It provokes a conformational

Neurokinin1 receptor antagonists
It is a new group of drugs used for PONV treatment thought to prevent both acute and delayed emesis.
These act mainly at nucleus tractus solitarius and areas of reticular formation blocking NK-1 receptors. They are more effective in inhibiting emesis than nausea.change of 5-HT_3
receptor through allosteric binding. Most
[42,43]

Aprepitant
Dose is 40 mg PO 1–2 h prior to surgery. It is an NK-1effective dose is 0.075 mg IV approved for 24 h.

Anticholinergic/antimuscarinic drugs
They block muscarinic receptors in the cerebral cortex and pons to induce antiemetic effects.

Transdermal scopolamine
It is a competitive inhibitor at postganglionic muscarinic receptors in the parasympathetic nervous system and acts directly on the central nervous system by antagonizing cholinergic transmission in the vestibular nuclei. It is applied as transdermal patch due to its short half-life, 1.5 mg is secreted over 72 h.

Side effects are visual disturbances, dry mouth, and dizziness.

Histamine receptor antagonists
These drugs block acetylcholine receptors in the vestibular apparatus and histamine receptors in the nucleus tractus solitarius.
Side effects are dry mouth, constipation, drowsiness, urinary retention, and blurred vision.

Dimenhydrinate
Dose is 1–2 mg/kg IV.

Meclizine
Dose is 50 mg per orally (PO) plus ondansetron 4 mg IV. It has longer duration of PONV effect than ondansetron.

Promethazine
Dose is 12.5–25 mg IV.

Dopamine antagonist
Metaclopramide

It is a strong D_2-receptor antagonist and blocks H_1 and 5-HT_3 receptors also. It enhances 5-HT_4 receptors and upper gastrointestinal tract motility to promote gastric emptying without affecting gastric, biliary, and pancreatic secretion. Intestinal transit time is decreased by increasing duodenal peristalsis. It increases gastroesophageal sphincter tone and decreases pyloric sphincter tone to prevent delayed gastric emptying associated with opioid use. Metoclopramide is a weak antiemetic; dose is 10 mg IV and its side effects include dyskinesia or extrapyramidal symptoms, headache, dizziness, and sedation.

receptor antagonist with a 40-h half-life. Aprepitant was significantly more effective than ondansetron for preventing vomiting at 24 h and 48 h after surgery and in reducing nausea severity in the first 48 after surgery.

Side effects are constipation, headache, pyrexia, pruritis.

Cospitant
Dose is 50–150 mg PO plus ondansetron 4 mg, not yet approved for use.

Rolapitant
Dose is 70–200 mg PO and has not been approved for use.

Corticosteroids
Dexamethasone
It blocks the synthesis of prostaglandins, which sensitizes nerves to other commonly involved neurotransmitters in emesis control. It also may have central effect by antagonizing 5-HT_3 receptors or corticosteroid receptors in the nucleus tractus solitarius. Its side effects are gastrointestinal upset, insomnia.

Preoperative dexamethasone 8 mg enhances the postdischarge quality of recovery in addition to reducing nausea, pain, and fatigue. It is administered at the time of induction due to relatively slow onset of action. A recent study reported that intraoperative dexamethasone 4–8 mg may confer an increased risk of postoperative infection. Weighing the risk–benefit ratio, a recent editorial suggests a single dose of dexamethasone 4–8 mg is safe when used for PONV prophylaxis. Recent studies showed significant increases in blood glucose that occur 6–12 h postoperatively in normal subjects. Those with impaired glucose tolerance, and type 2 diabetic and obese surgical patients receive dexamethasone 8 mg; hence, the use of dexamethasone is relatively contraindicated in labile diabetic patients.

Methylprednisolone
Methyl prednisolone 40 mg IV is effective for prevention of late PONV.

Haloperidol
Haloperidol <2 mg reduces the risk of side effects and QT prolongation.

Phenothiazines
Perphenazine
It prevents PONV at doses between 2.5 and 5 mg IV or IM.

Chlorpromazine
It is a D_2 receptor antagonist at CTZ and dosage is 10 mg IV; its side effect is severe sedation.

Other antiemetics
Propofol
It is used as part of total intravenous anesthesia (TIVA) to reduce baseline risk of PONV. Propofol has antiemetic properties even with subhypnotic dose range. Median plasma propofol concentration associated with antiemetic effect was 343 ng/ml, which is much less than sedation (1–3 mcg/ml) and induction (3–6 mcg/ml) plasma propofol concentration.

Alpha2agonists
These possess a direct antiemetic effect along with opioid-sparing effect. In a meta-analysis, perioperative systemic alpha-2-adrenoceptor agonists (clonidine and dexmedetomidine) showed a significant albeit weak and short-lived antinausea effect.

Mirtazepine
It is a specific serotonergic and noradrenergic antidepressant. The combination of mirtazapine 30 mg PO and dexamethasone 8 mg reduces the incidence of late PONV >50%.

Gabapentin
Gabapentin dose of 600 mg PO given 2 h before surgery effectively decreases PONV. Given an hour before surgery, gabapentin 800 mg PO is as effective as dexamethasone 8 mg IV, and the combination is better than either drug alone.

Midazolam

Midazolam 2 mg when administered 30 min before the end of the surgery was as effective against PONV as ondansetron 4 mg. Midazolam 2 mg given 30 min before end of the surgery decreased PONV more effectively than midazolam 35 mcg/kg premedication.

Intravenous fluids

IV fluid hydration is an effective strategy for reducing the baseline risk for PONV.

MANAGEMENT OF POSTOPERATIVE NAUSEA AND VOMITING

Strategies not effective for PONV prevention are music therapy, isopropyl alcohol inhalation, intraoperative gastric decompression, the proton pump inhibitor (esomeprazole), ginger root, nicotine patch to nonsmokers, and cannabinoids (nabilone and tetrahydrocannabinol).

Pharmacologic combination therapy that can be used are as follows:

1. Droperidol and dexamethasone
2. 5-HT_3receptor antagonist and dexamethasone
3. 5-HT_3receptor antagonist and droperidol
4. 5-HT_3receptor antagonist and dexamethasone and droperidol.

The 5-HT_3 antagonists have better antiemetic than antinausea efficacy but are associated with headache. These drugs can be used in combination with droperidol which has greater antinausea efficacy and is associated with lower risk of headache. The 5-HT_3 antagonists can also be effectively combined with dexamethasone. It has been suggested that when used as combination therapy, dexamethasone doses should not exceed 10 mg IV, droperidol doses should not exceed 1 mg IV, and ondansetron doses in adults should not exceed 4 mg and can be much lower. reduce baseline risk. A planned multimodal approach starting from preoperative period can significantly reduce the incidence of PONV. A multimodal approach to reduce PONV consisting of preoperative anxiolysis (midazolam), prophylactic antiemetics (droperidol at induction and ondansetron at end of surgery).

Postoperative nausea and vomiting prophylaxis and rescue

Depending on the level of risk, prophylaxis should be initiated with monotherapy or combination therapy using interventions that reduce baseline risk, nonpharmacologic approach, and antiemetics.

No prophylaxis is recommended for patients at low risk for PONV except if they are at risk of medical consequences from vomiting, for example, patients with wired jaw.

Antiemetic prophylaxis, although cannot eliminate the risk for PONV, can significantly reduce incidence. When developing management strategy for each individual patient with moderate and high risk, the choice should be based on patient preference, cost efficiency, level of PONV risk, patient's pre-existing condition.

CONCLUSION

The understanding of PONV mechanism and careful assessment of risk factors helps in PONV management. PONV prophylaxis should be considered for patients with moderate to high risk based on scoring system. Based on the level of risk, the patient can be treated with monotherapy or combination therapy of antiemetics along with nonpharmacologic approach and interventions for reducing baseline risk. A planned multimodal approach starting from preoperative period most likely ensures success in the management of PONV, which significantly improves the quality of patient care and is cost-effective.

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