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Review Article

Incidence and Management of Postoperativ Nausea and Vomiting: A Narrative Review

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ABSTRACT

Background: Postoperative nausea and vomiting (PONV) is viewed as nausea and/or vomiting or retching that occurs in the Post- anesthesia care unit within the first 24–48 h after surgery. The incidence of these adverse reactions is between 30 and 80% following elective surgery based on the type of surgery and anesthesia, and predisposing patient risk factors. The most commonly used criteria in the perioperative assessment of the risk-score is Apfel which is a tool to evaluate PONV. The risk-score depends on Four variables: female gender, PONV history or motion sickness, postoperative opioids, and smoking status.

Methods: Currently available evidence on MEDLINE, PubMed, Google scholar and Cochrane Evidence Based Medicine Reviews, in addition to the citation reviews by manual search of new anesthesia and surgical journals related to management post-operative nausea and vomiting were searched.

Results: This review of recent studies showed incidence and management of post-operative nausea and vomiting and way to prevent or reduce its incidence by using monotherapy or combination antiemetic therapy, multimodal approach and by using optimal anesthetic technique for reducing baseline risk PONV.

Conclusion: The causes of PONV are complex and multifaceted. Patient (gender, individual background, and medical condition); anesthesia type; and surgical procedure are all risk factors for PONV. PONV is better treated by preventing and/or minimizing PONV risk factors, as well as using prophylactic antiemetics in high-risk patients. There is no one PONV antiemetic drug or technique that is 100% appropriate for all patients at this time. If the first anti emetic is unsuccessful, a 2nd or 3rd anti emetic that targets a specific mid brain emetic receptor location may be needed. PONV prophylaxis should be considered for patients who have a low to high chance of contracting the virus, according to the scoring system. The patient may be treated with monotherapy or combination treatment of anti emetics, as well as non pharmacologic approaches and therapies to reduce baseline risk, depending on the severity of risk. A targeted multimodal solution beginning in the preoperative phase is more likely to ensure progress in the management of PONV, which increases patient care satisfaction while still being cost-effective.

Sedation Nausea is a disagreeable feeling that causes disturbances in the stomach area and makes you feel the imminent urge to vomit or retch. Often, it's transient, active retching also followed or increased salivation and tachycardia [1-2]. Vomiting is involuntary, forceful expulsion through the mouth and/or nose of the stomach contents [3-4].

The incidence of these adverse reactions is between 30 and 80% following elective surgery depending on the type of surgery and anesthesia, and patient risk factors

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predisposing [5-9]. The meaning of post-operative nausea and vomiting (PONV) is nausea and/or vomiting during 24 h following operation.

The physiology of PONV is complex, nausea and vomiting are primarily controlled in medulla oblongata from the vomiting center. It includes the reticular formation and the nucleus of the tractus solitarius (NTS). The vomiting center can be activated directly or indirectly by means of irritants from four main areas: the gastrointestinal tract, the cerebral cortex and thalamus, the vestibular region and the chemoreceptor trigger zone (CRTZ) [10].

PONV may increase peri-operative costs, increase peri-operative morbidity, prolonged stay in the post-anesthesia care unit, prolonged hospital stays, delay in the discharge time and lead to readmissions [11].

PONV is not generally fatal but in rare situations can cause significant dehydration, electrolyte imbalance, suture and dehiscence tension, venous hypertension and bleeding, gastric aspiration, esophageal rupture and life-threatening airway problems [12-13]. This affects the recovery process and after surgery patient satisfaction [14].

It begins as an emesis in the emetic center by several factors, which is summarized as an individual patient profile, surgical and anesthetic factors. Patients are known to profile for an increased incidence of PONV with relevant background factors such as through patients' age and sex and habits, PONV history, motion sickness, full stomach, smoking, anxiety, the use of opioids and pre-operative prolonged fasting, dehydration and hypovolemia [5, 15-16].

Patients' risks of developing PONV are increased in PACU by pain, opioids, hypovolemia, orthostatic hypotension, hemodynamic stability and oral intake initiation. Early ambulation and patient movement in the PACU increase the PONV baseline risk due to vestibular nerve stimulation, which causes motion sickness [16].

Gastric insufflation causes an increased PONV incidence as a result of bag-mask ventilation. In general, spontaneous ventilation via a supra-glottic airway has a lower risk than tracheal intubation [2]. The incidence of PONV after regional anesthesia procedures is commonly lower than the general anesthesia [15]. Longer duration of surgeries is related to an increased PONV incidence. Increased operating time by 30 minutes can increase the risk of PONV by 60%.

The prevention of pain and PONV is highly prioritized [8],for example- pelvic or Visceral pain causes postoperative emesis commonly [17]. Current PONV preventive and treatment strategies include proactive risk evaluation, PONV trigger avoidance, administration of preoperative prophylactic antiemetics and postoperative antiemetics rescue and anesthetic protocol optimization. The Apfel score is frequently used to estimate the risk of PONV before surgery [18].

Apfel's risk assessment tool is a frequently used preoperative assessment tool to evaluate the risk of PONV. The main risk factors for variability are female sex, PNOV history, motion sickness, non-smokers, and use of opioids postoperatively. One point is assigned to each factor, with risks of 0, 1, 2, 3 and 4, with associated probabilities of 10, 21, 39, 61 and 79 %, respectively. Every additional risk point, in other words, increases the chance by around 20%. The medium risk for patients with 0 or 1 is considered "low risk" for PONV, 2 or 3 and four high risk factors PONV [6, 19].

The first step in PONV prevention is risk factors assessment and reduction. Although nonpharmacologic therapy may play a significant role in the treatment of PONV, PONV therapy is mainly pharmacological, the cost of prophylactic treatment can be reduced by keeping the number of patients to be treated small by using a multi-mode approach to identify high-risk patients [9].

Objectives of the Study

Main Objectives

To procure the incidence and management of post-operative nausea and vomiting.

Specific objective

- To determine the possible causes or risk factors for nausea and vomiting after surgery.
- To determine which gender is more prone to post-operative nausea and vomiting.
- To assess the influence of post-operative nausea and vomiting on patient recovery.
- To clarify the optimal choice, anesthetic technique.
- To assess the availability of antiemetic medications and techniques for monotherapy and multimodal therapy.
- To evaluate the effectiveness of antiemetic use in postoperative nausea and vomiting management.
- To assess the understanding of health practitioners in selection of antiemetic for nausea and vomiting postoperatively.

Goals

To acquire the knowledge about the incidence and management of postoperative nausea and vomiting and to find out the ways to prevent or reduce it's occurrence.

Research Hypothesis

To procure the incidence and management of post-operative nausea and vomiting and to find a way to prevent or reduce its occurrence by anesthetic technique and antiemetics drugs.

Methods

This is narrative review study, we searched the best currently available evidence on MEDLINE, PubMed, Google scholar and Cochrane Evidence Based Medicine

Reviews. In addition, citation reviews and manual search of new relevant journals to management of post-operative nausea and vomiting were also searched. We searched the published studies from 2000-2020 by using these keywords: Nausea vomiting, incidence, postoperative, management. The data that were compiled from articles and measurements and analyses of these variables with their confounders, have all been performed by the single effort of researcher.

The goal was to review studies to procure the incidence and management of post-operative nausea and vomiting and way to prevent or reduce its incidence by using monotherapy or combination antiemetic therapy, multimodal approach and by using optimal anesthetic technique in reducing baseline risk PONV. All the selected reviews were limited to the English language.

Including Criteria

All available articles related to the research keyword and identified topic related to management of post-operative nausea and vomiting.

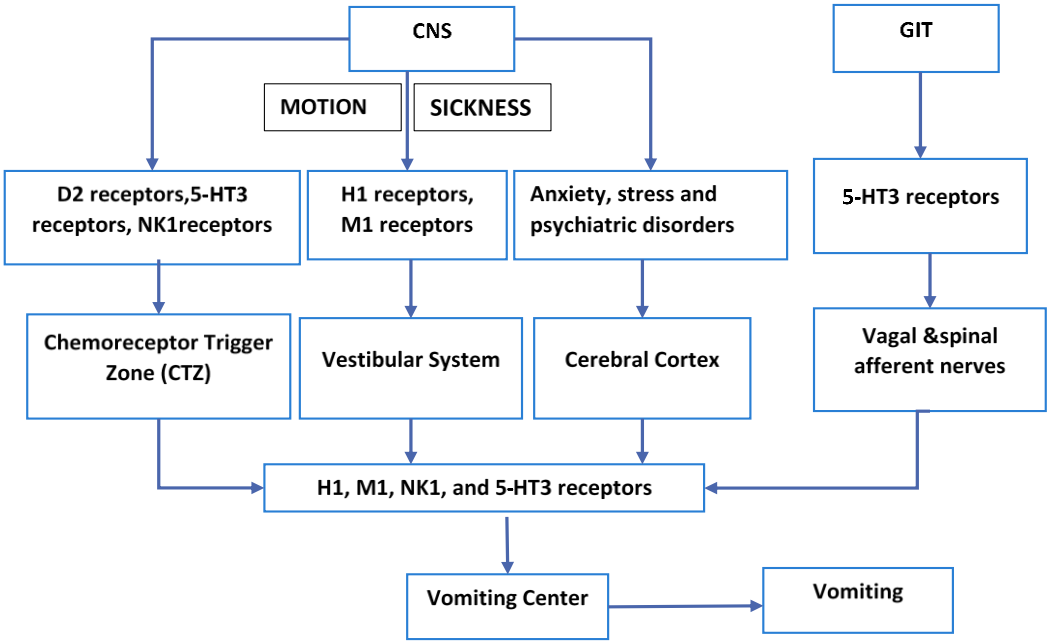
Exclusion criteria:

Were articles that do not conform to the topic, all articles which are not open access and all articles published or unpublished before 2000, children, pregnancy, eating disorders, renal or hepatic failure, CNS injury and vestibular disease.

Physiology of PONV

PONV is a physiological convoluted phenomenon that includes several neurophysiological pathways and both peripheral and central mechanisms of the receptor [20]. The vomiting center in the medulla primarily controls nausea and vomiting. At least five main PONV receptor systems are available: the chemoreceptor triggering zone, reflex afferent pathway from the cerebral cortex, the vagal mucosal pathways in the GI system, midbrain afferents, and neuronal pathway from the vestibular system. Stimulation by any of these afferent pathways is possible to activate the center of vomiting through dopaminergic, muscarinic (cholinergic), serotonergic, or histaminergic receptor [12] (Figure 1). PONV is generally not fatal [21] but, in uncommon cases, dangerous pathological situations can be caused by, dehydration, electrolyte imbalance, suture tensions and dislocation, venous hypertension and bleeding, esophageal rupture, aspiration of gastric contents, and life-threatening damage to the airway [22-23].

Figure 1- Physiology of PONV



NOT: - CNS: central nervous system, GIT: Gastrointestinal tract
D2: dopaminergic receptor, 5-HT3: 5-Hydroxytryptamine type 3 receptor
NK1: neurokinin 1 receptor M1: muscarinic receptor, H1: histaminergic receptors

Risk factors for PONV

The first step in PONV prophylaxis is to identify risk factors and populations that are at high risk of PONV.

The different risk factors for PONV are related to the patients, surgery, and anesthesia techniques (Table 1).

Patient related risk factors

The probability of PONV can be raised by a variety of patient conditions. The female gender, at 2.6 times greater risk, is considered to be the better general PONV predictor. Prior PONV history will be the next greatest factor. The first degree relatives of these patients may have an elevated chance of PONY, which indicates that a hereditary predisposition is present [24]. A major patient-related factor induced by the activation of histamine (H1) and muscarinic (M2) receptors in the vestibular system is motion sickness [8]. Smoking patients tend to have slightly lower PONV levels [25]. Smoking is thought to be due to the acclimatization of harmful elements of smoke such as tar, nicotine, and tobacco carcinogens by the user. The CNS receptors that induce PONV involves dopamine receptors, histamine receptors, cholinergic receptors, serotonin (5-HT3) receptors, and neurokinin receptors. It's possible that one of these receptors is affected by the anti-emetogenic influence of cigarette smoke to decrease the reaction of the receptor [26-27].

Surgical factors

Include surgery duration with each 30-minute raises the PONV risk by 60 %. A higher incidence of PONV can be caused by the longer contact to general anesthesia and usage of greater dose of opioid drugs (e.g., maxillofacial surgery and oral, ophthalmic, Laparoscopy, ENT, abdominal surgeries, Neurosurgery, gynecologic surgery, and cholecystectomy) [26].

Anesthesia-Related Risk Factors

Usage of opioids raises the underlying risk of PONV by activating opioid receptors in the postrema region at pre, intra-, and postoperative periods. Cyclopropane and ether were extremely emetogenic inhalation substances which had a 75%-80% chance of PONV. Whereas inhalation anesthetics may cause PONV in the first 0–2 hours after surgery, there are no variations in the incidence of risk of PONV among desflurane and sevoflurane or even between isoflurane and these agents [16]. It has been shown that nitrous oxide (N2O) raises the risk of PONV. Three pathways were suggested to lead to the rise in post-operative emesis linked to nitrous oxide.

1. Sympathetic nervous system activation of catecholamine release.
2. Variations in the middle ear pressure cause the membrane of the round window to traction and the vestibular system to stimulate.
3. As a consequence of the nitrous oxide and nitrogen exchange gas added into the GIT during mask breathing, increased abdominal distension [17].

Intravenous hypnotics like propofol and thiopentones have less PONV incidences than ketamine or etomidate.

The reversal of anticholinesterase muscle relaxant agents by agents such as neostigmine, has been shown to cause increased PONV incidence due to the muscarinic effect of such drug that increases GIT movement. However, it does not affect GI motility by substituting glycopyrrolate for atropine. This suggests that PONV may not be affected when anticholinesterase and cholinergic muscarinic antagonist are given in the usual ratio. The critical PONV-causing neostigmine dosage was estimated to be 2.5 mg. There was no indication of any emetogenic effect in lower doses, and when neuromuscular block reversal was omitted, the likelihood of residual muscle paralysis increased [28]. Regional anesthesia alone has a decreased incidence of PONV compared to general anesthesia. Low blood pressure can cause nausea and vomiting by vasodilatation following administration of a spinal or epidural block, with subsequent decreases in blood pressure and blood flow to the vomiting centers of the brain. In the operating room or PACU, orthostatic hypotension or hypotension of any origin may cause releases of CNS neuroreceptors that activate emetogenic neurochemicals, triggering nausea and/or vomiting. Suitable intravascular fluid volume replacement in a patient and vasopressor administration ephedrine, for example may able relieve nausea and vomiting of this particular cause [26, 29]. Postoperative discomfort may be a source of PONV, and it has been shown that the utilization of IV opioids in patients with pain and nausea causes nausea. Naloxone can overcome opioid analgesia and nausea, leading to a return to pain and nausea. In the PACU, the likelihood of a patient contracting PONV is raised by discomfort, antidepressants, hemodynamic stability, hypovolemia, oral intake. Because of vestibular nerve stimulation that induces motion sickness, Patient movement and early PACU ambulation raise baseline PONV probability. Hypotension may be caused by orthostatic changes, thereby lowering cortical infusion and blood supply to the vomiting center. Via vigorous preoperative bowel planning, blood loss, or inadequate IV fluid replacement, Orthostatic hypotension secondary to dehydration can occur. Crystalloid perioperative IV hydration fluid may reduce the chance of postoperative nausea [16].

Management Strategies

Histamine, dopamine 2, muscarinic, opioids, and 5-hydroxy tryptamine or serotonin are the receptors stimulated in nausea and vomiting pathway. For patient with a low risk of PONV, it appears logical to base a prophylaxis approach on Patient’s favorite, costeffectiveness, and a benefit-to-risk assessment. The approach to PONV prophylaxis should involve a combination of the2 antiemetics for patients at moderate

risk, while those at high risk need 2-3 antiemetics, considering using TIVA with propofol [26,30-32]. A combination antiemetic treatment is preferred in patients with a high PONV risk because 2 or more antiemetic agents acting on various receptors have improved efficacy compared to one single agent in patients with moderate and high PONV risks [26]. The antiemetic mixture has an additional effect on the reduction of the frequency of PONV. Interestingly, initial pharmacological treatment was found to be the most effective, with the benefit being less effective than that of the first intervention for each subsequent intervention. The combination of pharmacological therapies with non-pharmacological strategies, in particular to decrease patients baseline factor for a really multimodal approach in patients with an elevated PONV risk, the following considerations for each patient must be addressed in order to successfully management PONV: PONV risk evaluation and baseline risk reduction, prophylaxis, cost-effectiveness of therapy, and combination and rescue therapy (Figure 2) [33].

To reduce the baseline risk of PONV, multiple useful techniques are recommended: Regional and local anesthesia (e.g. local penetration and/or peripheral nerve blocks) are regularly utilized, during general anesthesia, propofol induction and maintenance injections are used, as well as controlled anesthesia treatment (MAC), perioperative opioid analgesics are reduced, volatile anesthetic doses are minimized, nitrous oxide and reverse medication usage is minimized, and nitrous oxide use is assured [26, 34-35] (Table 2). If GA is used, the risk of PONV can be minimized by substituting propofol injection for anesthesia maintenance instead of inhaled volatile anesthetics. The additive effects of a mixture of propofol and air/oxygen decreased the chance of early PONV by about 25 percent [38]. In current practice in high-risk adults, the recommended pharmacological antiemetics for PONV prophylaxis are 5-hydroxytryptamine receptorantagonists, serotonin receptor antagonists, neurokinin-1receptor antagonists, butyrophenones, corticosteroids, anticholinergics, antihistamines, and antagonists of mixed receptors [26].

Table 1- PONV Risk factor

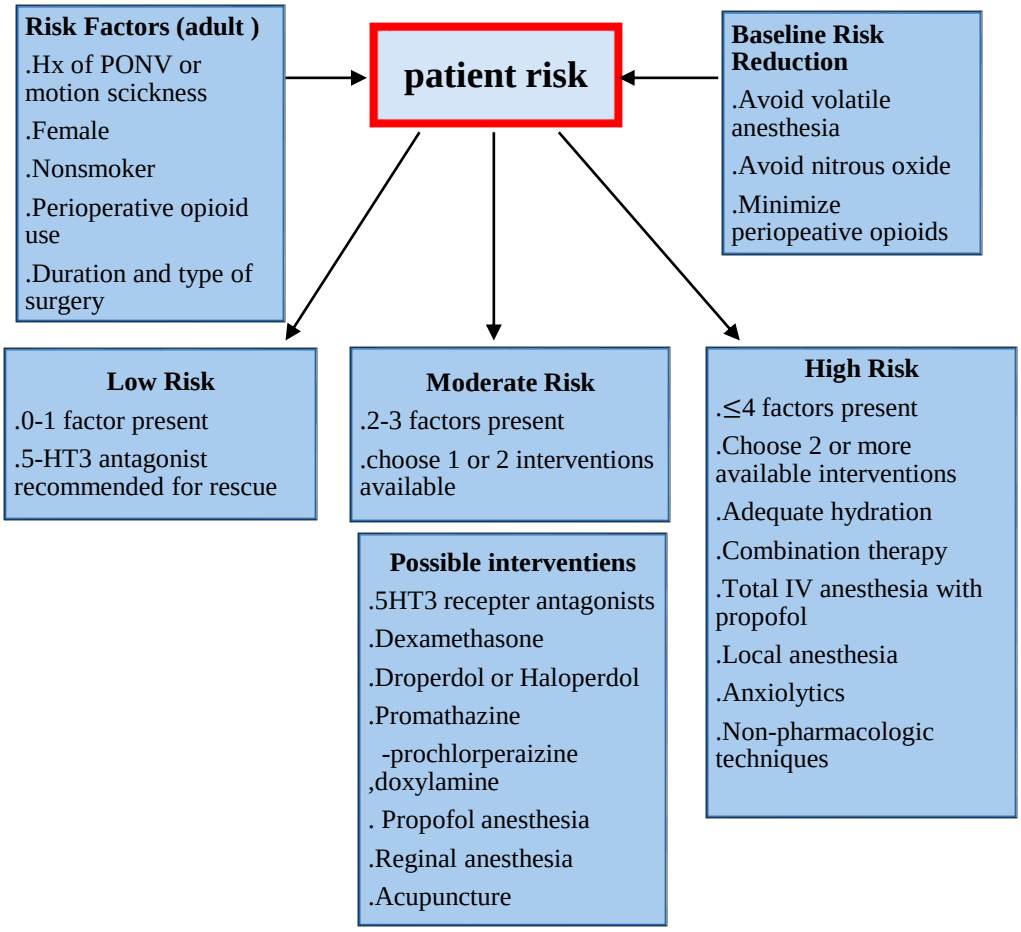
Patients factor	Anesthetic factor	Surgical factor
Female	Perioperative opioids	Duration of surgery
Non-smoker	Prolonged duration of anesthesia	Type of surgery
Previous PONV/ motion sicknes	Nitrous oxide (>50%)	ENT
Anxiety	Volatile agents	Plastic
Dehydration	Increased neostigmine doses (>3 mg)	Gynecology
Gastric distention		Abdominal
		Ophthalmologic
		Laparoscopic
		Orthopedic

Table 2- guidelines for different post-operative nausea and vomiting (PONV) risk factor having followed surgeries [39].

Mild risk (None or 1 risk factor)	Moderate risk (2 risk factors)	High risk (≥3 risk factors)
No prophylaxis required or monotherapy with a cost-effective antiemetic drug if there is a risk of medical sequelae from PONV	Choose a prophylactic combination of antiemetic medications	Start therapy with two or three prophylactic medications that act on different receptors
	When general anesthesia is needed, decrease preexisting risk factors by reducing volatile anesthetic usage, use of opioids for analgesia, nitrous oxide, and elevated doses of reversal medications	Minimize pre-existing risks by using opioid-reducing analgesia strategies
	Use neuraxial anesthesia, peripheral nerve blocks, and infiltration of local anesthesia	Reduce the use of opioids in the perioperative period Reduce volatile anesthetic usage, use of opioids for analgesia, nitrous oxide, and elevated doses of reversal medications (e.g., naloxone, flumazenil, and neostigmine)
	Utilize adjuvant non- pharmacologic options (e.g., acupressure and stimulation by electric acupoint)	Use neuraxial anesthesia, peripheral nerve blocks, and infiltration of local anesthesia

Treatment options
If prophylaxis fails or was not received, use antiemetic from different classes to prophylactic agent
Re-administer only if >6 hours after post-anesthesia care unit; do not re-administer dexamethasone or scopolamine

Figure 2- Management strategies

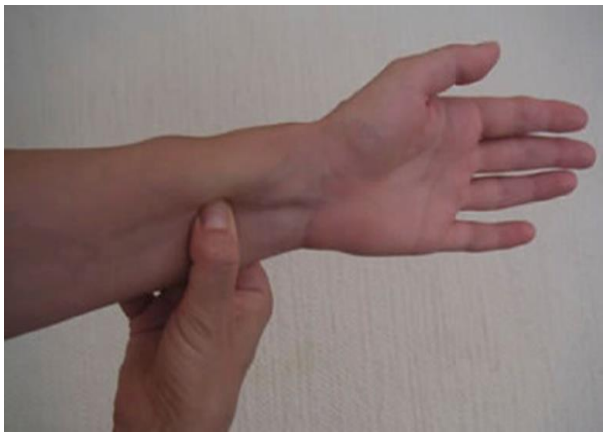


Non-pharmacologic treatment strategies for PONV

P6 point acupuncture and acupressure have been proposed as a beneficial prophylactic measure to avoid PONV (Figure2). Stimulation involves needle stimulation, electrical nerve stimulator transcutaneous, or pressure. Between flexor carpi radialis and palmaris longus, the P6 point lies 5 cm nearest to the ventral wrist crease. Prior to anesthesia induction, stimulation should occur. A meta-analysis of Cochrane (2009) showed decreased postoperative nausea, but no effect on vomiting [38]. Since preoperative anxiety was positive with PONV, the importance of good communication, reassurance, and a positive relationship with patients should not be ignored.

Sadly, there has been weak or no evidence that the role of psychological interventions and hypnosis in adult populations at present is of benefit [39].

Figure 3- Point of acupuncture for nausea and vomiting P6 position three Finger



widths between flexor carpi radialis and longus palmaris below the palmar crease.

Multimodal approach

In order to mitigate baseline risk, the multimodal approach integrates non-pharmacological and pharmacological prophylaxis with treatments. A proposed multimodal strategy beginning from the

preoperative phase will substantially reduce the incidence of PONV [40]. Pre-operative anxiolysis such as Midazolam, prophylactic antiemetics such as (Droperidol at the beginning and Ondansetron at the end of the operation), local anesthetic infiltration with propofol TIVA are a multimodal approach to PONV elimination, and ketorolac without nitrous oxide use had an average response rate of 80 percent relative to a response rate of 43 to 63 percent for patients undergoing either inhalation [41].

Prophylaxis and rescue for post-operative nausea and vomiting

Prophylaxis with monotherapy or combination therapy can based on risk level, be started with an intervention that decreases baseline risk, a non-pharmacological approach, and antiemetics [26]. For low-risk PONV patients, no prophylaxis is advised except where the risk is that vomiting will have medical consequences, for example in wired jaw patients [42]. While antiemetic prophylaxis never removes the risk of PONV completely, it can considerably minimize the incidence. When a management strategy is designed for every moderate and high risk patient, The decision should be based on the patient's preferences, cost effectiveness, PONV risk level, Pre-existing condition of the patient(carefully avoid QT-prolonging medications in QT-syndrome patients and TDS in patients with closed-angle glaucoma).When a patient has a PONV complaint, rescue treatment should be administered and, and at the same time, an examination should be actually performed to remove causing drugs or a mechanical main factor for nausea and/or vomiting, such as with as opioid PCA, abdominal obstruction or blood draining down the throat. Low-dose 5-HT3 antagonist therapy is prescribed for treatment if rescue therapy is needed, antiemetics of various clinical classes should be selected as medications used for prophylaxis, or if no prophylaxis is administered. The 5-HT3 antagonist dose used for therapy is smaller than the prophylaxis dose used (ondansetron 1 mg, tropisetron 0.5 mg, and granisetron 0.1 mg). A repeated prophylactic antiemetic dosage should not be given to patients if PONV happens within 6 hours of surgery. Each prophylactic medicine, except TDS, dexamethasone, aprepitant and palonosetron, can be treated with an emetic

episode lasting more than 6 hours [26]. As a rescue treatment for PONV, PC6 acupoint stimulation may also be useful. A clinical trial of moderate-risk patients undergoing laparoscopic surgery who developed PONV despite prophylaxis of droperidol or metoclopramide was performed by Coloma et al [43]. The electrical stimulation of PC6 resulting in a similar complete ondansetron rescue response time, and the addition of ondansetron rescue to PC6 acu-stimulation resulted in a slightly better full response rate.

Results

PONV continues to be a major burden for our patients. Despite the fact that it is rarely connected to life-threatening illness, its effects on patients appear to be significant, and it is frequently listed as one of surgery and anesthesia's unfavorable side effects. The first phase in implementing an effective management plan is defining risk factors and categorizing patients into various risk categories. Non-smoking condition, female gender, PONV history, motion sickness, as well as numerous anesthesia-related and surgery-specific aspects such as general vs local anesthetic, Anesthesia length and surgical type were all identified as risk factors. Antiemetic prophylaxis is not suitable for all surgical patients, but recognizing those who are at higher risk using obtainable risk criteria prove to be the most useful form of treatment and the best cost-effective. Antiemetic prophylaxis cannot completely remove the risk of PONV, but it can greatly minimize it. Patient’s favorite, cost-efficacy, and PONV risk level should all be considered when designing a management plan for each particular patient. The use of nonpharmacologic therapy and a decrease in baseline risk factors are the less likely to cause side effects among the treatments considered. For patients who are at a moderate to high risk of contracting PONV, prophylaxis should be considered. Prophylaxis should be started with mono- therapy or mixture therapy using treatments that minimize baseline risk, non-pharmacologic methods, and anti- emetics, dependent on the degree of risk. For patient at moderate and great risk of PONV, antiemetic combinations are recommended. Where rescue treatment is needed, the antiemetic should come from a various clinical class than the drugs used for prophylaxis, and it should be given in a different way. When PONV happens within 6 hours of treatment, patients don't take another dose of the prophylactic antiemetic. With the exception of TDS, dexamethasone, aprepitant, and palonosetron, all of the medications used for prophylaxis could be used to prevent an emetic episode that occurs more than 6 hours after surgery.

Conclusion

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