Postoperative Nausea and Vomiting
An Overview

An Essay

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بسم الله الرحمن الرحيم

وقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ
ورَسُولُهُ والْمُؤْمِنُونَ

صدق الله العظيم

سورة التوبة آية (١٠٥)

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List of Abbreviations

5-HT	:	5-hydroxytryptamine
BMI	:	Body mass index
BP	:	Blood pressure
C/E	:	Cost-effectiveness
CNS	:	Central nervous system
CSF	:	Cerebrospinal fluid
CT	:	Computerized tomography
CTZ	:	Chemoreceptor trigger zone
D	:	Dopamine
FDA	:	Food and Drug Administration
GIT	:	Gastrointestinal tract
IM	:	Intramuscular
IV	:	Intravenous
M	:	Muscarinic
MAC	:	Minimum alveolar concentration
NK1	:	Neurokinin-1
NSAIDS	:	Non-steroidal anti-inflammatory drugs
OR	:	Odds ratio
PACU	:	Postanesthesia care unit

List of Abbreviations (Cont.)

PCA	:	Patient controlled analgesia
PCEA	:	Patient controlled epidural anesthesia
PDNV	:	Postdischarge nausea and vomiting
PONV	:	Postoperative nausea and vomiting
POV	:	Postoperative vomiting
QTc	:	Corrected QT interval
RCT	:	Randomized controlled trial
TDS	:	Transdermal scopolamine
TIVA	:	Total intravenous anesthesia
UK	:	United Kingdom
USA	:	United States of America

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Introduction

Postoperative nausea and vomiting (PONV) are among the most common adverse events after surgery and anesthesia occurring in 30% of unselected inpatients and up to 70% of "high-risk" inpatients during the first 24 hours after emergence from anesthesia **(Gan, 2002).**

Nausea is the subjective sensation of urge to vomit in the absence of expulsive muscular movements.When severe, it is associated with increased salivary secretion, vasomotor disturbances and sweating **(Apfel et al., 2002)**, while vomiting is the forcible expulsion through mouth of the gastric contents **(Hornby, 2001).** PONV is classified as early occurring up to 2 to 6h after surgery or late occurring up to 24 or 48h after surgery **(Apfel et al., 2002).**

Although PONV is almost always self-limiting and non fatal, it can cause significant morbidity including dehydration, electrolyte imbalance, suture tension and dehiscence, venous hypertension and bleeding, esophageal rupture and life threating airway compromise **(Scuderi and Conlay, 2003).**

Risk factors for PONV are classified into well established, possible and disproved factors. Among the most important risk factors for PONV in adults are: patient-specific risk factors (e.g. female gender, nonsmoking status and history of motion sickness), anesthetic risk factors (e.g. use of volatile anesthetics, nitrous oxide and use of intraoperative and postoperative opioids) and surgical risk factors (e.g. increasing duration of surgical proc-edures) **(Gan et al., 2003).**

To decrease incidence of PONV, several anti-emetic strategies are available, e.g. use of propofol anesthesia or prophylactic administration of anti-emetic drugs, reducing

baseline risk factors which can significantly decrease the incidence of PONV, and reliable preoperative prediction of PONV risk factors which would enable anesthesiologists to selectively apply anti-emetic strategies **(Watcha and White, 1992).**

In children, the POV rate can be twice as high as in adults, which suggests a greater need for POV prophylaxis in this population. Children who are at moderate or high risk for POV should receive combination therapy with at least two prophylactic drugs from different classes **(Tong et al., 2014).**

In relation to regional anesthesia; although PONV have lesser frequency and severity compared with PONV due to general anesthesia, they may occur due to several different mechanisms (e.g. Systolic BP<80 mmHg, a block higher than fifth thoracic segment and the addition of vasoconstrictor to the local anesthetic) **(Carpenter et al., 1992).**

Definition, Classification, Physiology and Complications of Postoperative Nausea and Vomiting

Definition and classification:

Postoperative nausea and vomiting (PONV) is defined as nausea and/or vomiting occurring within 24 hours after surgery. It affects between 20% and 30% of patients. As many as 70% to 80% of patients at high risk may be affected **(Kovac, 2000).**

Postoperative nausea and vomiting encompasses three main symptoms (nausea, retching and vomiting) that may occur separately or in combination after surgery **(Kovac, 2000).**

Nausea is defined as a sensation associated with awareness of the urge to vomit**;** it is accompanied by gastrointestinal tract (GIT) relaxation, duodenal peristalsis and vegetative symptoms**.** Generally, it precedes vomiting **(Habib et al., 2006).**

Retching (also known as dry heaving) is the rhythmic and spasmodic contractions of the respiratory muscles, diaphragm, chest wall, and abdominal muscles, without the expulsion of gastric contents. The patient's mouth and glottis are closed **(Scuderi and Conlay, 2003)**.

Vomiting is defined as the forceful expulsion of stomach contents through the mouth, where the diaphragm is fixed during inspiration and the abdominal wall muscles contract **(Habib et al., 2006).**

Vomiting is usually started by retching and rhythmical contractions of the respiratory muscles. Vomiting and

retching are subjective patient symptoms **(Scuderi and Conlay, 2003)**.

Postoperative nausea and vomiting may take place in single or multiple episodes which may last minutes, hours, or even days. PONV is classified as early, occurring up to 2 to 6 hours after surgery, or late, occurring up to 24 or 48 hours after surgery, with the exact cut-off times depending upon the individual investigator's definition. As may be inferred from this lack of a standard cut-off time, the delineation is somewhat arbitrary and is related to the patient's location at the time of evaluation for the symptoms, e.g. the post anesthesia care unit, surgical or other ward, or home. However, there are suggestions that early and late PONV may differ at least somewhat in their pathogenesis. The use of volatile anesthetics may be a main cause of early PONV **(Scuderi and Conlay, 2003)**.

Physiology of Vomiting:

The central nervous system (CNS) areas connected with balance, vasomotor activity, salivation, respiration and eye motion control are located close to the vomiting center, moreover, these areas are interconnected. The proximity of these areas is responsible for physiological vegetative reactions observed in PONV, such as salivation, sweating, frequent gulping, pallor, tachypnea, tachycardia, heart rhythm disturbances, pupil dilation and motion sickness **(Habib et al., 2006)**.

Vomiting is a neurologically conducted, coordinated reflex in which visceral reflexes in the medulla oblongata are integrated, including their coordination and time synchronization with somatic components **(Brady et al., 2003)**.

The vomiting act has two phases. In the retching phase, the abdominal muscles undergo a few rounds of coordinated contractions together with the diaphragm and the muscles used in respiratory inspiration. For this reason, an individual may confuse this phase with an episode of violent hiccups.In this retching phase nothing has yet been expelled. In the next phase, also termed the expulsive phase, intense pressure is formed in the stomach brought about by enormous shifts in both the diaphragm and the abdomen. These shifts are, in essence, vigorous contractions of these muscles that last for extended periods of time - much longer than a normal period of muscular contraction. The pressure is then suddenly released when the upper esophageal sphincter relaxes resulting in the expulsion of gastric contents. At the same time, the epiglottis closes off the entrance to the lower airways, preventing aspiration and the soft palate lifts to close the posterior nasal aperture. Breath is held approximately in the middle of inspiration. Individuals who do not regularly exercise their abdominal muscles may experience pain in those muscles for a few days. The relief of pressure and the release of endorphins into the blood stream after the expulsion causes the vomiter to feel better **(Scuderi and Conlay, 2003)**.

Both vomiting and retching are brain stem reflexes. On the other hand, nausea is coordinated from the cortex. Nausea and vomiting are protective reflexes to prevent the absorption of toxins (which trigger chemoreceptors in the GIT), but may also occur in response to olfactory, visual, vestibular and psychogenic stimuli **(Rahman and Beattie, 2004).**

The mechanism of the vomiting reflex was first described by Borison and Wang in 1953 to be a complex act involving the respiratory, gastrointestinal, and abdominal musculature controlled by the vomiting centre which is situated in the lateral reticular formation close to the nucleus

tractus solitarius in the brain stem (medulla oblongata) **(Yates et al., 2014)**.

The vomiting centre can be triggered by stimuli from the periphery: the oropharynx and the gastrointestinal tract as input from mechanoreceptors and chemoreceptors. It is carried via the vagus nerve and involve serotonin 5-hydroxy-tryptamine (5HT) and dopamine (D) receptors. The mediastinum, renal pelvis, peritoneum and genitalia are other sites of peripheral stimulation. Stimulation from the CNS evolve from cerebral cortex, labyrinth, the visual centre, the vestibular portion of the eighth cranial nerve, and the chemoreceptor trigger zone (CTZ) located in the area postrema at the base of the fourth ventricle.Therefore, inputs include those from the vestibular system, the cardiovascular system, the pharynx and more complex stimuli from higher cortical centres responding to pain, fear and anxiety **(Figure 1) (Kovac, 2000)**.

The vomiting centre integrates these various inputs and then coordinates the efferent branches of cranial nerves V(trigeminal), VII(facial), IX(glossopharyngeal) and X(vagus) and organises the muscular contractions and cardiovascular responses occuring during emesis. When the vomiting centre is stimulated, a complex series of neural impulses coordinates the simultaneous relaxation of the gastric muscles and contraction of the abdominal muscles and diaphragm, expelling vomit from the stomach **(Aitkenhead et al., 2007)**.

Nausea, often the precursor to vomiting, is triggered by a low level of the same stimuli responsible for the vomiting reflex but the exact mechanism underlying the sensation of nausea is unclear. It is often accompanied by salivation, sweating and pallor **(Taylor and Pickford, 2003)**.

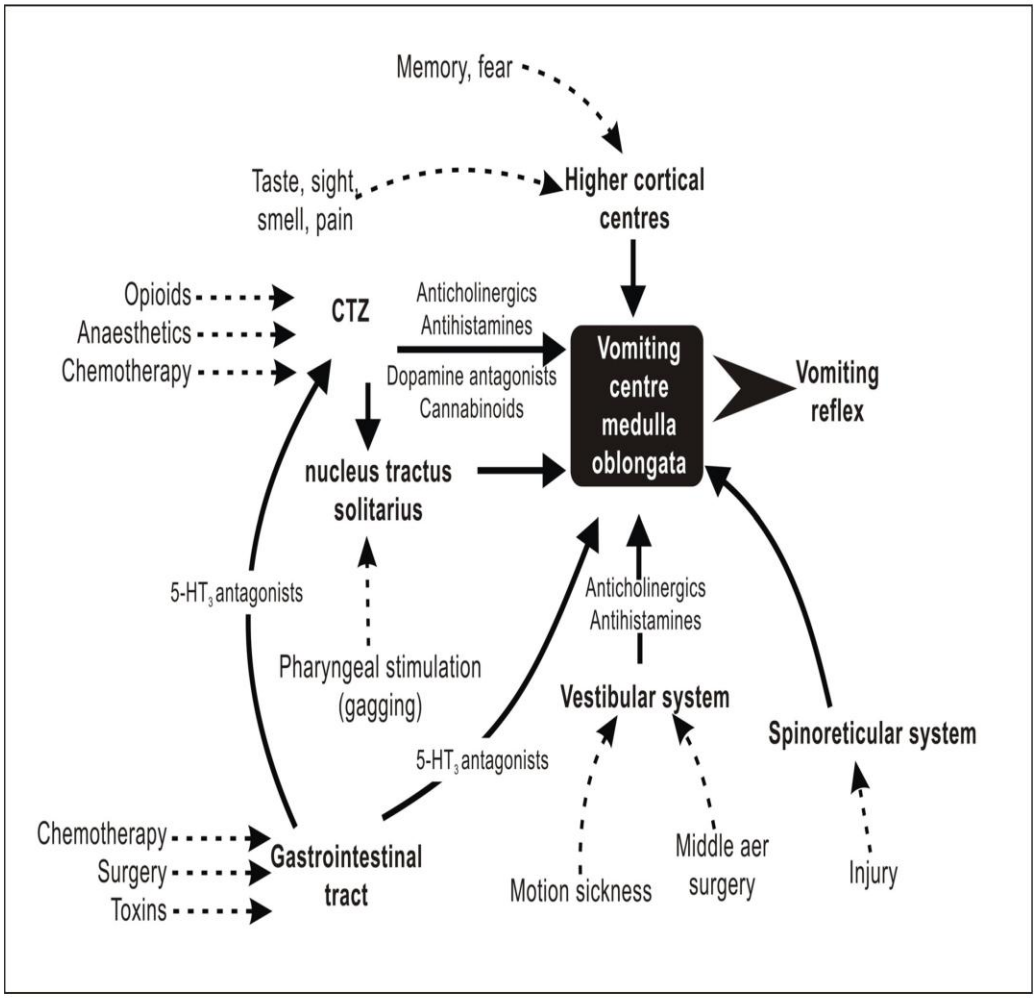

Figure (1): Vomiting pathway (Kovac, 2000)

Many different types of surgery stimulate the vomiting centre as do various perioperative drug types and anaesthetic agents, explaining why nausea and vomiting are such common complaints following surgery **(Taylor and Pickford, 2003)**. As the area postrema has no effective blood-brain barrier, CTZ can be directly stimulated by chemicals in the cerebrospinal fluid (CSF) and blood. The CTZ has high concentrations of encephalin, dopamine, and opioid receptors. The area postrema is rich in opioid, dopamine (D) and serotonin (5-HT) receptors. The nucleus of

the solitary tract contains high concentrations of encephalin, histamine, muscarinic (M), and cholinergic receptors. Recently, substance P and neurokinin-1 (NK1) receptors were found to be involved in the regulation of emesis **(Figure 2) (Gan, 2007)**.

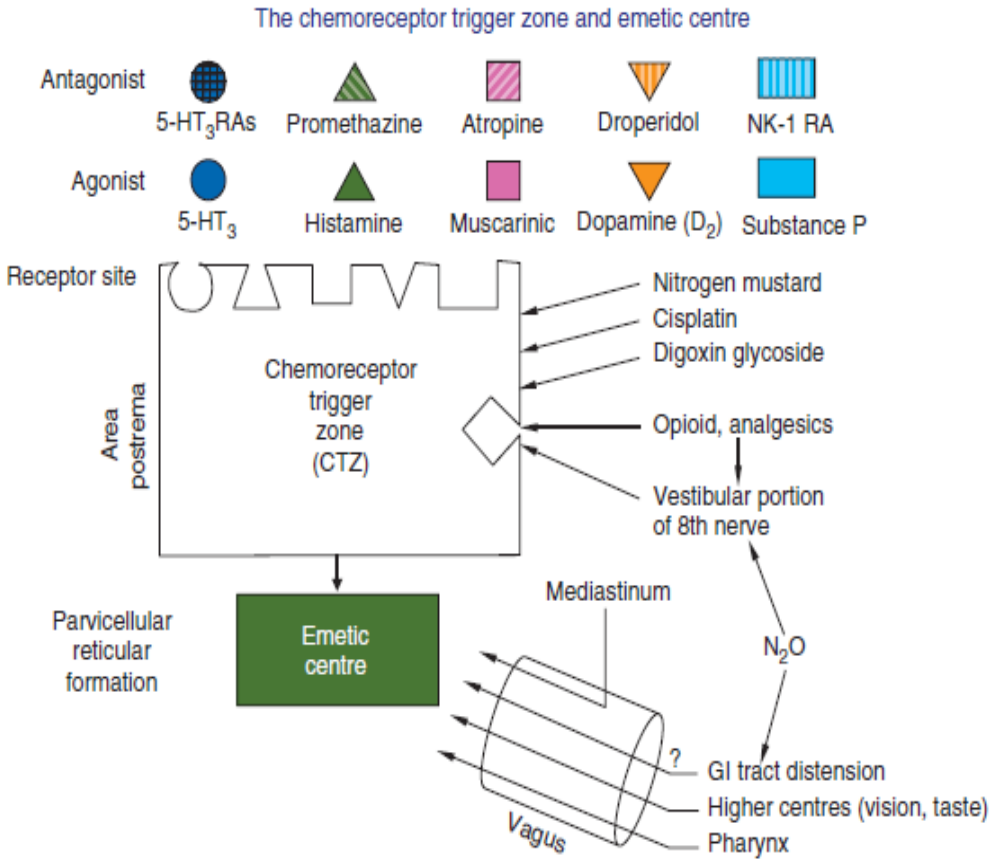

Figure. (2): The Pathophysiology of Emesis (Gan, 2007)

Before vomiting occurs, there may be a period of antiperistalsis, in which rhythmic contractions occur up the digestive tract instead of downward. This may commence as far down as the ileum, with the anti-peristaltic wave pushing contents of the lower small intestine upwards into the duodenum and stomach within a few minutes. Then,