POSTOPERATIVE NAUSEA AND VOMITING

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ABSTRACT
The vomiting reflex evolved as a defensive one centered mainly on the gastrointestinal tract. It is also a symptom of many diseases of the gastrointestinal tract, and other systems. Its occurrence with nausea in the postoperative period, poses a challenge to surgeons and anesthetists alike. To avoid the unwanted effects of postoperative nausea and vomiting in patients, pre, intra and postoperative factors that contribute to its occurrence should be prevented or treated. Antiemetics, acupuncture and other drugs are used to prevent and treat postoperative nausea and vomiting. Those that manage patients in the postoperative period should endeavour to make postoperative nausea and vomiting as unacceptable as postoperative pain.

Key Words: Postoperative, Nausea, Vomiting, Narcotics, Antiemetics

INTRODUCTION
With recent technological advancement, and resultant improvement in anaesthetic-related mortality and life threatening morbidity, attention has now been focused on the relief of postoperative pain and emetic symptoms. While it is true that much effort has been spent on the control of postoperative pain, not enough attention has been paid to the problem of postoperative nausea and vomiting (PONV).\(^1,2\)

Nausea and vomiting are regarded as side effects undesirable clinically, but in the natural world they have specific functions contributing to the survival of the animal. Nausea often precedes vomiting. The incidence of nausea usually exceeds that of vomiting, and vomiting itself may relieve nausea. Nausea and vomiting have been associated with the use of general anaesthetics for surgical procedures, but not all postoperative vomiting is due to the anaesthetic agents.\(^3,4\). Vomiting is a physiological mechanism, which may act either as a warning sign or as a therapeutic measure.\(^1,4,5\). Postoperative vomiting is most often a purposeless response to an abnormal stimulus, which is psychological, physical, or pharmacological.\(^4\). However, the persistence of vomiting after surgery may denote a serious complication, which must be given attention and not masked by giving antiemetic drugs or sedatives.

Nausea is an unpleasant sensation referred to the pharynx and upper abdomen, and is associated with a desire to vomit or the feeling that it is imminent.\(^3\) It may be brief or not, it may also precede vomiting or occur in isolation. Vomiting is the forceful expulsion of upper gastrointestinal tract
contents via the mouth. Retching is similar to vomiting, in that it involves the activation of the same muscle groups, but there is no expulsion of gastrointestinal contents. Vomiting is not the same as regurgitation or oesophageal reflux, neither of which is forceful nor involves the same muscle activation. PONV still occurs with a high frequency and is distressing to patients and potentially detrimental to their postoperative recovery. The commonest cause of postoperative nausea and vomiting is the administration of opioids either intraoperatively or in the postoperative period. PONV are considered by many patients to be specific complications of anaesthesia. PONV is common after general anaesthesia, and prophylactic administration of antiemetics has been suggested for those patients at risk.

Very few anaesthetic agents these days cause emesis, it’s a fact that some patients are prone to suffer following anaesthesia. Despite recent advances in modern anaesthesia, only modest progress has been made in the understanding and treatment of PONV.

PATHOPHYSIOLOGY

Vomiting is a reflex, with three major components; emetic detectors, integrative mechanisms and motor outputs.

Emetic detectors
The major function of the vomiting reflex is to guide against the accidental ingestion of toxins in the food, it is therefore necessary for the gut to have detection systems capable of activating the reflex. The vagus is the major nerve involved in the detection of emetic stimuli. Mechanoreceptors located in the muscular wall of the gut are activated by contraction and distention of the gut; while chemoreceptors located in the mucosa of the upper gut, monitor several features of the intraluminal environment. They respond to mucosal stroking, acid, alkali, hypertonic solution, temperature and irritants.

Area postrema: Located in the caudal part of the fourth ventricle in the region of the obex, it is one of the circumventricular organs of the brain and is outside the blood-brain barrier and the cerebrospinal fluid-brain barrier. When cells of this area termed chemoreceptor trigger-zone for emesis, are stimulated, this in turn activates the vomiting centre.

Vestibular system: The vestibular labyrinthine system is essential for induction of emesis by motion stimuli; so sudden head movement should be avoided after treatment to minimize any labyrinthine input to the vomiting centre. The movement of patients on trolleys after surgery may also induce vomiting, through this system.

Higher influences: Inputs from the higher centres appear to have facilitatory role in modulating the sensitivity of the brain stem emetic mechanism, rather than acting as primary detectors.

Miscellaneous inputs: Unpleasant taste can induce vomiting, nausea and gagging can be evoked by mechanical stimulation of pharyngeal afferents to the brain stem in the glossopharyngeal nerve. In myocardial infarction, ventricular cardiac afferents may induce nausea and vomiting when activated.

Organisation of the vomiting reflex
Both autonomic and somatic nerves mediate the motor components of the reflex. These pathways have non-emetic functions. Vagal innervations of the stomach mediate gastric relaxation for food storage. These pathways are activated in a unique pattern.
Vomiting can be considered to be a stereotyped motor programme involving coordination between the autonomic and somatic nervous systems\(^5\). The vomiting centre is used widely to describe the central emetic coordinating mechanism\(^5, 12\). The coordination of the motor components of the reflex occurs in the brain stem. The vomiting reflex can be conveniently divided into two, consecutive phases, pre-ejection and ejection.

**Pre-ejection**
The prodromal phase is characterized by the sensation of nausea. There are several visible signs such as cold sweating, cutaneous vasoconstriction, and pupillary dilatation, mediated by sympathetic nerves and salivation mediated by parasympathetic nerves. There are other changes such as tachycardia and reduction in gastric secretion. There is relaxation of the proximal stomach just before ejection, via vagal afferent nerves activating postganglionic neurons in the stomach wall using vasoactive intestinal peptides or nitric acid as neurotransmitters\(^3\). At the same time, a retrograde giant contraction originates in the mid-small gut and travels towards the stomach. This is under vagal control with acetylcholine as the neurotransmitter.

**Ejection**
This comprises retching and vomiting, with oral expulsion of gastrointestinal contents only during vomiting\(^3\). Both vomiting and retching, involve principally contractions of the somatic muscles of the abdomen and the diaphragm\(^5\). During retching and vomiting the abdominal muscles and the entire diaphragm contract synchronously, but during vomiting the peri-oesophageal diaphragm relaxes, to facilitate passage of gastric contents into the oesophagus. The actual expulsion of gastric contents is caused by compression of the stomach by the descending diaphragm, and the contracting abdominal muscles under the influences of somatic motor neurones\(^5, 8\).

The reason for anaesthesia and surgery inducing vomiting is that some feature of this treatment is capable of activating the emetic detectors. It is likely that there is not one single feature of the surgical environment that is the single cause of PONV, but this is probably multifactorial with a differing contribution from each factor depending upon the clinical situation\(^15\). The factors include food, psychological stress, and the indication for surgery in the pre-operative period. Food is not an emetic stimulus, except when consumed in large quantities, so the problem here is probably that of interaction between stimuli or sensitisation to one stimulus by another, in this case, food and the anaesthetic agent(s). The forthcoming operation may induce stress in some patients and this can lead to release of stress hormones like ACTH, growth hormone and prolactin, with possible involvement in PONV\(^3, 5\). Anxious patients may swallow large quantities of air before operation (aerophagy) producing distention of the upper gastrointestinal tract, and thus contribute to the genesis of PONV\(^3\).

Postoperative factors like premedication and intubation may contribute to PONV. The main classes of premedicant agents used are analgesics and antiemetics. The commonly used analgesics are morphine and pethidine and have been studied in relation to PONV\(^6, 9\). These drugs in analgesic doses decrease gastric emptying, increase the sensitivity of the emetic reflex to activation by labyrinthine stimulation, enhance release of 5-HT from the small intestine and cause release of vasopressin (ADH) from the posterior
posterior pituitary, thus contributing to PONV\textsuperscript{3, 11}. Stimulation of pharyngeal mechanoreceptive afferents, that project to the brain stem, during intubation can evoke the gagging reflex and if continued lead to retching and vomiting\textsuperscript{6}.

Intraoperative factors, that are contributors to PONV are the anaesthetic and the surgical procedure. The state of the anaesthesia itself contributes to the emesis of the anaesthetic agents\textsuperscript{11}. The incidence of PONV is greater with volatile than with intravenous anaesthetics and hence the physical effects of the anaesthetics could contribute to PONV. Manual ventilation with a mask may lead to distention and activation of abdominal vagal and splanchnic afferents, which in turn trigger emesis. The anaesthetics may induce nausea and vomiting by causing disruption of gastrointestinal motility, which may be compounded by the effects of surgery itself on gut function. The effects of anaesthetics on blood pressure may be compounded also by haemorrhage and surgical manipulation \textsuperscript{3, 11, 13}. Hypotension is more likely to cause nausea and vomiting during spinal anaesthesia. The vasodilatory effects of halothane, enflurane and isoflurane on cerebral blood vessels can cause an increase in intracranial pressure and contribute an additional trigger to emesis. The effects of the surgical procedure, to PONV are divided into the general effects of any surgical procedure and the effects of specific types of surgical procedure that are associated with a high incidence of PONV. The motility of the gastrointestinal tract is reduced by the anaesthetics, and surgery especially abdominal procedures with extensive manipulation\textsuperscript{12}. Certain surgical procedures are known to have high incidence of PONV, examples are ophthalmic surgery, ear, nose and throat surgery by activation of the oculoemetic reflex and vestibular afferent pathways involved in motion sickness respectively. During abdominal and gynaecological surgery, there is some displacement, manipulation and traction on the intestine and the mesentery, even when the intestine is not the organ for the surgical procedure. The procedures are signaled to the central nervous system via vagal and splanchnic afferents that invest the intestine\textsuperscript{3}.

PONV usually lasts less than 24 hours, and being most intense during the first 2 hours, although the precise pattern depends upon many factors\textsuperscript{12}. The factors already discussed above may occur in the postoperative period, especially if they have along time course or may initiate secondary processes with prolonged effects.

Morphine and other opioids are the most likely to cause PONV, of the drugs given in the pre-operative period\textsuperscript{3, 9}. They have a direct emetic effect, sensitising the vestibular system and by inhibiting gastric motility. The rate of recovery of anaesthesia, affects the incidence of PONV as sedation itself suppresses the emetic reflex. The use of neostigmine to facilitate the reversal of neuromuscular block has been associated with increased incidence of PONV\textsuperscript{14}. The role of pain in the genesis of PONV is difficult to assess from a mechanistic viewpoint. Pain induces general arousal or alerting of the central nervous system, it may be that the patient becomes alert enough to experience the nausea generated by other inputs. Thus pain need not cause nausea but merely facilitate its expression.

**CONSEQUENCES OF PONV**

PONV is unpleasant and aesthetically displeasing to both the patient and their caretakers, is also associated with
detrimental effects that may increase morbidity and mortality. The consequences may be classified into physical, metabolic and psychological.

**Physical**
Retching and vomiting are fairly violent (active) and intense physical acts, and may place some stress on certain structures particularly if prolonged. These include oesophageal tears leading to mediastinitis\(^1\) and rupture resulting in haemorrhage (Mallory Weiss Syndrome), rib fractures, gastric herniation, muscular strain and fatigue and rupture of cutaneous vessels in the upper body. There may also be wound dehiscence and bleeding at the operative site, with or without haematoma formation, raised intracranial and intraocular pressure can occur from postoperative vomiting, with bleeding of skin flaps in plastic surgery. The stress and strain on wounds after surgery following vomiting can increase the postoperative pain. The main physical problem of PONV is aspiration of vomitus in the postoperative period, and triggering of cardiorespiratory reflexes and its attendant risk of increased morbidity and mortality\(^1,12\).

**Metabolic**
With persistent vomiting, fluid and electrolyte imbalances, dehydration and alkalaemia may occur, especially in the paediatric population\(^1,3,13\).

**Psychological**
The nausea and vomiting associated with an operation, may induce an aversion to surgery\(^3\). A patient experiencing PONV on an occasion may expect the same experience with subsequent surgery. The implication of all these consequences may be delayed hospital discharge, and consequently increased financial burden on the system, as the patients may require extended time in recovery room, increased attention from nurses and physicians, additional drugs, intravenous fluids and supplies.

The incidence of PONV has remained fairly constant at between 10%-30% in recovery room during the first 24 hours after anaesthesia in several large series\(^1\). PONV is affected by many factors, including age, body habitus, gender of the patient, delayed gastric emptying, anaesthetic history, motion sickness, anxiety, premedication, anaesthetic technique, and medication, postoperative analgesia and regional blocks and the type and duration of surgery\(^11,15\).

**MANAGEMENT OF PONV**
Antiemetics are now the main stay of therapy for postoperative nausea and vomiting (PONV)\(^16\). There are several types of antiemetics used in the management of PONV. These include gastrointestinal prokinetic drugs with antidopaminergic actions (e.g. prochlorperazine, perphenazine) and butyrophonones (e.g. droperidol) have antiemetic properties resulting from antidopaminergic actions. Central anticholinergic action is associated with antiemetic activity and this is seen in drugs such as hyoscine, atropine, and in some antihistamine receptor type 1 antagonists (e.g. cyclizine). It is possible that the anticholinergic effect of these drugs is responsible for their antiemetic activity. Metoclopramide and domperidone act primarily as antidopaminergics and therefore are used as antiemetics. Cisapride has no antidopaminergic effects, and therefore little antiemetic activity. Side effects that may occur with their use include extrapyramidal reactions such as dystonia and Parkinsonian reactions. Phenothiazine a derivative of prochlorperazine has been used
extensively in the management of PONV. Promethazine a derivative of phenothiazine is still used as premedication and has effects on PONV but its sedative action limits its use considerably.

Butyrophenones, these are potent neuroleptics, but its only droperidol that is used extensively in anaesthesia. The side effects are similar to these of phenothiazines. Droperidol has alpha-adrenergic receptor blocking properties, and may cause hypotension during anaesthesia.

The anticholinergics, such as hyoscine or atropine are centrally and peripherally acting, and have antiemetic activity. The development of a transdermal preparation of hyoscine is an attempt to alleviate the problems of short half-life and dose dependent side effects. Atropine is not used after anaesthesia in managing PONV. Cyclizine is the only antihistamine used extensively as an antiemetic, others are used for prevention of motion sickness. These drugs exhibit histamine type-1 receptor antagonist activity. Sedation and dry mouth are a consequence of its antimuscarinic action.

Acupuncture has been used in the prevention of PONV, it is effective in some circumstances, and is free from side effects.

The 5-Hydroxytryptamine subtype 3 (5HT3) receptor antagonists' represent a major break through in the management of emesis, as they are highly effective and possess a low side effect profile. The group includes granisetron, tropisetron, dolasetron, batanopride and zacopride. Tropisetron prevented PONV better than Metoclopramide and placebo in a recent study. It also reduced the need for rescue antiemetic significantly. Ondansetron is the prototype of this class of drugs. It is a carbazole, with a highly selective, competitive antagonism at the 5-HT3 receptor, but with little effect on 5-HT1, 5-HT2, and P1, muscarinic, histaminic, dopaminergic or GABA receptors. Side effects with Ondansetron are minor and include headache, and constipation. Although Supplemental oxygen reduced the risk of PONV better than ondansetron in a study by Goll and Colleagues. They recommended it because, oxygen is inexpensive and essentially risk free, but this may not be so in developing countries. Propofol has become popular for induction and maintenance of anaesthesia, because it is associated with rapid awakening and a markedly decreased incidence of PONV. Midazolam has also been used to treat persistent PONV.

The steroid dexamethasone was more effective than saline in preventing nausea and vomiting, associated with epidural morphine for post-caesarean analgesia, as reported by Wang and Colleagues.

CONCLUSION

Postoperative nausea and vomiting is detrimental to patients. The factors that contribute to PONV should be treated. To decrease morbidity and mortality from PONV efforts must be made to prevent or treat it by those who manage patients in the postoperative period.

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