

Postoperative nausea and vomiting: causes and treatments



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Postoperative nausea and vomiting is the nausea and vomiting symptoms which occurred after a surgery, medicines intake or anaesthesia usage. Around 18 to 30 of surgical patients have PONV and the nausea and vomiting symptoms are usually self-limiting in most cases. 1 Uncomplicated PONV usually resolve within 24 hours after an operation whereas intractable PONV involve various triggering factors and resist to medical treatment, making it harder to treat. Studies revealed that most patients dislike chronic PONV more than postoperative pain as it is a more distressing illness and it may lead to several serious clinical consequences if left untreated.

In the case of repeated vomiting, PONV patients might suffer from dehydration and have a higher chance of developing hiatal hernia, a condition where the upper part of stomach protrudes into the thorax through the opening of diaphragm. Other than that, patients might also experience anorexia, gastrointestinal discomfort, headache, weakness, dizziness and nausea while not vomiting. Chronic vomiting can also cause complications like dental damage and sore throats due to exposure of oesophageal lining and mouth cavity to the low pH gastric acid. Moreover, PONV may induce serious problems like pulmonary aspiration, electrolyte abnormalities, wound dehiscence, increased pain and oesophageal rupture. 4, 5 Despite causing patients discomfort, patients also have to pay more for the delayed hospital discharge. Each incidence of vomiting has increased postanesthetic care unit (PACU) stay duration by 20mins. Therefore, to reduce the unanticipated hospital admission and the financial burden brought by PONV, there is a need to understand the disease pathophysiology so that precise and

mechanism-based treatment strategies can be developed to tackle the emesis problem.

The vomiting centre and the chemoreceptor trigger zone (CTZ) are the two main parts of the brain controlling the vomiting action. The vomiting centre is located within the medulla oblongata and the emesis action is initiated via the stimulation of five primary afferent pathways. They are the chemoreceptor trigger zone, vagal mucosal pathway of the gastrointestinal system, neuronal pathways from the vestibular apparatus system, inputs from the periphery glossopharyngeal nerve and reflex afferent pathways from cerebral cortex C2, 3 and midbrain afferents. Next, efferent nerve impulses are sent to various place of the body such as the pharynx, larynx, diaphragm, intercostals muscles and gut to initiate the vomiting reflex. During the ejection phase of the vomiting reflex, the diaphragm and abdominal muscles simultaneously contract and the elevated intra-abdominal pressure leads to the throw up and expulsion of gastric contents. A variety of receptors are participated in the emesis action. They are the histaminergic(H1), dopaminergic(D2), serotonergic(5-HT3), muscarinic and neurokinin-1 receptors. Consequently, pharmacological agents which target on these receptors can be utilized to treat PONV. However, the British National Formulary (BNF) had advised that antiemetic agents should only be used once the causative factor for nausea and vomiting was identified. This is because the use of antiemetic is sometimes dangerous and inappropriate in clinical cases like diabetic ketoacidosis, digoxin or antiepileptic overdose. 6 Hence, the aetiology and possible causative factors of PONV should be

investigated to guide the planning of the pharmaceutical management steps and the antiemetic selection for treating PONV.

There are patient-specific factors, surgical factors and anaesthetic risk factors which contribute to PONV prevalence. Patients who aged 6 to 16 year old, female, non-smoker, obese or have a history of motion sickness or PONV are proven to be the high-risk patient group. Moreover, patients who have chemotherapy, migraine and gastroparesis problems are also susceptible to PONV. Other causative factors include elevated intracranial pressure, metabolic abnormalities, gastroduodenal ulcers, dehydration and infections of the gastroesophageal lining.

As for the surgical factors, PONV is related to the premedication side-effect, prolong fasting, conditions of gastric inflation during mask ventilation, use of long-acting opioids, nitrous oxide, volatile anaesthetics and high dose neostigmine in surgery. In addition, frequent head movement of patient and early intake of food after surgery can also potentiate the nausea problem. 1 Some types of operations have higher chance of developing PONV, they are the gynaecological surgery, ear, nose and throat operation, intra-abdominal and squint correction surgery. Furthermore, the surgical duration is also an important contributor which predisposes patients to a higher risk of PONV. Every 30 minutes extension in surgical time can increase risk of PONV by 60% as patient is taking in more anaesthetics into the body. Hence, healthcare team should control and minimize the surgery duration such that risk of getting PONV is reduced.

Although it is not relevant to discuss anaesthetic techniques in this case scenario, it is important to note that regional anaesthesia should be preferred over general anaesthesia during surgical process. According to SOGC guideline, there is an 11-fold increase in the PONV risk when using general anaesthesia rather than regional anaesthesia. Apart from that, volatile anaesthesia, long-acting opioid and neostigmine should also avoid in surgery as these agents predispose patient to PONV. If the use of general anaesthesia is unavoidable in a surgery, propofol can be a suitable induction agent because it induces less PONV incidence.

A thorough assessment should be carried out to serve as a rationale for the management plan of PONV. The past medical history, frequency and nature of the vomiting episode, blood electrolyte test and physical examination can be evaluated to identify the severity of disease condition and the aetiology of PONV. Subsequently, the appropriate pharmacological agents which target on the responsible pathway of emesis can be given.

Many antiemetic preparations are available in the market and patients can choose between formulations of solution, buccal tablets, rectal suppository and subcutaneous (SC), intravenous (IV) or intramuscular (IM) injections when oral route is not feasible. 6 As no single agent provides complete control in emesis, most hospital has adopted a multimodal approach and a combination strategy where different antiemetics which target on different receptors are utilized in the treatment of PONV. 1 Combination therapy becomes the preferable way to treat PONV and the generally used combination is 5-HT₃ receptor antagonists with droperidol or dexamethasone.

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Granisetron and ondansetron are examples of 5-HT₃ or serotonin receptor antagonists. They exert their effects in the chemoreceptor trigger zone and at vagal afferents of the gastrointestinal tract. Previous studies showed that no single agent performed exceptionally well than the others of same class as all 5-HT₃ antagonists illustrated similar safety and efficacy profile. Yet, a recent meta-analysis which includes 85 randomized controlled, double-blind studies with 15, 269 patients involvement had established that the antiemetic effect of granisetron is significantly superior to ondansetron and dolasetron. Ondansetron was also found to be more cost effective than granisetron. 1-2mg of granisetron or 4-8mg of ondansetron can be delivered in intravascular route at the end of surgery for PONV treatment. Long-acting serotonin antagonist with higher binding affinity to 5-HT₃ receptors, palonosetron, is also available in the market with a long half-life of about 40 hours. Patients receiving these agents might experience headache, constipation and dizziness problems.

Droperidol is a butyrophenone which acts competitively on central dopaminergic receptors in the chemoreceptor trigger zone (CTZ). It is applied in 0.625-1.25mg IV route at the end of surgery. A systematic review of 24 randomized studies was carried out by Schaub and team, they concluded that droperidol decreases PONV incidence regardless of the dose given to patients. However, this drug is only used as a third-line antiemetic for intractable PONV when other alternative treatments failed because droperidol can lead to adverse effects associated with QT prolongation and torsades de points, sedation, anxiety, hypotension and extrapyramidal symptoms. Due to its possibility in causing fatal arrhythmia,

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electrocardiographic monitoring is compulsory each time upon its usage.

Nonetheless, a double-blinded randomized clinical study which included 120 patients stated that there was insufficient evidence to prove the QTc prolongation effect induced by droperidol after surgery.

Dexamethasone is classified under corticosteroids and often delivered in a 4 to 5mg 'one-off' dose via IV or IM route. 19 The exact mechanism of action is unknown but it is related to the peripheral inhibition of prostaglandin synthesis and its ability to reduce 5-HT turnover in the CNS. Although dexamethasone is not licensed for the indication of PONV, this drug is as effective as other conventional antiemetic drugs like droperidol and serotonin antagonists. A single blinded, randomized-controlled interventional study had illustrated that the administration of dexamethasone is useful for the reduction of PONV episodes (30% in contrast to 70% of the placebo group). 20 Moreover, Ormel et al. illustrated that the addition of dexamethasone to droperidol and ondansetron showed a profound amplification in the efficacy profile of these triple agents combination. It stands as a good alternative for PONV treatment due to the advantage of cost-effectiveness issue and its characteristic of long action duration. As dexamethasone can increase plasma glucose level, it is not recommended for diabetic patient. Furthermore, unfavorable side-effect like postoperative euphoria, impaired wound healing, irritability and adrenal suppression can happen in patient taking long-term corticosteroids.

Metoclopramide is a gastroprokinetic agent which acts on the D2 receptors of the gastrointestinal tract. It can accelerate the gastric emptying rate of gastroparesis and GI obstruction patients. 2, 6 Despite blocking the D2

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receptors, it also has antagonist action on 5-HT₃ receptors in the CTZ and vomiting centre when delivered in high doses. 5 to 20mg dose of metoclopramide in subcutaneous, oral or IV route is commonly taken by patient before meal and before bed. 6 This medicine is commonly administered as combination therapy because there is conflicting evidence stating that metoclopramide alone is ineffective for PONV and it should not be use unless the causative factor for PONV is gastric stasis. Yet, a recent meta-analysis has proved that 10mg IV metoclopramide does well in preventing nausea and vomiting problems after the general anaesthesia surgery. As with the phenothiazines discussed below, both drugs have limited use in practice due to the adverse reactions like extrapyramidal effects and dystonia disorder particularly in pediatric and young adults population.

Phenothiazines is an example of strong dopamine antagonist which also act on medullary CTZ. Promethazine, prochlorperazine and perphenazine belong to this group and take part in the prophylaxis and treatment of PONV. 24 Prochlorperazine is often administered as a 12. 5mg deep intramuscular injection or in a 3 to 6mg dose buccal preparation 12 hourly after the surgery. These agents show superior efficacy in treating opioid-induced PONV. However, high-dose metoclopramide and phenothiazines are now less likely used in clinical practice because of their significant side effects like acute dystonic reactions, sedation, dizziness and extrapyramidal symptoms. 9, 25 A systematic analysis consisting of 19 non-randomized and randomized clinical trials had demonstrated that most studies supported the effectiveness of promethazine in reducing PONV occurrence when compared

to placebo and that combination therapy is always preferable and more effective than promethazine alone.

Cyclizine is an antihistamine drug which blocks the H₁ sympathetic pathway in the vomiting centre. The antimuscarinic and antihistamine properties of cyclizine render it to become an antiemetic drug in PONV treatment. A randomised double-blinded study which involved the participations of 960 women had shown that patients who received cyclizine monotherapy showed a slightly greater antiemetic effect than granisetron alone (PONV incidence of 24% with cyclizine compare to 23% in granisetron group).²⁶ Cyclizine can be given orally, intramuscularly or intravenously, with common antimuscarinic side-effects like sedation and dry mouth. Severe heart failure patient should avoid taking this medicine because it leads to detrimental haemodynamic effect.⁶ The acidic pH of cyclizine at 3.2 also causes pain and irritancy to body upon injection.¹⁰ As a result, patients usually have 50mg of cyclizine IV injection every 8 hours after proper dilution. A lower dose of 25mg in oral, IM or IV preparations can also be applied in elderly patient.

Scopolamine has anticholinergic property which inhibits the muscarinic as well as the histaminergic receptors in the vestibular apparatus and the nucleus of the tractus solitarius.^{3, 9} Patients who undergo middle ear surgery or use opioids as postoperative anaesthetics are recommended to take scopolamine for their profound efficacy in reducing PONV.³

Scopolamine requires 2 to 4 hours for onset of duration. Hence, a fast-acting antiemetic or a loading bolus dose is needed in urgent case. It is available in transdermal form as a 1.5mg patch which can be placed behind the ear.
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This slow-release formulation can have sustained effect up to 72 hours. Apfel C et al. had reported that transdermal scopolamine had significantly reduced the risk of PONV when compared to the placebo group although it has the main side-effects of dry mouth, sedation and visual disturbances. 28 Furthermore, a comparative study between the combination use of ondansetron plus scopolamine patch and ondansetron alone also proved that the earlier group significantly decrease the nausea and vomiting incidence after surgery.

Other than a mechanism-based approach, less conventional therapeutic agents can also be used to treat intractable PONV cases. An antidepressant with a novel indication, mirtazapine, is able to ease the nausea and vomiting symptoms because it can antagonize 5-HT₃ receptors. A small scale randomized trial which compared the therapeutic outcome of mirtazapine and ondansetron had showed that patients using mirtazapine were less anxious and had fewer PONV episodes than the ondansetron group. Next, olanzapine which is recognized as an atypical antipsychotic drug also proved to have potential in treating PONV. It can inhibit several receptors such as the dopamine, acetylcholine, histamine and 5-HT₃ receptors. Ibrahim M et al. had conducted a randomized controlled study which involved 82 surgical patients. The result proved the efficacy and safety profile of olanzapine against PONV especially during the late postoperative stage. Other than medications approach, non-pharmacological interventions also show potential therapeutic efficacy in PONV management.

Acupuncture, acustimulation or acupressure serves as a good alternative or adjuvant therapy for PONV patients as it shows good tolerability and safety <https://assignbuster.com/postoperative-nausea-and-vomiting-causes-and-treatments/>

profile. The P6 point (Neiguan) which located at 5cm near to the ventral wrist is the target site of these alternative approaches. Transcutaneous electrical stimulation delivered to the P6 point of the pericardium meridian has been proved to be an efficient way in preventing emesis. Patients only complain of light side-effects like needle fainting, allergy, needle site pain, anxiety or lethargy problems when using this method.

In order to solve the labour intensive and time-consuming issues of traditional Chinese acupuncture, the acupressure and acustimulation wristband are introduced in the market (Sea-Band and ReliefBand). Sea-Band applies steady, continuous pressure on the P6 point whereas ReliefBand is a watch-like device which conducts low current to P6 point via electrodes in contact with the skin. Based on the well-established efficacy profile and good evidence-base literature support, healthcare professionals can involve more acupuncture interventions in treatment practice as part of the multimodal approach.

In this case, the intractable emesis symptoms experienced by the old woman might indicate the failure of prophylaxis treatment or the need to start a primary antiemetic treatment. Before the initiation of a rescue treatment, a bedside examination and a patient interview should be done to find out whether the PONV symptom is associated to issues such as morphine analgesia, surgical pain management, infection, intestinal obstruction, hypotension, hypoxia, blood in the pharynx, anxiety or removal and insertion of nasogastric tube.

5-HT₃ antagonist is the recommended drug for patients who previously do not receive a prophylaxis treatment. Patient can start with a low dose regimen such as ondansetron 1 mg, dolasetron 12.5 mg and granisetron 0.1 mg. If drugs for prophylaxis had been given but fail, patients can then try other class of antiemetics to tackle more diverse receptor pathways. For instance, Habib et al. had found that the failure of prophylactic ondansetron or droperidol can be replaced with rescue agents like promethazine (12.5-25 mg IV), prochlorperazine (12.5 mg IM) or cyclizine (25-50 mg IV or IM) to achieve a better outcome. This is because consensus guideline support that the repeat use of 5-HT₃ antagonist within the initial 6 hours postoperative period provides no extra recovery response. If patient use dexamethasone as prevention agent, small dose 5-HT₃ antagonist (25% of prophylactic dose) can then be given as a rescue approach. A study also concluded that the cost-effectiveness of ondansetron in low dose treatment group was higher than that in the high dose prophylactic group.

Moreover, in the case of the aggressive treatment failure, such as those who had taken 5-HT₃ antagonist, droperidol and dexamethasone altogether but failed, repeat dosing of same prophylactic regimen except dexamethasone can only be considered 6 hours after the surgery though the optimal dosage and timing for readministration still remain unknown. Transdermal scopolamine can also be prescribed for outpatients as it is a more convenient preparation than the parenteral drugs.

Prolong use of opioids for pain control after surgery should also be minimized as side-effects like nausea and vomiting are correlated to the prescribed dose. Alternative analgesics like NSAIDs can be used to substitute the <https://assignbuster.com/postoperative-nausea-and-vomiting-causes-and-treatments/>

causative opioids. In persisting case, pharmacist can review the prescription and anaesthetic charts to ensure adequate maintenance of analgesia, antiemetic and oxygen supply. Dose escalation under safety and therapeutic dosage range can also be worked on. However, pharmacist should be cautious on polypharmacy problem as it may aggravate nausea and vomiting in susceptible patient. Non-oral drug preparations can be considered over oral route to avoid burdening of patient with excessive pills at one time. If necessary, the acupuncture treatment can also be applied to attempt a multimodal approach.

Pharmacist should also concern about the possible dehydration risk that might be encountered by chronic PONV patients. For this reason, the blood pressure, hydration and perfusion level of patients have to be checked on a regular basis. Patients should be told to report of symptoms like dry or sticky mouth, sunken eyes, reduced urination or dark yellow urine. If constipation or diarrhea happens, intravenous fluid replacement therapy, osmotic or stimulant laxative can be given to solve the issues. For the dietary measures, patients should avoid oily or spicy food which might aggravate the nausea. Small, frequent meal is preferable over big heavy meal as light meal reduce the possibility of gastric discomfort.

Patients should be advised to not move around too often to avoid triggering the vomiting centre. Furthermore, in post-discharged nausea and vomiting (PDNV) case, the antiemetic efficacy profiles are different from PONV's as they have dissimilar underlying cause. Droperidol should be avoided as it is ineffective in treating PDNV. 2 If the patient still not responsive to all these approaches, specialist intervention should be initiated to treat intractable <https://assignbuster.com/postoperative-nausea-and-vomiting-causes-and-treatments/>

nausea and vomiting symptoms. Serious causative factors like surgical complication might be suspected and further investigations are required to treat this disease.

In a nutshell, the optimization management of PONV disease requires the participation of the multimodal approach. Patients should be treated accordingly after the accurate disease assessment and further modifications of treatment approaches like (dose-adjustment, introduction of new agents or alternative approaches) can be done to control patient's nausea and vomiting symptoms. Lifestyle modification and non-pharmacological interventions also play an important part in treating PONV. Proper patient education about symptoms management should be delivered and follow-up session can be arranged to assess patient's rehabilitation progress. Apart from that, reassurance and full supportive care from healthcare teams also play an important role in reducing patient distress and anxiety level.