

# [Nursing processes for emesis management](https://assignbuster.com/nursing-processes-for-emesis-management/)

Nausea and vomiting are common complications of multiple conditions, procedures, therapies, and events such as motion sickness, pregnancy, anesthesia (general, regional, or local) or radio/chemotherapy. Symptoms can be debilitating for many patients, and in the case of post-operative nausea and vomiting (PONV) physical damage may result, such as rupture of sutures, stitches, and esophageal tissue, and metabolic problems, such as electrolyte imbalances and dehydration (Golembiewski et al, 2005; Gan 2006). In severe cases of PONV, although rare, aspiration of gastric contents may occur, resulting in pulmonary sequelae, such as pneumonia or pneumothorax (Scuderi and Conlay 2003; Bremner and Kumar 1993). Thus effective treatment of PONV, possibly through multimodal antiemetic prophylaxis, is an important are of research (Skledar et al. 2007).

This essay will consider two commonly used, well-recognized antiemetic treatments namely cyclizine and prochlorperazine. Both represent very old drug therapies, with cyclizine having been launched as an antiemetic in 1953, and prochlorperazine as an antipsychotic in 1957 (Broccatelli, 2010), its use as an effective antiemetic emerging soon thereafter (Finn et al, 2005). These drugs are commonly used on most wards in my practice setting and therefore it is vital for nursing staff to understand their respective pharmacodynamic (PD) and pharmacokinetic (PK) profiles. Prior to prescribing it is also important that the nurse have relevant knowledge regarding how these drugs work, how their PD and PK properties are altered by disease processes such as kidney/liver failure and whether there are any relevant contraindications or precautions. Additionally, the potential for drug-drug interactions and the dose appropriate for the patient’s age and weight should be ascertained if beneficial patient orientated outcomes are to be achieved. These issues will be comprehensively discussed within this essay.

## Pharmacology of emesis

There are a plethora of drugs on the market to treat emesis, however, deciding upon an appropriate and effective treatment for patients requires the cause of the underlying nausea and vomiting to be ascertained. This is because the symptoms can manifest as a result of a number of underlying pharmacological processes, as will now be described.

Vomiting is a complex reflex action controlled by the vomiting centre (VC) in the medulla region of the brain, an important part of which is the chemotrigger zone (CTZ); stimulation of this in turn leads to VC stimulation which ultimately leads to vomiting (Goodman & Gilman, 1996). Neurotransmitter mediated stimulation of the VC can arise from both peripheral and central impulses (Shanbhag, 2008). Thus gastrointestinal irritation, motion sickness and vestibular neuritis all manifest in nausea and vomiting as a result of neurotransmitter release. The three main neurotransmitters involved in the control of vomiting are acetylcholine (ACh; via muscarinic-receptors), dopamine (via dopaminergic receptors), histamine (via H-1 receptors), and serotonin (via 5-HT3 receptors) (Shanbhag, 2008). Inhibition or antagonism of these receptors achieves emetic control.

The VC has neurons which are rich in muscarinic cholinergic and histamine containing synapses and is directly stimulated by the vestibular input (e. g. through motion sickness), whilst dopamine and serotonin release are involved in the visceral stimuli pathway (e. g. through chemotherapy treatment) and also in the CTZ stimulation pathway as shown in Figure 1. Thus drug classifications of anti-emetics arise on the basis of which of the three pathways that they target (Flake et al., 2004). Selective serotonin receptor antagonists and antidopaminergics target the visceral stimuli and the CTZ, whilst the antihistamines and anticholinergics target the vestibular input pathway (Hornby , 2001; Flake et al., 2004).

## Etiology of Nausea and Vomiting

Cyclizine’s anti-emetic effects are not fully understood but it is thought that it works by blocking the transmission of information from the labyrinthine apparatus in the inner ear (i. e. the vestibular pathway) to the VC (Goodman and Gillman, 1996).

Cyclizine may also target the CTZ and it thought to exhibit some ACh muscarinic receptor blockade which probably contribute to the antiemetic potential thus operating at several pathophysiological levels. However, a side effect of ACh blockade is sedation in some individuals along with the potential for certain deliriant and hallucinogenic effects, probably responsible for cyclizine’s abuse potential (Bailey and Davies, 2008). Cyclizine produces its antiemetic effect within two hours and it lasts approximately four hours (emc, n. d.).

The exact mechanism of prochlorperazine’s antiemetic action is also unclear, but the drug is thought to inhibit apomorphine induced vomiting by blocking dopamine D2 receptors centrally in the CTZ and possibly peripherally through dopaminergic receptors in the intestine (Perwitasari, 2011).  However, it also has some potential to block anticholinergic and alpha-adrenergic receptors, and therefore can also result in sedation along with muscle relaxation, and orthostatic hypotension (Kelly, 2000). Following intramuscular administration prochlorperazine has an onset of action within ten to twenty minutes and a duration of action of three to four hours (globalrph, n. d.).

## Indications and dosage form

Cyclizine is indicated for the control of postoperative and drug-induced vomiting and in motion sickness (BNF, 2012; emc, n. d.). It is given by mouth at a dose of 50mg tablets up to three times a day or parenterally as a 50mg in 1ml solution intramuscular (im) or intravenous (iv) injection again at a frequency of up to 3 times a day (Reynolds, 1993). The recommended dose in children aged 6-12 years is lower: 25 mg up to 3 times daily. For motion sickness, it is recommended that tablets be taken 1-2 hours before departure. Cyclizine can also be given for vertigo and, morning sickness in pregnancy, and to combat opioid nausea. It is also prescribed for radiation sickness (medsafe, n. d.) and PONV (Cholwill et al., 1999), indeed it is given iv before the induction of general anaesthesia at half the recommended dose, to increase the lower oesophageal sphincter tone thus reducing the hazard of regurgitation and aspiration of gastric contents (medsafe, n. d.).

Although prochlorperazine is classified as an antipsychotic, its principal use nowadays is in the treatment of severe nausea and vomiting of various causes including, PONV, vertigo and motion sickness (BNF, 2012). It has several dosage forms: tablet (5mg: one or two tablets 3-4 times daily), syrup (5mg in 5ml: 5-10 ml 3-4 times daily), suppositories (25mg twice daily), dissolvable tablet (buccal tablet 3mg: one or two tablets twice a day in adults and children aged 12 years and over), im injection (12. 5mg in 1ml; 5-10mg repeated every 3-4 hours with a maximum daily dose of 40mg) and iv injection (2. 5 -10 mg by slow IV injection or infusion with a maximum daily dose of 40mg). The oral (and buccal) route is the only method of administration recommended for children, and it is not recommended in children younger than 12 years (BNF, 2012). The different dosage form of prochlorperazine provides the nurse with flexibility for example the elderly and children may prefer the syrup or buccal tablet, or in dysphagia suppositories or intra-muscular injections could be more appropriate.

Cyclizine and prochlorperazine are both considered first line treatments for nausea secondary to vertigo and motion sickness (Quigley, 2001) and are first line treatments in many hospitals in PONV (NHS, Salisbury; NHS Plymouth). A review by Matchar, et al. (2003) has suggested that oral prochloperazine may also be used as an adjunct in the treatment of nausea associated with migraine (Matchar et al, n. d.). No randomized controlled trial has been found which formally compares efficacy of cyclizine and prochlorperazine, however, two studies comparing cyclizine with perphenazine in ameliorating drug-induced emesis, have shown the former to have comparable antiemetic efficacy to this related phenothiazine drug (Dundee et al., 1975; Chestnutt and Dundee, 1986). These studies are featured in a Cochrane report (Stevenson, 2006) which investigates drugs for preventing PONV and highlights eight drugs which reduce PONV by a similar amount in this patient group, cyclizine being one. The report concluded, therefore, that the most important question to answer when treating emesis is “ What are the types and risks of side effects experienced by patients exposed to these antiemetics?” Thus safe and effective prescribing requires the nurse to identify patient variables or comorbidities relevant to the drug’s side effects, for example heart failure patients should not be prescribed cyclizine and individuals susceptible to visual disturbances should avoid prochlorperazine as per the drugs’ contraindications. It is noteworthy that both drugs may be prescribed in the later stages of pregnancy if considered appropriate by a doctor (Schaefer, 2007; CKS, n. d.).[1]

The choice of antiemetic would depend upon the precise cause of the nausea in conjunction with the specific receptor affected. However, since several different neurotransmitters stimulate the CTZ, combining drugs with different mechanisms of action can often be more effective than increasing the dose of one individual drug (King and Brucker 2011). Indeed, combinations of antiemetics are often used in palliative care (NHS Scotland, n. d.). Notably, vomiting of unclear or mixed origin may respond to a phenothiazine such as prochlorperazine because, in addition to acting on dopamine and serotonin receptors in the CTZ, it also acts at the VC and vestibular area.

Cyclizine and prochlorperazine are both commonly used anti-emetics in palliative care where nausea and vomiting are present in up to 70% of patients with advanced cancer (NHS Scotland, n. d.). Treating this patient population requires particular vigilance, since there may be a number of underlying reasons for and comorbidities contributing to the nausea and vomiting, and antiemetics may be inappropriate. Consideration for causes of the symptoms might include intestinal obstruction or constipation, anxiety, raised intracranial pressure (ICP), oesophageal candida, severe pain or hypercalcaemia all of which might warrant interventions other then antiemetics. Conversely, should the nausea and vomiting be identified as drug induced, then anti-emetics such as cyclyzine or prochlorperazine might be appropriate. Raised intracranial pressure stimulates vomiting centre via pressure receptors and can be problematic in patients with known or suspected brain metastases. Notable, cyclizine can be given to such patients, especially where corticosteroids are contraindicated (NHS Scotland, n. d.).

## Pharmacokinetics

Cyclizine, like most antihistamines, is well absorbed from the GI tract. After oral doing the effects develop within 30 minutes, are maximal within 1-2 hours and lasts for 4-6 hours. A single oral dose of 50 mg cyclizine in healthy adult volunteers resulted in a peak plasma concentration of approximately 70 ng/mL, occurring at about two hours after drug administration. The plasma elimination half-life is approximately 20 hours.[2]Cyclizine is extensively metabolised in the liver via N-demethylation to the inactive metabolite norcyclizine (Figure 4), which is widely distributed throughout the tissues and has plasma half-life of approximately 20 hours. This metabolite has minor antihistaminic activity compared to parent drug. A single 50 mg dose of cyclizine when given to an adult male volunteer, results in less than 1% of the total dose administered being excreted as parent drug in the urine over a 24 h period. Thus urinary excretion of metabolite rather than parent drug is the major route of elimination for cyclizine. The metabolism is thought to be mediated through CYP 2D6 and therefore exhibit inter-subject variability dependent upon the CYP 2D6 genotype as demonstrated by Vella-Brincat et al. (2012) in their study of the PK of cyclizine (Appendix 1) and its major metabolite (Appendix 2) in palliative care patients receiving sub-cutaneous cyclizine. Results indicated that the metabolic ratio of parent drug to metabolite differed significantly according to CYP2D6 genetics.[3]

Prochlorperazine is reasonably well absorbed from the GI tract and highly protein bound. It undergoes extensive metabolism both in the gastric mucosa and on first pass through the liver via the cytochrome P450 enzyme system (CYP 2D6 and CYP 3A4)[4]to inactive metabolites, which are subsequently excreted in the urine. Parent drug has a plasma half-life of between 4 and 8 hours, the precise half-life differing according to the mode of administration. An im injection produces its antiemetic effect in 5-10 minutes and it lasts for 3-4 hours. Onset of effects are related to the mode of administration hence the pharmacokinetic profile, thus an oral dose would have a slightly slower onset of action but would last longer compared with an im injection.[5]According to Finn et al (2005), although the drug has been accepted as a useful anti-emetic for over half a century, its therapeutic success has been limited by its low and variable absorption and high first-pass metabolism. However, the development of a new buccal formulation has improved the PK, since studies demonstrate that buccal administration of prochlorperazine produces plasma concentrations more than twice as high as an oral tablet, with less than half the variability (Finn et al., 2005)[6](Figure 5). When placed in the buccal cavity between the upper lip and the gum the formulation forms a gel from which the prochlorperazine is released and absorbed. The plasma levels achieved at steady-state on a dosage regimen of one 3mg buccal tablet twice daily are similar to those observed with the standard oral dosage of one 5 mg tablet taken three times daily. The elimination half-life of prochlorperazine in this formulation is 9 hours. The safety and efficacy of this relatively new formulation has also been demonstrated by Bond[7](1998) in a randomised, double-blind, double-dummy trial in patients with vestibular disorders.

## Side effects

By virtue of their pharmacology, cyclizine and prochlorperazine are both central depressants and can cause impairment of performance (Benson, 2001). Consequently, the pharmaceutical data sheets for both drugs have warnings regarding their potential to interfere with the ability to drive or operate machinery safely due to their ability to cause drowsiness (BNF, 2012). Despite the fact that cyclizine is one of the older antihistamines it is considered less potent in this regard compared to others in its class (Broccatelli, 2010), however, there is considerable variability in response to this side effect which can range from slight drowsiness to deep sleep. For this reason in practice, when one drug is not effective or poorly tolerated then it is justifiable to give another drug or combination of drugs (Benson, 2001). This unwanted side-effect is also a feature of prochlorperazine especially in the elderly, and often diminishes with continued treatment of both drugs (emc, n. d.).

Cyclizine’s other more common side-effects include headache and psychomotor impairment plus antimuscarinic effects, such as urinary retention, dry mouth, blurred vision, and gastrointestinal disturbances (BNF, 2012). Less common side effects are palpitations and arrhythmias, also dizziness, hypotension, muscular weakness and poor coordination (Goodman and Gilman, 1975).

Prochlorperazine commonly causes CNS related side effect such as acute dystonia or dyskinesia, however these tend to be transitory (usually occur within the first 4 days of treatment) and are more common in children and young adults. Dopamine antagonists like prochlorperazine can also cause extrapyramidal effects, QT prolongation and even severe hypotension, especially in the elderly (emc, n. d.). Muscle spasms and restlessness are other reported side effects.

## Interactions

Cyclizine exhibits pharmacological interactions with other drugs due to antagonism of its action (donepezil, galantamine, rivastigmine) or enhanced anticholinergic actions (tacrine, trimethobenzamine, triprolidine, trospium). Pharmacokinetic interactions may arise since cyclizine is an inhibitor of the hepatic CYP 2C9 isozyme system, which is involved in an NADPH-dependent electron transport pathway. This isozyme oxidizes a variety of structurally unrelated compounds, including steroids, fatty acids, and xenobiotics and contributes to the wide pharmacokinetics variability of the metabolism of drugs such as S-warfarin, diclofenac, phenytoin, tolbutamide and losartan. Pethidine and propanidid are also listed as having a potential to interact with cyclizine. Cyclizine also acts as an inhibitor of estrogen sulfotransferase, the enzyme responsible for estradiol metabolism.

Prochloperazine has a plethora of interactions, both pharmacological and pharmacokinetic. The pharmacokinetic interactions are largely due to competitive metabolic interactions at the hepatic CYP 3A4 and CYP 2D6 enzymes. The CYP 3A4 isozymes are responsible for a variety of oxidation reactions e. g. caffeine 8-oxidation, omeprazole sulphoxidation, midazolam 1′-hydroxylation and midazolam 4- hydroxylation, plus metabolism of structurally unrelated compounds, including steroids, fatty acids, and many other xenobiotics. Whilst the CYP 2D6 isozymes are responsible for the metabolism of many drugs and environmental chemicals, via oxidative transformation along with metabolism of drugs such as antiarrhythmics, adrenoceptor antagonists, and tricyclic antidepressants.[9]Consequently, the data sheet for prochlorperazine lists many drugs with interaction potential including adrenaline, amphetamine, carbamazepine, clonidine, desferrioxamine, guanethidine, levodopa, lithium, phenobarbital and propranolol.

## Managing Drug Therapy

When managing the care of a patient, nursing staff must initially thoroughly assess the patient, then identify significant interactions between core drug knowledge (PD, PK, ADRs, interactions, contraindications) and the patient’s core variables (health status, age and gender, life-style and diet, environments, culture). Thereafter the nurse can plan and implement suitable interventions, which will maximise therapeutic effects whilst minimising adverse effects (Aschenbrenner and Venable, 2008). In order to achieve such objectives the nurse should ensure administration of the appropriate medication is given through a suitable route on a regular basis or as required, with ongoing patient evaluation and monitoring.

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## Administration Precautions

Due to its centrally acting effects, patients taking cyclizine should avoid alcohol and other depressants e. g. hypnotics or tranquillisers. Food may reduce irritation to cyclizine and since there is no interaction with food, this drug can be taken without regard to meals. The datasheet indicates it should be used with caution in hepatic disease, whilst in renal impairment there is a need for dose reduction (BNF, 2012). Cyclizine should also be used with caution in patients with severe heart failure. Other anticholinergic effects include visual disturbances, and sedation, which can make them dangerous for the elderly population or younger patients. Further, cardiovascular side effects e. g. hypotension, tachycardia, and palpitations have been reported, plus minor GI effect e. g. dry mouth and constipation. Cyclizine has a well-known abuse potential (Ruben et al. 2006). In opiate dependents receiving long-term methadone cyclizine is often taken in large doses intravenously to provide a more intense high. Thereafter the addict experiences depressive mood changes and a craving for cyclizine. Many individuals receiving long-term prescriptions of oral methadone have been identified as being habitual abusers of cyclizine.[11]Consequently, there is considerable reticence by pharmacists in prescribing the drug, and alternative treatments are generally sought. Obviously in the hospital setting there is little opportunity for such abuse, and the efficacy and cost-effectiveness of the drug would therefore take precedence over its abuse potential (Barber, 1995; Philips and Thompson, 1997).

Although prochlorperazine being an antipsychotic phenothiazine drug can be employed in psychiatry, in lower doses it is usually prescribed for its anti-emetic properties. Patients taking the drug should take with a full glass of water, avoid excessive quantities of coffee or tea (containing caffeine) and also avoid alcohol. Prochlorperazine should be used with caution in patients with renal and hepatic impairment and cardiovascular disease; also in Parkinson’s disease, epilepsy and in patients with a history of glaucoma. While the drug does not deliver the euphoria that is associated with many commonly abused drugs, it still has some abuse potential since it can alter mood and perception, but not to the extent of cyclizine. Moreover, dependence and tolerance can develop, which can drive the individual to continue to seek more of the drug[12]and result in overdose, characterised by symptoms of central nervous system depression to the point of somnolence or coma. Agitation and restlessness may also occur in overdose. Other possible manifestations include convulsions, EKG changes and cardiac arrhythmias, fever and autonomic reactions such as hypotension, dry mouth and ileus.

## Managing Drug Therapy

Nausea and Vertigo: In emetic patients, antiemetics should only be prescribed when the underlying cause is known, indeed antiemetic administration may be harmful when the cause can be treated, e. g. in diabetic ketoacidosis or digoxin/antiepileptic overdose. In addition to motion sickness cyclizine can be given to patients with nausea caused by mechanical bowel obstruction and raised intracranial pressure.[13]Once a decision has been made that antiemetic drug treatment is appropriate, the drug and the dosage form should be chosen according to the aetiology of vomiting along with core drug knowledge and patient variables. Thus prochloperazine is useful for episodes of more severe nausea and vomiting e. g. associated with diffuse neoplastic disease, radiation sickness, and the emesis caused by drugs such as opioids, general anaesthetics, and cytotoxics. Indeed, prophylactic use may be required if severe nausea is anticipated such as following chemotherapy treatment. (Aschenbrenner and Venable, 2008). Prochorperazine may be a suitable choice because of its dosage forms, thus rectal suppositories can be useful in patients with persistent vomiting or with severe nausea and the buccal tablet dosage form is also useful in such instances. However, during use of phenothiazines it is important to monitor severe dystonic reactions, especially in children. It is recommended as a second-line treatment for vomiting in pregnancy after promethazine.[14]

Whereas the efficacy of cyclizine in treating nausea and vomiting has already been unequivocally proven, it is only available in tablet and injectable form. Nevertheless, cyclizine may be the choice of drug over prochlorperazine in children since in this patient population the latter can only be administered orally (BNF, 2012), and therefore requires patient compliance for success.

There is no evidence that either of the two drugs is superior to the other in terms of efficacy; also despite cyclizine’s longer plasma half-life compared with prochlorperazine, the duration of action is similar at around 4 hours. The adverse event profiles do however differ slightly, because of the differing underlying pharmacology of these two drugs. This is an important consideration in the choice of drug, alongside special precautions which, as described earlier, must be considered in conjunction with patients’ co-morbidities. It is also noteworthy that educating patients and their families regarding the drug of choice is important; for example warning patients against consuming alcohol with both prochlorperazine and cyclizine and warning patients against driving or operating machinery if susceptible to drowsiness with either drug.

In summary, both cyclizine and prochloperazine have similar safety, tolerability and toxicity profiles despite their differing modes of action on a cellular level. Tolerability in terms of drowsiness is a potential problem for both drugs, but is generally dependent upon the individual patient’s susceptibility, warranting a trial and error type approach when determining which is the optimal drug of choice. Also, due to the drugs both being substrates of CYP 2D6 their phamacokinetic profiles may exhibit inter-subject variability by virtue of the different phenotypes of this enzyme which exist in the population. This differing pharmacokinetic profile would logically translate into a varied response in terms of therapeutic effects. Likewise, their potential to interact with other drugs is inextricably linked with their metabolism, namely metabolic competition at the cytochrome P450 enzyme receptor sites. Thus both drugs have the potential to interact with a wide range of other medications. Moreover, since both drugs are extensively metabolised in the liver, with excretion of metabolites in the urine, there is a need for caution in renal and hepatic disease. Cyclizine and prochlorperazine appear to be similarly efficacious with regard to their treatment of emesis caused by motion sickness. The literature is inconclusive regarding which drug would be more superior for PONV, or vertigo, and even though it has been suggested that prochlorperazine should be chosen over cyclizine when the nausea is severe, there does not seem to be any compelling evidence for this and many hospitals tend to choose cyclizine over prochlorperazine in their antiemetic protocols/guidelines. The most compelling evidence for choosing prochlorperazine over cyclizine in the primary care setting would be the high abuse potential with cyclizine. However, in the secondary care setting this is of minimal concern. Therefore a more compelling reason for choosing prochlorperazine over cyclizine in this setting might largely hinge on the greater flexibility in formulations available for prochlorperazine. Whereas both drugs can be given orally as a tablet, when patients are vomiting this may be inappropriate. The buccal tablet or rectal suppository, which is available for prochlorperazine, and is less invasive than an injection formulation may be more acceptable to many patients in such cases.

To conclude, the present essay has demonstrated that the nursing process for effectively dealing with emesis is challenging and complex. Here we have witnessed the plethora of facts which the nurse must take into account prior to prescribing the antiemetic drugs cyclizine and prochlorperazine, and that even after attempting to optimise drug selection on the basis of such facts, success cannot be guaranteed. Ongoing monitoring of patient response/progress with the possibility of altering or augmenting the chosen drug therapy is necessary to improve outcomes, ensure patients receive optimal care, and that they enjoy maximal therapeutic success with minimal side effects.

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