

Wyoming Drug Utilization Review

Antiemetics

Janette Collins, PharmD

Nausea and vomiting (NV) is an unpleasant symptom related to many underlying causes including vertigo, motion sickness, pregnancy, gastroenteritis, postoperative surgical procedures, migraines and chemotherapy treatment. Often resolving the underlying cause will alleviate the symptoms of NV.¹

Anticholinergics, antihistamines, dopamine receptor antagonists, serotonin antagonists, neurokinin -1 receptor antagonists, corticosteroids, cannabinoids and, in select cases, herbals and vitamins are antiemetics commonly prescribed to treat NV.¹ Antiemetic drugs are classified by their primary action and several of these drugs demonstrate affinity for more than one receptor site, allowing for broader treatment coverage for different types of NV. If significant drug interactions or adverse effects occur during therapy, it is recommended to discontinue the antiemetic and switch to another class when possible.¹

Anticholinergics: Anticholinergics work on the muscarinic receptors and are commonly used for the treatment of vertigo and motion sickness.¹ Scopolamine (TransDerm Scop) is the most commonly used anticholinergic. Side effects include dry mouth, drowsiness, urinary retention and vision disturbances. It is contraindicated in patients with narrow angle glaucoma. Caution should be used in patients with impaired liver or kidney functions, pyloric

obstruction or urinary bladder neck obstruction and the elderly. Kidney and liver function should be monitored.^{2,3}

Antihistamines: Antihistamines bind histamine and muscarinic receptors. The following are commonly recommended for treatment of vestibular nausea: diphenhydramine (Benadryl), dimenhydrinate (Dramamine), meclizine (Antivert) and doxylamine (Unisom, Aldex AN).¹ Side effects include dry mouth, urinary retention, drowsiness and vision disturbances. Use with caution in patients with asthma, emphysema, chronic bronchitis, glaucoma, or enlargement of the prostate gland. Monitor breathing, urine output and vision changes.^{2,3}

Dopamine receptor antagonists: Dopamine agonists target D2-dopamine, muscarinic and histamine receptor site and include phenothiazines, butyrophenones, and benzamides.¹

Phenothiazines include prochlorperazine (Compazine), chlorpromazine (Thorazine) and promethazine (Phenergan). Common side effects of phenothiazines are orthostatic hypotension, xerostomia and drug-induced tardive dystonia. Rare but severe side effects are prolonged QT interval, torsade de pointes and neuroleptic malignant syndrome. They are contraindicated in patients receiving large amounts of CNS depressants. Drug interactions include CNS depressants, anticoagulants and antiseizure meds.^{2,3} Monitor for sedation, clotting and seizures.

Droperidol (Inapsine), a butyrophenone, is a short-acting tranquilizer used for postoperative NV.¹ Butyrophenones exhibit a similar side effect profile and antiemetic efficacy as the phenothiazines. Droperidol is contraindicated in patients with known or suspected QT prolongation. Possible interactions can occur between droperidol and drugs that have a potential for QT prolongation.^{2,3} Monitor for heart rate, blood pressure and sedation.

Metoclopramide (Reglan) is a benzamide that works on central and peripheral dopamine D2 receptors at low doses, and higher doses cause serotonin antagonism. Metoclopramide can freely cross the blood-brain barrier which can lead to neurological side effects.¹ Common side effects are fluid retention, constipation, dystonia, drowsiness and restlessness. Rare severe side effects

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P & T Committee Meeting Update

The P&T Committee met for its bimonthly business meeting on November 18, 2010. Highlights of this meeting include:

Maria Kidner, DNP, FNP-BC, APRN accepted the open position on the Committee. She will fill the position vacated by Joe Farrell, PAC.

Issues have been identified with billing of compound drugs. Information will be sent to pharmacies detailing the correct way to bill these products and pharmacies will be given until February 1, 2011 to comply. Failure to comply after this date may result in recovery of paid amounts.

The following criteria were approved:

Silenor: 30-day trial of preferred insomnia agent and 30-day trial of liquid doxepin, followed by manual prior authorization and justification for use of Silenor.

Tobradex ST: 5 day trial and failure of Tobradex, followed by manual prior authorization and justification for use of Tobradex ST.

Pradaxa: Approve for patients with atrial fibrillation and relative contraindications to warfarin.

Aricept: Approve for patients with dementia. All other diagnoses will require prior authorization.

Welchol: 6 month trial and failure of each unique preferred agent.

Altanax: 7 day trial and failure of two preferred agents in the previous three months.

Topical corticosteroids: 2 week trial and failure of all generics of similar potency in the previous three months.

Gilenya: Non-preferred MS agent. Trial and failure of an interferon, Copaxone and Tysabri, or an inability to use Tysabri.

Epogen: Procrit is preferred. Manual prior authorization required with justification for use of Epogen as it is the same product.

The Cymbalta criteria will be modified to allow use for chronic pain associated with osteoarthritis of the knee.

The 2011 Preferred Drug List has been drafted and is available for review on the DUR website (www.uwyo.edu/DUR).

All proposed prior authorization criteria will be posted for public comment at www.uwyo.edu/DUR. Comments may be sent by email to alewis13@uwyo.edu or by mail to: Wyoming Drug Utilization Review Board, Dept. 3375, 1000 E. University Avenue, Laramie, WY 82071. Comments should be received prior to January 3, 2011.

The next P&T Committee meeting will be held February 17, 2011 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

The DUR offices will be closed December 20, 2010 through January 3, 2011.

2011 P & T Committee Meeting Dates

February 17, 2011
May 19, 2011
August 18, 2011
November 17, 2011

Meeting time:
9 am - 3 pm

Location:
Laramie County Community College
Cheyenne

All meeting dates and times are subject to change.

Antiemetics continued

include cardiac dysrhythmia (reversible) and neuroleptic malignant syndrome. Metoclopramide is contraindicated in patients with seizure disorders and with other drugs that cause extrapyramidal effects. Drug interactions include anticholinergic drugs, narcotic analgesics, alcohol, sedatives, hypnotics, tranquilizers and monoamine oxidase inhibitors. Monitor for hypotension, sedation and stomach pain.^{2,3}

Serotonin receptor antagonists: Serotonin antagonists affect 5HT₃ receptors and have a broad range of treatment coverage for NV.¹ The serotonin antagonists available are ondansetron (Zofran), granisetron (Kytril), dolasetron (Anzemet), and palonosetron (Aloxi). The more common side effects consist of headache, asthenia, constipation and dizziness. Rare but serious side effects consist of bronchospasm and anaphylaxis. Contraindications include medications that can cause QT prolongation.^{2,3}

Neurokinin-1 receptor antagonists: NK-1 antagonists bind NK-1 receptors and are used in the treatment of chemo-induced nausea and vomiting (CINV) and postoperative NV. Available drugs are aprepitant (oral Emend) or fosaprepitant (intravenous Emend). Side effects include hypotension, pruritus, constipation, diarrhea, nausea, headache, hiccoughs, and fatigue. Rare but serious side effects are sinus tachycardia, angioedema, Stevens-Johnson syndrome, febrile neutropenia, and neutropenic sepsis. Use caution when administered with other medications that use the CYP3A4 pathway as aprepitant has an inhibitory effect on several medications. Diltiazem can increase the blood concentration levels of aprepitant when used concurrently.^{2,3,5}

Corticosteroids: Corticosteroids' mechanism of action for the treatment of NV is not clearly understood. They are commonly used for pregnancy-induced nausea and CINV. Dexamethasone (Decadron) is the most widely studied corticosteroid for NV.¹ Common side effects of corticosteroids include insomnia, increased energy, and gastrointestinal effects. Rare but serious side effects of hyperglycemia, primary adrenocortical insufficiency and glaucoma are of more concern in long term therapy (\geq 6 months).²⁻⁴ Drug interactions include anticoagulants; prothrombin time should be monitored.^{2,3,5}

Herbals and Vitamins: Studies on ginger have shown it to be beneficial for certain types of NV. Pyridoxine (Vitamin B₆) has been shown to help reduce NV in mild pregnancy-induced nausea. Side effects are minimal with both these products.¹

Treatment Recommendations:

Vertigo and motion sickness: 1st line: scopolamine, diphenhydramine, dimenhydrinate and promethazine.⁴⁻⁵

Migraine headache with nausea: 1st line- metoclopramide, prochlorperazine.

Migraine with nausea: 1st line: metoclopramide, prochlorperazine and serotonin antagonists.⁵

Pregnancy-induced nausea: Mild NV: 1st line: pyridoxine plus doxylamine; 2nd line: diphenhydramine.

Hyperemesis gravidarum: 1st line: promethazine; 2nd line: serotonin antagonists and corticosteroids.⁵

Gastroenteritis: 1st line: prochlorperazine; 2nd line: serotonin antagonist.^{5,6}

Postoperative NV: 1st line: serotonin antagonists; 2nd line: droperidol and dexamethasone.^{5,7}

CINV: 1st line: serotonin antagonists, dexamethasone and aprepitant. CINV is an extremely specialized field and there is insufficient space to thoroughly cover the proper dosing recommendations in this article.¹

Understanding and utilizing the most beneficial therapy when deciding on the appropriate antiemetic medications will increase positive therapeutic outcomes. Therefore, determining the cause of the emesis and the receptors affected is the first step toward choosing the therapy which will result in improved efficacy.

References

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