



Therapeutic brief

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PROCHLORPERAZINE: A new look at an old drug

Prochlorperazine (Stemetil®, Stemizine®) is an antipsychotic medication frequently used in the treatment of dizziness and nausea. Evidence suggests it may be being initiated as part of a *prescribing cascade*.

Adverse drug reactions (ADRs) can be a serious consequence of prescribing any medication and new symptoms should be considered drug-related until proven otherwise. Drug-induced symptoms in an older person are often mistaken for a new disease or attributed to ageing. Prescribing cascades occur as a new drug is prescribed to treat symptoms arising from the unrecognised adverse effect. The patient is then at risk of developing additional ADRs related to the new and unnecessary treatment.

Veterans, who have many co-morbidities and multiple drug therapies, are at particular risk for prescribing cascades. Analysis of the DVA database indicates that prescribing certain drugs - including metformin, NSAIDs, statins and calcium channel blockers - is associated with a subsequent prescription for prochlorperazine (see page 3).¹

This module asks doctors to first consider 'Is this drug-induced?' when assessing their veteran patients with dizziness or nausea. It also aims to clarify the risks associated with long-term use of prochlorperazine, in particular the development of permanent tardive dyskinesia or the initiation of further prescribing resulting from prochlorperazine-induced Parkinsonism.

Key points

- ✓ Consider 'Is this drug-induced?' when assessing patients with dizziness or nausea.
- ✓ Avoid long-term use of prochlorperazine; short-term use may be appropriate.

Dizziness

Dizziness is a general term which means different things to different people. It is a well recognised problem among the older population and evaluation can be challenging due to a wide range of possible diagnoses. The reported prevalence varies depending on the definition used but has been estimated at 47% of men and 61% of women aged over 70 years.² The natural decline in vision and visual-vestibular reflexes make older adults susceptible to dizziness. However, it is not appropriate to attribute dizziness to the normal ageing process; most people will have an identifiable cause which is benign and self-limiting.

Table 1. Factors that predispose to dizziness³

Factor
Postural hypotension
Impaired balance
5 or more medications
Previous MI
Anxiety trait
Impaired hearing
Depressive symptoms



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Side effects of many drugs used in the elderly, such as postural hypotension, may compound underlying pathologies and result in dizziness. Asking 'Is this drug-induced?' and reviewing medication will identify potentially problematic drugs.

Table 2. Drugs commonly used in the elderly that may cause dizziness

Drug
Antihypertensives
Anxiolytics
Antidepressants
Anticholinergics
Acetylcholinesterase inhibitors
Antipsychotics
Anticonvulsants

Conditions causing dizziness

It is important to clarify what patients mean when they complain of dizziness. Conditions causing dizziness can be grouped as follows.⁴

Vertigo

A sensation in which the environment seems to be spinning; usually episodic, begins abruptly and often associated with nausea or vomiting.

- **Benign paroxysmal positional vertigo** – typically presents with brief episodes of vertigo associated with a change in head position often while turning in bed. Most cases remit spontaneously.
Treatment: repositioning manoeuvres e.g. Epley manoeuvre, Brandt-Daroff exercises.
- **Acute labyrinthitis** – characterised by sudden onset of severe vertigo and often nausea/vomiting; probably viral in origin.
Treatment: short term anti-emetics.
- **Meniere's disease** – characterised by paroxysmal vertigo lasting minutes to hours plus hearing loss, tinnitus, nausea and vomiting.
Treatment: lifestyle modifications, intermittent anti-emetics/vestibular suppressants/diuretics.
- **Vertebrobasilar insufficiency** – atherosclerotic disease of the vertebral and basilar arteries which may be compounded by compression from cervical vertebrae during head turning/extension results in acute vertigo, often with focal neurological effects.
Treatment: control risk factors for atherosclerosis, antiplatelet drugs.

Presyncope

Usually described as a sensation of impending faint or loss of consciousness.

- **Postural hypotension** – can result from medications or autonomic dysfunction.
Treatment: address underlying cause; reduce or withdraw medication if possible.
- **Vasovagal attacks** – parasympathetic hyperactivity causes a decrease in cardiac output leading to a reduction in cerebral perfusion; can be caused by swallowing, defaecation, micturition and pain.
Treatment: address underlying cause.
- **Decreased cardiac output** – results from any cardiac condition causing impaired cardiac output e.g. heart failure, MI, aortic stenosis.
Treatment: address underlying cause.

Dysequilibrium

Characterised by unsteadiness or imbalance when standing which disappears when lying down.

- **Vestibular loss** – occurs with slow unilateral or bilateral vestibular loss; can be caused by ototoxic drug exposure especially with renal impairment.
Treatment: medication review, address underlying cause; vestibular rehabilitation may be helpful.
- **Proprioceptive and somatosensory loss** – can occur with peripheral neuropathy; osteoarthritis of the cervical spine may lead to proprioceptive disturbance.
Treatment: address underlying cause, employ fall prevention strategies and gait re-training.
- **Parkinsonism including Parkinson's disease** – due to the disease or treatments, disturbance of posture and motor control often results in dysequilibrium.
Treatment: ensure not drug-induced Parkinsonism by reviewing medication; vestibular rehabilitation exercises and physiotherapy may help reverse deconditioning.
- **Multiple neurosensory impairments** – results from impairment of one or more systems used in postural control, such that other systems are unable to compensate; common abnormalities include visual impairment, physical deconditioning and medication side effects. It is a diagnosis of exclusion.
Treatment: medication review, targeted strategies such as vision correction and strength/balance training.

Up to 15% of patients presenting with dizziness will have an underlying psychiatric disorder such as anxiety and the exact cause of dizziness remains uncertain in approximately 10% of people.⁵

Nausea

Nausea is a non-specific symptom with diverse aetiology. The sensation of nausea can be caused by drugs, toxins, hypoxia, uraemia and acidosis. Higher CNS centres can be stimulated by sights, smells or emotions. Chronic nausea can be a clinical challenge because of diagnostic difficulty and symptom control. The main factor influencing drug choice is the underlying cause of nausea or vomiting.

Table 3. Causes* of nausea and vomiting⁶

Cause
Drugs (see table 4)
Alcohol
Infections - GI or non GI such as meningitis, pneumonia
Endocrine e.g. uraemia, Addison's disease
Cardiac e.g. heart failure, myocardial ischaemia
GI disorders e.g. Gastro-oesophageal reflux disease , peptic ulcer, hepatitis, GI malignancies, inflammatory bowel disease
CNS e.g. migraine, raised intracranial pressure
Labyrinthine e.g. Meniere's disease
Psychiatric illness e.g. anxiety, depression
Hypercalcaemia
Organ failure
Motion sickness

*Causes of nausea and vomiting which are commonly missed are highlighted.

Adverse drug reactions are such a common cause of nausea that it is vital to take a drug history (including complementary and alternative medicines) and ask 'Is this drug-induced?' to avoid a prescribing cascade. In many cases drug-induced nausea is self limiting but with certain drugs it may be an indication of dose-related toxicity requiring dose adjustment (e.g. digoxin, lithium, SSRIs).

Table 4. Drugs commonly used in the elderly that may cause nausea

Drug
Cardiovascular medications (including antihypertensives, antiarrhythmics and diuretics)
Analgesics (including anti-inflammatories)
Antithrombotic agents
Antidepressants
Oral hypoglycaemics
Antibiotics
Acetylcholinesterase inhibitors

Prochlorperazine

Prochlorperazine (Stemetil[®], Stemizine[®]) is a piperazine phenothiazine antipsychotic which blocks dopamine receptors in the brain including the chemoreceptor trigger zone. Other drugs in this class include Fluphenazine (Modecate[®]) and Trifluoperazine (Stelazine[®]). All have a propensity to cause extrapyramidal side effects with 'moderate frequency'; that is an incidence of greater than 10%.⁷ Therapeutic Guidelines state that long-term symptomatic treatment of chronic dizziness or vertigo with prochlorperazine is 'not good practice' and that 'the long term efficacy of any drug in the prevention of recurrent vertigo is unproven'.⁷

Prochlorperazine is often initiated to treat unrecognised side effects of another drug.

Risk* of receiving a prochlorperazine script is raised by:

- 50% after initiation of a statin
- 40% after initiation of an NSAID
- Between 20 – 30% after initiation of a bisphosphonate, sulphonamide, metformin, calcium channel blocker, opioid, ACE inhibitor or angiotensin 2 antagonist

*Sourced from prescription symmetry analysis. DVA database June 2009.

The Adverse Drug Reactions Advisory Committee (ADRAC) currently holds details of over 1,000 adverse reactions related to the use of prochlorperazine.^{8,9} These include acute dystonic reactions, more prevalent in younger adults and children, and other extrapyramidal disorders such as Parkinsonism and tardive dyskinesia, which are more likely to affect older patients.

Prochlorperazine should not be used in patients with known Parkinson's disease.

The risk of adverse drug effects from prochlorperazine, including sedation and falls, is increased by the concurrent administration of another antipsychotic medication.

Drug-induced Parkinsonism

Studies have shown all-cause Parkinsonism to be very common among those over 65 years and its prevalence increases markedly with age: 14.9% in those 65–74 years, 29.5% in those 75–84 years and 52.4% in those 85 years and older.¹⁰

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The clinical features of idiopathic Parkinson's disease and drug-induced Parkinsonism (DIP) are very similar; as a result DIP is frequently missed in clinical practice.¹¹ One study showed patients on antipsychotics were 5.4 times more likely than controls to be initiated on treatment for Parkinson's disease within 90 days of starting their antipsychotic medication and 70% of these patients were left on the antipsychotic.¹²

DIP typically occurs in elderly patients treated with dopamine receptor blockers (such as prochlorperazine, metoclopramide, haloperidol or risperidone) and may account for up to 20% of Parkinsonism cases in a community setting.¹³ Women are more commonly affected than men and the presence of dementia is a risk factor for the development of DIP with antipsychotic medications like prochlorperazine.¹⁴

Once DIP is recognised, discontinuation of the dopamine receptor blocker usually leads to recovery over weeks to months.

Tardive dyskinesia

Tardive dyskinesia (TD) is characterised by involuntary movements of the face, mouth or tongue, and sometimes the head, neck, trunk or limbs. It typically occurs after long-term use of dopamine receptor blocking agents such as prochlorperazine, metoclopramide and antipsychotic drugs; up to one third of people treated for 10 years with conventional antipsychotics will

develop TD.^{15,16} Total cumulative drug exposure is an important factor but TD can develop after relatively brief treatment periods at low doses or with sudden cessation of treatment.^{17,18} Newer antipsychotic drugs can also cause TD. Risk factors for the development of TD include increasing age, female gender and dementia.

There is no known effective treatment for TD.

Practice points

- ✓ Patients may be reluctant to volunteer information about medications from alternative healthcare providers or excessive alcohol intake and may need to be asked directly.
- ✓ When any medication is ceased, monitor for recurrence of original symptoms.
- ✓ Consider a Home Medicines Review (HMR) / Residential Medication Management Review (RMMR) to help identify prescribing cascades.

For further information

More information regarding therapeutic options in the management of nausea and vertigo can be found in the Australian Medicines Handbook 2010¹⁶ and Therapeutic Guidelines⁷.

References

1. Veteran's Datamart, University of South Australia, QUMPRC. Accessed June 2009
2. Eaton, D and Roland PS. Dizziness in the older adult, part 1. Evaluation and treatment strategies. *Geriatrics* April 2003, Vol 58, no.4
3. Tinetti Mary E, Williams CS and Gill TM. Dizziness among Older Adults: A Possible Geriatric Syndrome. *Ann Intern Med.* 2000;132: 337-344
4. Eaton, D and Roland PS. Dizziness in the older adult, part 2. Treatments for the causes of the four most common symptoms. *Geriatrics* April 2003, Vol 58, no.4
5. Branch WT et al. Approach to the patient with dizziness. Literature review May 2009. www.uptodate.com Viewed September 7 2009
6. Duggan, A and Al-Sohaily, S. How to treat: Nausea. *Australian Doctor* 23 March 2007
7. Acute vertigo and recurrent vertigo [revised 2007 Jan]. In: eTG complete [CD-ROM]. Melbourne: Therapeutic Guidelines Limited; 2009 July.
8. ADRAC Summary for prochlorperazine. Adverse Drug Reactions Advisory Committee, www.tga.gov.au Viewed September 17 2009
9. ADRAC Case line listing for prochlorperazine, 2000-2009. Adverse Drug Reactions Committee, www.tga.gov.au Viewed September 17 2009
10. Bennett, DA et al. Prevalence of parkinsonian signs and associated mortality in a community population of older people. *NEJM* 1996, Vol.334, No.2: 71-76
11. Stephen PJ and Williamson J. Drug-induced Parkinsonism in the Elderly. *The Lancet* Nov 10, 1984.
12. Esper, CD and Factor, SA. Failure of recognition of Drug-Induced Parkinsonism in the Elderly. *Movement Disorders*, Vol.23, NO.3, 2008, 401-404
13. Wenning, GK et al. Prevalence of movement disorders in men and women aged 50-89 years (Bruneck Study cohort): a population-based study. *Lancet Neurol* 2005; 4: 815-820
14. Tison, F et al. Parkinsonism and exposure to neuroleptic drugs in elderly people living in institutions. *Clinical Neuropharm* 1999, Vol.22, No.1: 5-10
15. Kenney, C et al. Metoclopramide, an increasingly recognised cause of Tardive Dyskinesia. *J Clin Pharmacol* 2008; 48: 379-384
16. Australian Medicines Handbook, Adelaide: Australian Medicines Handbook Pty Ltd 2010
17. MIMS Prescribing Information for Stemetil. www.mims.com.au Viewed September 7 2009.
18. Alberts VA, Catalano G and Poole M. Tardive Dyskinesia as a result of Long-Term Prochlorperazine Use. *Southern Medical Journal*, Oct 1996, Vol.89, No.10, 989-991