



Therapeutic Brief

39

www.veteransmates.net.au

Topic 39: Thinking clearly about the anticholinergic burden

Older people can be particularly sensitive to the anticholinergic effects of medicines.¹ Adverse effects may arise from an individual anticholinergic medicine, and from the cumulative effects of multiple medicines with varying degrees of anticholinergic properties.²⁻⁴

The anticholinergic burden may be unintentionally increased by medicines prescribed with other mechanisms of action intended, but also having anticholinergic effects, such as antihistamines, tricyclic antidepressants and antipsychotics.² In addition, medicines not typically thought of as having anticholinergic effects, such as citalopram, mirtazapine and metoclopramide, when added to other strongly anticholinergic medicines, may tip the balance of the cumulative anticholinergic burden and result in significant adverse effects.^{2,4,5}

Older Australians commonly use medicines with anticholinergic effects; at any point in time 21-33% of Australians aged over 60 years use at least one medicine with anticholinergic effects.⁶⁻⁸ A cumulative anticholinergic burden in older people with co-morbidities who are taking multiple medicines is associated with an increased risk of confusion, cognitive and physical decline, delirium, hospitalisation and death.^{2,3,9-11}

This therapeutic brief provides information on anticholinergic adverse effects and outlines steps to take to reduce the anticholinergic burden.

Inside

- 2 Ask yourself and your patient: What are the adverse effects and potential outcomes?
- 3 Ask: What is the burden?
- 4 Ask: Can the burden be reduced?
- Insert – Potential strategies to reduce the anticholinergic burden

Key points

- Medicines that contribute to an anticholinergic burden are medicines:
 - prescribed for their anticholinergic effects
 - prescribed with other mechanisms of action intended but also having anticholinergic effects, and
 - not typically thought of as having anticholinergic effects.
- A high anticholinergic burden in older people is associated with an increased risk of cognitive decline.
- Be alert to anticholinergic adverse effects in your older patient.
- Consider reducing the anticholinergic burden where possible.



✓ Ask yourself and your patient: What are the adverse effects and potential outcomes?

Anticholinergic adverse effects may be subtle or severe (see Figure 1). In older people, the effects may be overlooked and considered part of the natural ageing process or attributed to the progression of underlying disease.^{1, 5} Consequences of blurred vision, dizziness or memory loss from an anticholinergic burden may include loss of independence, falls or motor vehicle accidents.^{1, 12} Acute confusion or delirium may result in hospitalisation, functional and cognitive decline or aged care facility placement.^{13, 14}

Be alert to possible anticholinergic adverse effects in your older patient, as the anticholinergic load differs between medicines, and individuals differ in their ability to tolerate them.⁴

Consider that any worsening of chronic conditions, new symptoms or adverse events may be the result of medicines with anticholinergic effects, especially if they occur after changes in the medicine regimen.^{4, 13}

Avoid treating adverse effects with medicines.¹³

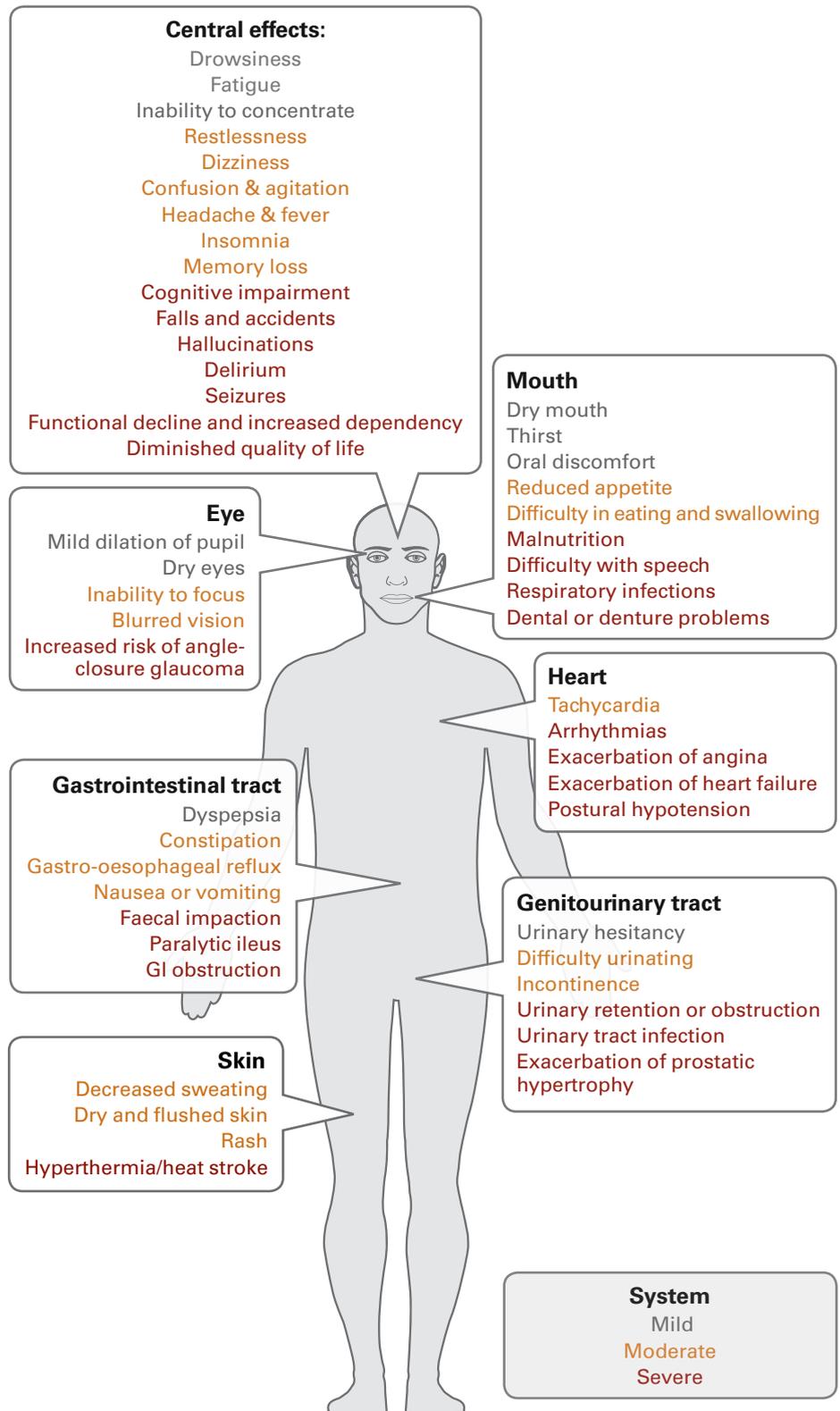


Figure 1: Anticholinergic adverse effects and potential outcomes^{2, 12, 13, 15}

✓ Ask: What is the burden?

While exact quantification of a medicine's anticholinergic effect is difficult,¹⁶ it is estimated one medicine with strong anticholinergic effects is likely to cause two or more anticholinergic adverse effects in more than 70% of older patients.¹⁷ Additionally, older patients prescribed two or more anticholinergic medicines are at a significantly increased risk of hospitalisation for confusion or dementia.¹⁰ Table 1 lists some of the commonly used medicines with anticholinergic effects in older veterans.

Individual pharmacokinetic and pharmacodynamic variability, the number of medicines, dosages prescribed, drug interactions, and prevalence and severity of co-morbidities may also influence cumulative anticholinergic burden and severity of adverse effects.^{4, 18}

The increase in the number of medicines, including prescribed and self-prescribed over the counter medicines used by many older people, may contribute to an unintended high anticholinergic burden.^{2, 3, 11} Herbal preparations such as knotweed (*polygonum aviculare*) as well as over the counter medicines for coughs and colds, antihistamines, travel sickness products and antidiarrhoeals may have anticholinergic properties.⁴

Ask your patient specific questions about self-prescribed medicines they may be taking.

Anticholinesterases and anticholinergic medicines

Where possible avoid using anticholinesterases, such as:

- donepezil
 - galantamine
 - rivastigmine
 - pyridostigmine
- with anticholinergic medicines; anticholinergic medicines antagonise the therapeutic effect of anticholinesterases.⁴

Be alert to the cholinergic effects of anticholinesterases. Avoid prescribing anticholinergic medicines to compensate for the cholinergic effects of anticholinesterases. If an anticholinergic medicine is prescribed, and you stop the anticholinesterase, the effects of the anticholinergic medicine may be magnified.¹²

Table 1: Commonly used medicines with anticholinergic effects in older veterans^{12, 16}

	Antipsychotics	Antidepressants	Bladder antispasmodics	Antihistamines	Opioids	Inhaled medicines	Other medicines
Higher anticholinergic effects	chlorpromazine clozapine trifluoperazine	amitriptyline clomipramine dothiepin doxepin imipramine nortriptyline	darifenacin* oxybutynin propantheline solifenacin* tolterodine*	cyproheptadine promethazine	tapentadol	acridinium glycopyrronium ipratropium tiotropium	benztropine homatropine
Lower anticholinergic effects	haloperidol lithium carbonate olanzapine prochlorperazine quetiapine risperidone	citalopram fluoxetine fluvoxamine mirtazapine paroxetine		cetirizine fexofenadine loratadine	codeine fentanyl methadone morphine oxycodone tramadol		alprazolam amantadine baclofen carbamazepine clonazepam colchicine diazepam digoxin disopyramide domperidone entacapone frusemide loperamide metoclopramide ranitidine temazepam theophylline

Note: The list of medicines is based on Duran et al.'s 2013 Systematic review of anticholinergic risk scales in older adults (reviewing 7 studies, one of which was Australian), the Australian Medicines Handbook, Martindale: The Complete Drug Reference and expert opinion.

Note: *these medicines are not available on the PBS/RPBS



Ask: Can the burden be reduced?

Step 1: Assess your patient for adverse effects

Assess your patient for anticholinergic symptoms including dry mouth, constipation, blurred vision, increased heart rate, heat intolerance, sedation and mild confusion or memory loss. In your older patient, these symptoms can develop into serious problems (see Figure 1).¹

Step 2: Review your patient's medicines

Identify medicines to consider ceasing or substituting: target medicines of lesser benefit to your patient.¹⁹ Assess whether your patient is taking their medicines as prescribed, potential adverse effects, such as risk of falls and cognitive decline, indications, time of benefit and interactions.²⁰ Consider recommending a Medicines Review (HMR or RMMR) by an accredited pharmacist. Ask the pharmacist to specifically consider the anticholinergic burden. Consider consulting the opinion of a geriatrician in difficult cases.

Step 3: If problematic, ask the question: is a medicine essential?

If a medicine is not essential, can it be ceased? Ceasing a medicine with anticholinergic effects may not always be possible. Consider, in consultation with your patient, their goals and expectations, co-morbidities and individual preferences when making a decision.^{4, 19}

Once you have confirmed the medicines to be ceased and a plan has been developed with your patient, begin by ceasing one medicine at a time. Monitor your patient closely and gradually taper the medicine.¹⁹ Talk to your patient about possible withdrawal effects, such as anxiety, nausea, vomiting, headache and dizziness. Advise your patient to talk to you if any of these symptoms worry them.²¹

If a medicine is essential, ask these questions:

- **Is there a safer alternative treatment option? (see Insert)**
- **If not, can the dose, frequency or duration of the medicine be reduced?**

When a medicine with anticholinergic effects is essential and the dose, frequency or duration cannot be reduced, advise your patient of non-pharmacological measures to minimise the impact of adverse effects. Examples include artificial tears for dry eyes and increased water intake and a high fibre diet for constipation.⁵

References

1. Feinberg M. The problems of anticholinergic adverse effects in older patients. *Drugs and Aging*. 1993;3(4):335-348.
2. Tune L. Anticholinergic effects of medication in elderly patients. *Journal of Clinical Psychiatry*. 2001;62(suppl 21):11-14.
3. Campbell N. et al. The cognitive impact of anticholinergics: a clinical review. *Clinical Interventions in Aging*. 2009;4:225-233.
4. Australian Medicines Handbook Aged Care Companion. Fourth edition, Adelaide: Australian Medicines Handbook Pty Ltd. 2014.
5. Mintzer J. & Burns A. Anticholinergic side-effects of drugs in elderly people. *Journal of The Royal Society of Medicine*. 2000;93:457-462.
6. Sittironnarit G. et al. Effects of anticholinergic drugs on cognitive function in older Australians: results from the AIBL study. *Dementia and Geriatric Cognitive Disorders*. 2011;31:173-178.
7. Gnjidic D. et al. Drug burden index and physical function in older Australian men. *British journal of clinical pharmacology*. 2009;68(1):97-105.
8. Gnjidic D. et al. A pilot randomized clinical trial utilizing the drug burden index to reduce exposure to anticholinergic and sedative medications in older people. *The Annals of Pharmacotherapy*. 2010;44:1725-1732.
9. Gnjidic D. et al. Impact of high risk drug use on hospitalization and mortality in older people with and without Alzheimer's disease: a national population cohort study. *PLOS ONE*. 2014;9(1):e83224
10. Kalisch Ellett L. et al. Multiple anticholinergic medicine use and risk of hospital admission for confusion or dementia. *National Medicines Symposium - Medicines in Health: Shaping our Future*; Brisbane: May 21-23 2014.
11. Fox C. et al. Anticholinergic medication use and cognitive impairment in the older population: the Medical Research Council Cognitive Function and Ageing study. *J Am Geriatr Soc*. 2011;59:1477-1483.
12. Australian Medicines Handbook, Adelaide: Australian Medicines Handbook Pty Ltd 2014.
13. Karimi S. et al. Anticholinergic burden: clinical implications for seniors and strategies for clinicians. *The Consultant Pharmacist*. 2012;27(8):564-582.
14. Kalisch L. et al. Prevalence of preventable medication-related hospitalizations in Australia: an opportunity to reduce harm. *International Journal for Quality in Health Care*. 2012;24(3):239-249.
15. Elliot R. & Lee C. Anticholinergic load and adverse outcomes in older people. *Australian Pharmacist*. 2009;28(11):970-975.
16. Duran C, Azermai M. & Vander Stichele R. Systematic review of anticholinergic risk scales in older adults. *European journal of clinical pharmacology*. 2013;69:1485-1496.
17. Rudolph J. et al. The anticholinergic risk scale and anticholinergic adverse effects in older persons. *Arch Intern Med*. 2008;168(5):508-513.
18. Sumukadas D. et al. Temporal trends in anticholinergic medication prescription in older people: repeated cross-sectional analysis of population prescribing data. *Age and Ageing*. 2013;0:1-7.
19. Woodward M. Deprescribing: achieving better health outcomes for older people through reducing medications. *Journal of Pharmacy Practice and Research*. 2003;33:323-328.
20. Hilmer S, Gnjidic D. & Le Couteur D. Thinking through the medication list. Appropriate prescribing and deprescribing in robust and frail older patients. *Australian Family Physician*. 2012;41(12):924-928.
21. Scott I. et al. Deciding when to stop: towards evidence-based deprescribing of drugs in older populations. *Evidence Based Medicine*. 2013;18(4):121-124.
22. eTG complete. Melbourne: Therapeutic Guidelines Limited. 2014 March. Available at: <http://online.tg.org.au/ip/desktop/index.htm> [Accessed July 2014].



Insert: Potential strategies to reduce the anticholinergic burden^{4, 12}

Urinary incontinence

- Consider potential contributing factors, such as disease or pharmacological causes.
- Consider lifestyle and physical or behavioural therapies before using medicines.
- If prescribing anticholinergics, monitor for adverse effects, especially cognitive function, and cease after 4 weeks if no improvement in urinary symptoms.
- Darifenacin and solifenacin may be less likely to cause cognitive impairment or dry mouth than oxybutynin, but may contribute to constipation.
- For further information contact the Continence Foundation of Australia at: www.continence.org.au
- See Module 26: The impact of commonly used medicines on urinary incontinence at: www.veteransmates.net.au/TB_urinaryincontinence

Depression

- Treat mild to moderate depression with psychotherapies such as cognitive behavioural therapy, mindfulness and interpersonal therapy, supportive counselling and problem-solving techniques as first line therapies where possible.
- If prescribing medicines, consider escitalopram or sertraline: they have less potential for drug interactions.
- If prescribing a tricyclic antidepressant (TCA), consider nortriptyline as there is a lower incidence of anticholinergic adverse effects than for other TCAs.²²

Behavioural and psychotic disorders including those associated with dementia

- Exclude secondary causes of behavioural disturbances such as pain, infection, faecal impaction or depression.
- Initiate behavioural therapies and changes to the environment before considering medicines.
- If antipsychotics are indicated, consider one with low anticholinergic effects such as risperidone or haloperidol. NOTE: haloperidol is for short term use only.

COPD

- Assess for and treat comorbidities commonly associated with COPD, such as cardiovascular disease, anxiety, depression and osteoporosis.
- Encourage and support smoking cessation: it is the single most effective way to improve long term outcomes and reduce mortality in COPD patients.
- Consider multidisciplinary rehabilitation programs such as exercise training, advice about nutrition and psychosocial support programs.
- Consider annual influenza vaccinations: they reduce serious illness and mortality in COPD patients.
- If prescribing anticholinergics and your patient is experiencing adverse effects, consider ipratropium before tiotropium as it may not have as many anticholinergic adverse effects.
- Avoid prescribing short and long acting anticholinergic medicines in combination as the anticholinergic effects will be magnified.
- Consider combined long acting beta2 agonists with inhaled corticosteroids to reduce exacerbations.
- See March 2017: *COPD Keeping Well this Winter* for further information at www.veteransmates.net.au/topic-46-therapeutic-brief

Allergies

- Antihistamines are effective in relieving itch due only to histamine release.
- Intranasal corticosteroids are the most effective treatment for allergic rhinitis.
- Consider loratadine or fexofenadine for chronic urticaria: they have reduced anticholinergic effects.

Pain

- Consider physical, psychological and social factors that may be contributing to pain.
- Consider non-pharmacological therapies and a multidisciplinary approach to management.
- If amitriptyline is prescribed for neuropathic pain and causing adverse effects, consider gabapentin or pregabalin instead.
- See Modules 35: Managing neuropathic pain: a stepwise approach at: www.veteransmates.net.au/TB_neuropathicpain
- See Module 38: Chronic musculoskeletal pain: Changing the way we think about pain at: www.veteransmates.net.au/TB_musculoskeletalpain