

DELIRIUM AND ANTICHOLINERGIC DRUG BURDEN

Delirium is common among older people in residential aged care and is associated with poor outcomes, such as functional and cognitive decline and increased mortality. Medicines with anticholinergic properties are commonly prescribed in older persons. However, anticholinergic medicines are a risk factor for delirium and should be used judiciously.

Delirium

Delirium or acute confusion is a serious disturbance in mental abilities that results in confused thinking and reduced awareness of the environment.

Reduced awareness of the environment may result in:

- An inability to stay focused on a topic or to switch topics
- Getting stuck on an idea rather than responding to questions or conversation
- Being easily distracted by unimportant things
- Being withdrawn, with little or no activity or little response to the environment

Behavioural changes may include hallucinations, restlessness, agitation or combative behaviour, calling out, being quiet and withdrawn, disturbed sleep habits or reversal of night-day sleep-wake cycle.

Emotional disturbances may appear as anxiety, fear, or paranoia, depression, irritability or anger, apathy, personality changes, or rapid and unpredictable mood shifts.

Delirium usually develops rapidly, within hours or a few days. It may often fluctuate throughout the day and symptoms tend to get worse during the night. Delirium prolongs hospital stays, increases the need for care and is associated with increased mortality.

Dementia and delirium may be particularly difficult to distinguish, and people may have both conditions. The onset of delirium occurs within a short time, while dementia usually begins with relatively minor symptoms that gradually worsen over time. The appearance of delirium symptoms can fluctuate significantly and frequently throughout the day.

While people with dementia have better and worse times of day, their memory and thinking skills stay at a fairly constant level during the course of a day. People with dementia are more vulnerable to medicines with anticholinergic effects.

There are many predisposing and contributing factors to delirium, including:

- Severe or chronic illness
- Changes in metabolic balance (e.g. low sodium)
- Infection
- Surgery
- Alcohol
- Drug withdrawal
- Medications

Medications associated with delirium include benzodiazepines, opioid analgesics and medications with an anticholinergic effect.

Anticholinergics

Medications with anticholinergic properties are prescribed for a range of common problems in older age, including:

- Urinary incontinence and overactive bladder
- Depression
- Parkinson's disease
- Gastrointestinal complaints

Medicines with anticholinergic effects include:

- Antidepressants (e.g. amitriptyline, doxepin, dosulepin, imipramine, nortriptyline, mianserin)
- Antipsychotics (e.g. chlorpromazine, olanzapine, clozapine)
- Inhaled bronchodilators (e.g. acclidinium, glycopyrronium, ipratropium, tiotropium, umeclidinium)
- Medicines for overactive bladder (e.g. darifenacin, oxybutynin, propantheline, solifenacin, tolterodine)
- Antiparkinsonian drugs (e.g. amantadine, benztropine, trihexyphenidyl)
- Sedating antihistamines (e.g. cyclizine, cyproheptadine, dexchlorpheniramine, diphenhydramine, dimenhydrinate, pheniramine, promethazine)
- Antispasmodics (e.g. belladonna alkaloids, atropine, hyoscine)

Tricyclic antidepressants (amitriptyline, doxepin, dosulepin, imipramine, nortriptyline) are usually not appropriate for older people.

If being used for treating neuropathic pain, nortriptyline is more appropriate as it has less anticholinergic activity.

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Some herbal preparations also have anticholinergic properties. There are many more medications (e.g. furosemide, digoxin, prednisone, warfarin, tramadol, isosorbide nitrate) with minimal anticholinergic activity which may contribute to the cumulative anticholinergic burden.

A comprehensive medication review (RMMR) will identify medicines with anticholinergic properties and provide advice for alternatives and deprescribing. Residents who develop delirium should have medicines recently started or dose increased reviewed by a pharmacist and the prescriber. Sometimes it is clear which medication is responsible for an episode of delirium because of a temporal relationship.

Anticholinergic burden

Accumulation of anticholinergic effects from one or more anticholinergic medications leads to anticholinergic burden. Anticholinergic burden is a strong predictor of cognitive and physical impairments in older people living in residential care. In addition, the use of medicines with anticholinergic properties is a strong independent predictor of mortality and an increased risk of hospitalisations. The cumulative adverse impact of multiple concurrent anticholinergic medicines is an indicator for suboptimal prescribing in older adults.

Anticholinergic side effects

Older people are more susceptible to side effects from anticholinergic medicines and adverse outcomes. Overall, inappropriate and unnecessary use of medicines with anticholinergic properties have a negative effect of quality of life and lead to poorer physical function. Blurred vision, urinary retention, and constipation are known peripheral adverse effects of anticholinergic drugs. These conditions are also risk factors for delirium.

Other anticholinergic side effects include:

- Dizziness
- Drowsiness
- Dry mouth
- Mild cognitive impairment
- Falls
- Hypotension
- Confusion
- Narrow angle glaucoma

In addition, anticholinergics may decrease sweating and cause hyperthermia.

Anticholinergics should not be prescribed with acetylcholinesterase inhibitors for dementia, including:

- Donepezil (Aricept, Aridon)
- Galantamine (Reminyl, Galantyl, Gamine XR)
- Rivastigmine (Exelon)

Deprescribing anticholinergics

If there is no alternative to use of a medicine with anticholinergic properties and the resident is experiencing cognitive symptoms such as poor memory, then reducing the dose may help to ameliorate these symptoms.

Ceasing anticholinergics should be usually considered when adverse effects are evident, and the benefits are not significant.

In general, anticholinergics should be weaned gradually by 25-50% of the daily dose every 1-4 weeks. Alternate day dosing can be used if dosage forms are limited. If the reason for deprescribing is due to serious adverse effects such as delirium or worsening confusion, faster weaning or abrupt cessation can be considered.

Withdrawal symptoms can occur within one to three days of dose reduction. Withdrawal symptoms include irritability, anxiety, insomnia, sweating and gastrointestinal effects.

They are usually mild, can be highly variable and can last up to 6-8 weeks. If severe symptoms such as severe anxiety, tachycardia, orthostatic hypotension, severe insomnia occur, the previous lowest effective dose should be restarted. Tapering can then be recommenced after 6-12 weeks at a lower weaning rate (e.g. 5-12.5% of daily dose each month) then stop.

A deprescribing guide for anticholinergic drugs for urinary incontinence is available at <https://www.nswtag.org.au/deprescribing-tools/>

Summary

Delirium is a common disorder in the geriatric population, which can manifest as a decline in cognition, attention or consciousness. Medicines with anticholinergic actions can precipitate delirium and are associated with adverse outcomes related to physical function, cognition and falls in older people. Use of anticholinergics associated with hospital admission, longer length of hospital stay, institutionalisation, and of all-cause dementia and mortality in older people. This strong association with impairment of cognitive and functional outcomes should prompt regular review of medications to identify anticholinergic medicines and provide advice on discontinuation.

References

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