Older people with dementia may be particularly susceptible to cognitive impairment associated with anticholinergic and sedative medicines. Medicines with anticholinergic and sedative properties may result in adverse events by increasing the anticholinergic and sedative load. Last month’s newsletter focussed on anticholinergic burden of one of more medicines with anticholinergic activity. This newsletter will build on that information, with a focus on the adverse effects from cumulative anticholinergic and sedative load.

**Anticholinergic side effects**

Studies have consistently associated anticholinergic adverse effects with cognitive impairment. These medicines have a limited place in people with dementia. A common drug-drug interaction is the use of cholinesterase inhibitors (donepezil, rivastigmine, galantamine) and anticholinergic medicines (e.g. oxybutynin, benztropine), resulting in loss of efficacy of both medicines.

Antipsychotics, antidepressants, medicines for urinary incontinence and antihistamines, as well as many other common medicines, have anticholinergic side effects, including:

- Confusion
- Hallucinations
- Delirium
- Dry mouth
- Pupil dilatation/blurred vision
- Urinary retention
- Constipation
- Tachycardia

**Medicines with sedative properties**

Medications with sedative effects are known to adversely affect physical and cognitive function, such as memory, psychomotor performance, falls and fractures, and postural sway.

The cumulative effect of taking one or more medicines with sedative properties is termed the ‘sedative load’. Medicines with sedative properties include:

- Benzodiazepines
- Antidepressants
- Antipsychotics
- Anticonvulsants
- Antihistamines
- Opioid analgesics

Many anticholinergic medicines also have sedative properties, for example, olanzapine or quetiapine, making older people who are using medications from both classes, and who are already at risk from polypharmacy, more vulnerable to adverse drug events and their consequences.

Medicines with sedative properties have been linked to symptoms of depression, worsening cognition, respiratory depression, impaired muscle strength, and falls and fractures.

**Concomitant use**

Anticholinergic and sedative medications are prescribed in older adults to treat medical conditions that usually occur later in life, such as urinary incontinence, sleep and pain disorders, dementia, chronic obstructive pulmonary disease (COPD), and mental health conditions.

Medicines with weak anticholinergic or sedative properties may also cause adverse events by contributing to an older person’s anticholinergic and sedative load.

**Drug Burden Index**

The Drug Burden Index (DBI) is a pharmacological risk assessment tool that measures the burden of anticholinergic and sedative medications in older adults. DBI measures the effect of dose-related cumulative exposure to both anticholinergic and sedative medications on physical and cognitive function in older adults. Studies have shown psychotropic medication prescribing is as high as 80%, and anticholinergic medicine use is at least 50%, and up to 80% in dementia-specific units in aged care facilities. So the potential for DBI to identify inappropriate prescribing in older people is significant.

The dose of each anticholinergic and sedative medication is used to determine a score from 0 to 1.
for each medicine in these classes. It has been shown that each additional unit of DBI had a negative effect on physical function similar to that of three additional physical morbidities.

Increasing DBI scores have been associated with significant functional impairment in older people. The DBI has been shown to be superior to the Beers explicit criteria in predicting functional decline, and has been associated with poorer physical and cognitive performance, falls, frailty and reduced functional capacity. Exposure to medicines that increase DBI also contributes to the downward spiral in function that characterises frailty.

High DBI score-associated outcomes include:
- Poorer physical function
- Poorer balance and falls
- Frailty
- Poorer cognition and memory
- Reduced mortality
- Increased hospitalization
- Increased GP visits

Residents with dementia may be particularly susceptible to these outcomes. There is dose-response relationship between higher DBI exposure and hospitalisation and mortality in people with and without Alzheimer’s disease. Increasing DBI exposure is associated with longer length of hospital stay and higher number of admissions in people with and without Alzheimer’s disease. An Australian study showed an individual’s fall risk increases with the doses and numbers of anticholinergic and sedative medications taken.

Medication review
Residents in aged care facilities may benefit from Residential Medication Management Reviews (RMMRs) on admission, after introduction of new medicines and with any change in clinical status, especially cognitive function. It has been shown that DBI scores of participants were significantly lower after the pharmacist-led RMMR intervention.

Barriers to reducing regularly scheduled drug burden index medicines include:
- Resident’s attitude to failed previous attempts to reduce/cease dose
- Discomfort with altering a specialist-initiated prescription
- Unaware that resident taking medications with anticholinergic/sedative effects

Shared-decision making between residents and their family and the healthcare team of doctors, nurses and pharmacists may help to break down these barriers.

Deprescribing
The DBI can guide deprescribing to reduce exposure to anticholinergic and sedative medications. Reducing DBI, through dose reduction or cessation of anticholinergic and sedative drugs, can prevent or reduce cognitive decline, falls, and other functional impairments.

A tapering strategy is usually required for residents taking benzodiazepines long-term. A 20-25% reduction every week or two is usually well tolerated. Cessation of benzodiazepines when used for insomnia often results in problems with recurrence (in an exaggerated form) of the insomnia as a part of a discontinuation syndrome. Other withdrawal symptoms include anxiety, insomnia, nightmares, changes to memory and concentration as well as muscle spasms.

Discontinuation of antipsychotics should be gradual, particularly if use has been long term. It is recommended to reduce the dose by 50% every two weeks then stop after two weeks on the minimum dose.

Symptoms of antidepressant discontinuation syndrome typically occur within one week of ceasing the drug. They are usually mild, and resolve over ten days or less.

Anticholinergic medicines should also be tapered slowly. Abruptly stopping anticholinergic drugs can lead to an anticholinergic discontinuation syndrome characterised by cholinergic rebound, symptoms of which include nausea, sweating, and urinary urgency.

Summary
Anticholinergic and sedative medications are commonly used in older people and are associated with adverse clinical outcomes. Older people with dementia often experience impaired physical and cognitive function with medicines with anticholinergic and sedating properties. The DBI tool may be used to identify high-risk prescribing in older people in residential aged care facilities.

References