A hip fracture is a devastating event for many older people. Every day, more than 40 Australians break their hip. Most are aged 65 years or over, and more than half are aged 85 or over. Benzodiazepines and other hypnotics are associated with increased hip fracture rate.

A previous newsletter discussed the Drug Burden Index (DBI), 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. It has clearly been shown that DBI scores of residents are significantly lower after collaborative medication reviews between general practitioners and pharmacists (RMMRs).

Falls risk
Risk factors for falls may be intrinsic (factors related to the individual) or extrinsic (factors relating to a person’s environment). Intrinsic risk factors include problems with vision, muscle weakness, poor balance, older age, cognitive impairment, a history of falling, fear of falling, use of medications causing drowsiness or confusion and conditions affecting bone structure, such as osteoporosis. Extrinsic risk factors include tripping hazards; such as uneven ground, loose rugs or clutter, wet or slippery surfaces, slippery footwear, poor lighting and lack of handrails on stairs.

There is a well-established association between psychotropic medications (hypnotics, antidepressants, antipsychotics) and falls.

Hip fractures
Most hip fractures are associated with a fall. Hip fractures are associated with repeat fractures and substantial morbidity and mortality. It has been reported that one third of older people die within the year following hip fracture. Many who survive face significantly reduced capacity to carry out activities of daily living and one third require admission to residential care.

Fracture risk
According to a recent systematic review and meta-analysis of published studies, short term use (up to 14 days) of benzodiazepines increases the risk of hip fracture by 140%, whilst medium term use (15 to 30 days) carries a 53% increased risk, and long term use (longer than one month) a 20% increased risk. The review showed a similar risk with benzodiazepine-related drugs (Z-drugs), with little or no difference between their respective risks.

Another large study showed that people with Alzheimer’s disease who are prescribed benzodiazepines have a 43% increased risk of hip fracture compared to people not taking benzodiazepines. People with Alzheimer’s disease are already more susceptible to falls and are twice as likely to experience hip fracture. This study found that benzodiazepines increase that risk even further. It also showed the risk of hip fracture was higher in patients with Alzheimer’s disease taking benzodiazepine within the first six months of treatment, with figures showing that between one and six months of treatment the fracture risk was 2.61 times higher. Benzodiazepines increased the hip fracture risk as much as Z-drugs. The authors concluded that benzodiazepines should only be used in the short-term or intermittently to treat behavioural symptoms associated with Alzheimer’s disease.

Hypnotics
Benzodiazepines and Z-drugs are used to treat anxiety and sleep disorders. Z-drugs include zolpidem (Stilnox) and zopiclone (Imovane). Benzodiazepines can be classified as short, medium or long-acting:
- Short-acting – alprazolam (Kalma, Alprax), oxazepam (Serepax, Alepam, Murelax), temazepam (Normison, Temaze, Temtabs)
- Medium-acting – bromazepam (Lexotan), lorazepam (Ativan)
- Long-acting – diazepam (Valium), flunitrazepam (Hynodorm), nitrazepam (Mogadon, Alodorm)

Guidelines recommend short-term use of benzodiazepines of 2 to 4 weeks, as part of a broader treatment strategy.
management plan that includes other pharmacological or non-pharmacological measures.

Both insomnia and drugs used to treat it may increase the risk of falls in older people. There is no evidence that the risk of hip fracture differs between short-, medium- and long-acting benzodiazepines. The risk of hip fractures also appears to be dose-related; people using higher doses of benzodiazepines are at the highest risk of hip fracture.

Medications with sedative effects (including hypnotics and antianxiety drugs) are known to adversely affect physical and cognitive function, such as memory, psychomotor performance, falls and fractures, and postural sway. Long term prescription of hypnotics carries well documented risks of dependence and cognitive impairment. Cognitive dysfunction associated with long-term use may not be fully reversible.

Due to the potential for these adverse effects, benzodiazepines and Z-drugs should be used at the lowest dose and for the shortest time possible. A definite time limit should be established with the resident and carers at commencement of therapy.

Withdrawal

Suddenly stopping hypnotics can cause withdrawal symptoms in dependent people. Reducing or tapering the dose too quickly can also cause withdrawal symptoms. These withdrawal symptoms may include:
- Anxiety, irritability
- Dysphoria, psychosis
- Insomnia, nightmares, hallucinations
- Sweating, tremors
- Memory impairment
- Hypertension, tachycardia
- Seizures

Discontinuation syndrome

After stopping benzodiazepines, insomnia can return in an exaggerated form and short term changes to sleep patterns can occur. The time to fall asleep (sleep latency) may be increased; and sleep may be more disturbed or shorter in duration. These changes usually only last less than a week, and should be managed by reassurance and non-drug sleep hygiene measures rather than recommencement of benzodiazepines.

Deprescribing

Deprescribing is the planned and supervised process of dose reduction or stopping of medication that might be causing harm or might no longer be providing benefit. The goal of deprescribing is to reduce medication burden and harm while maintaining or improving quality of life.

A 20-25% reduction in benzodiazepines every one to two weeks is usually well tolerated. This tapering strategy should be used for all residents to minimise the risk of withdrawal symptoms. More gradual dose reduction may be needed for some residents after long-term use. The majority will tolerate tapering by 15-20% per step over 6 to 8 weeks.

Summary

Benzodiazepines and Z-drugs increase the risk of hip fracture by at least 50%, with the greatest risk occurring when these medicines are newly prescribed. Falls prevention strategies should be implemented at the commencement of hypnotic therapy to reduce the risk of falls and subsequent fractures. All hypnotics should be used at the lowest dose for the shortest period of time. Non-pharmacological approaches for the management of insomnia and anxiety should be considered to reduce the risk of falls and subsequent hip fracture, particularly in the older frail people.

References

J Am Med Dir Assoc 2016;87:e15-87.

Further information

Deprescribing guide http://cpsedu.com.au