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BENZODIAZEPINES AND DEMENTIA

Benzodiazepines are commonly used to treat anxiety, insomnia, agitation, alcohol withdrawal and seizures. Anxiety symptoms and sleep disturbances are common among residents in residential aged care. However, benzodiazepines are potentially inappropriate for older persons. Older persons are particularly vulnerable to neurocognitive side effects of benzodiazepines. Chronic benzodiazepine use is associated with cognitive function decline and an increasing risk of dementia.

Benzodiazepines

Benzodiazepine use is common in residential aged care facilities (RACFs), partly because residents in RACFs have a high prevalence of sleep and anxiety disorders. People with dementia have higher rates and increased severity of sleep disorders than people without dementia. The prevalence of regular benzodiazepine use in Australian RACFs ranges from 12 to 42%.

Short-acting benzodiazepines include alprazolam, oxazepam and temazepam. Temazepam is suitable choice for managing insomnia as it has a fast onset of action. Lorazepam and bromazepam are considered medium-acting, and clobazam, clonazepam, diazepam, flunitrazepam and nitrazepam have a long duration, more than 24 hours.

Diazepam, lorazepam and oxazepam are used for anxiety disorders, although they should not be used as first-line therapy, because of potential harms including increased risk of falls, memory problems, accidents, daytime sedation and dependence. Antidepressants are first-line treatment for severe anxiety.

Benzodiazepines should only be used short-term for 2 to 4 weeks or intermittent use only. The hypnotic efficacy of benzodiazepines appears to reduce within 4 weeks.

Benzodiazepines are associated with modest improvements in time to fall asleep (sleep latency) and longer sleep duration. However, they suppress deep sleep which has a restorative effect. Short-acting as-needed benzodiazepines are associated with lower night-time sleep quality and longer day-time napping compared to long-acting regular benzodiazepines. In most cases the risk of adverse effects such as falls and fractures and cognitive impairment, outweighs any benefit for sleep quality.

Factors associated with long-term use of benzodiazepines include the following:

- female gender
- diagnosis of Alzheimer's disease
- schizophrenia
- bipolar disorder
- depression
- coronary artery disease
- asthma/chronic obstructive pulmonary disease

Dependence can occur due to long-term use. Regular use for more than one month risks development of dependence, particularly at higher doses. The risk increases with the duration of use. The highest rate of dependence is in older people.

People with current or previous alcohol and drug problems are at increased risk of developing benzodiazepine dependence.

Adverse effects

Common adverse effects include drowsiness, oversedation, light-headedness, ataxia, slurred speech, blurred vision and increased salivation. Benzodiazepine use is associated with a greater risk for hospitalisations, emergency department visits, outpatient visits, and higher health care costs. Benzodiazepine use is also associated with an increased risk of falls, and memory and cognitive impairment among older adults.

Dependency on benzodiazepines may occur after as little as 2 to 4 weeks of continuous hypnotic use.

There is also emerging evidence that the use of benzodiazepines may increase the risk for developing dementia among older adults.

Benzodiazepines and dementia

There is some evidence of an association between past or current benzodiazepine use and the risk of dementia. It appears that the risk of dementia increases with cumulative doses of medication, longer treatment duration, and when long-acting benzodiazepines are used. Current users have a higher risk for dementia than past users.

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Prodromal symptoms of dementia which include sleep disturbances, anxiety and depression can occur 10 years preceding a diagnosis of dementia. These symptoms and conditions may prompt the prescription of benzodiazepines.

A proposed mechanism is that benzodiazepines promote beta-amyloid accumulation in the brain. Others have suggested benzodiazepines could precipitate the onset of dementia or mental decline by altering or impairing higher mental activities.

A Canadian study showed a 50% increase in the risk of Alzheimer's disease among those who had used benzodiazepines in the past. People using long-acting benzodiazepines for more than three months were at greater risk. The authors also suggested benzodiazepine use might also be an early marker of a condition associated with an increased risk of dementia.

A large review of published trials found the odds of dementia were 78% higher in those who used benzodiazepines for more than 30 days compared with non-users.

The risk of dementia association with past use of benzodiazepines decreases as duration since discontinuation increases. After 3 years discontinuation, the risk of dementia has been shown to be similar to that of never-users.

Discontinuation

It is unclear whether cognitive impairment after chronic benzodiazepine use is permanent or reversible after discontinuation. One study showed light users of benzodiazepines were no longer at risk of dementia one year after discontinuation. However, the risk of dementia among heavy users remained high, even after 3 years of discontinuation.

After short-term use, benzodiazepines can usually be stopped abruptly. For people who have taken benzodiazepines for several months, reduction of the dose at a rate of 15% of the starting dose per week is likely to be well tolerated. Other recommendations for deprescribing include reducing the dosage by approximately 25% of the original dose every 1 to 4 weeks.

Substitution with an equivalent dose of a longer-acting benzodiazepine such as diazepam is now not recommended, as the same adverse effects and outcomes can occur. Substitution with diazepam is no more effective than weaning short-acting benzodiazepines. Slower weaning (e.g., 12.5%) may be necessary if discontinuation symptoms occur. Alternate day dosing can aid with weaning if dosage forms are limited. The rate of reducing the dose should be titrated against symptoms.

Typical symptoms of benzodiazepine withdrawal include:

- anxiety
- insomnia
- irritability
- myoclonic jerks
- palpitations
- sensory disturbances

Abrupt discontinuation among people taking higher doses may trigger seizures.

About a third of people taking benzodiazepines long-term may have difficulty in reducing or stopping them. If recurrent/withdrawal symptoms occur, the previous lowest tolerated dose should be maintained for 6 to 12 weeks, followed by a lower weaning rate over many months.

Non-pharmacological support including sleep hygiene measures and cognitive behavioural therapy (CBT) should be offered.

Summary

Benzodiazepines may increase the risk of dementia among older persons. The risk appears to be dose and duration dependent. Long-acting benzodiazepines and long-term use should be avoided in older people. Short-acting benzodiazepines should be used at the lowest dose for the shortest duration.

References

Therapeutic Guidelines
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