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Benzodiazepines and risk of dementia

At least half of all residents of Australian residential aged care facilities have dementia. Use of psychotropic medications in residential aged care is high, with nearly two-thirds of residents prescribed antidepressants, antipsychotics or benzodiazepines. Use of psychotropic medications before entering residential care is also high, and nearly one-third of residents are prescribed at least one benzodiazepine during their first three months of residential care. The RedUSe study identified that 20% of residents were prescribed regular benzodiazepines. Another study identified that over 30% of benzodiazepines are charted 'as-needed'.

The Choosing Wisely Australia and the Australian and New Zealand Society for Geriatric Medicine recommendations against prescribing benzodiazepines or other sedative-hypnotics to older adults as first choice for insomnia, agitation or delirium.

Benzodiazepines are commonly used to treat anxiety, insomnia, agitation, alcohol withdrawal and seizures. However, use of benzodiazepines is associated with poor outcomes. Benzodiazepines increase the risk of falls, especially among older people. There is also emerging evidence that the use of benzodiazepines is associated with an increased risk of developing dementia among older adults.

Benzodiazepine use

Insomnia is a leading indication for chronic benzodiazepine use in residential aged care.

Benzodiazepines are widely prescribed to control disruptive behaviour and sleep disturbances in people with dementia. Short-acting benzodiazepines (alprazolam, oxazepam, temazepam) may be appropriate in the short-term to manage these symptoms. Behavioural and psychological symptoms of dementia (BPSD) are common in residential aged care. Symptoms include agitation, aggression, anxiety, delusions, sleep disturbances, and hallucinations.

Benefits

Benzodiazepines are not recommended for the long-term treatment of anxiety disorders. SSRI and SNRIs antidepressants are effective long-term, even in the absence of depression. Benzodiazepines may be useful for a 2 to 4 week course to control symptoms until antidepressants take effect. They then should be tapered and stopped.

Benefits of benzodiazepines for treatment of insomnia are short-lived. Any effect is lost after 14 consecutive nights. Long-acting benzodiazepines (diazepam, flunitrazepam, nitrazepam) are inappropriate for the treatment of insomnia in older people.

Benzodiazepines may be beneficial for symptoms associated with dementia, such as anxiety, irritability and insomnia. Regular use should be limited to less than 2 weeks. They may also be useful as single doses to allay anxiety and agitation when they can be anticipated, for example prior to a dental visit. The Australia Medicines Handbook (AMH) Aged Care Companion recommends oxazepam 7.5mg 1 to 3 times a day, with a maximum of 30mg daily.

Harms

Benzodiazepines are considered potentially inappropriate medicines (PIMs) in older persons. Long-term use of benzodiazepines is associated with an increased risk of falls, dependence and withdrawal syndromes. Older people are particularly vulnerable to other side effects such as oversedation, ataxia, confusion, memory impairment, incontinence and respiratory depression. Benzodiazepine use is also associated harms across several cognitive domains including reduced visuospatial ability, speed of processing, and visual learning.

Prescribing tools such as the Beers criteria and the Screening Tool of Older People's Prescriptions (STOPP) list short-acting and long-acting benzodiazepines as potentially inappropriate in older people, recommending their use for only up to 4 weeks duration. There is a risk of dependence even with short-term use.

Benzodiazepines can worsen cognitive impairment in persons with dementia, and lead to a higher rate of side effects such as amnesia, confusion, and sedation.

Dementia risk

Benzodiazepines are frequently prescribed in patients with Alzheimer's disease. A diagnosis of dementia is associated with long-term use of benzodiazepines. Long-term use is associated with accumulation of cognitive deficits that lead to an increased risk of dementia.

Benzodiazepines may precipitate the onset of dementia or cognitive decline by impairing or altering mental activities. The prescription of benzodiazepines may be a consequence of prodromal symptoms of dementia. Benzodiazepine use may also be an early marker of dementia. Persistent mid-life anxiety and depression may be associated with a higher chance of dementia in older people.

Some studies report accelerated cognitive deterioration in association with benzodiazepine use. Other studies highlight that cumulative exposure to benzodiazepines longer than 3 months may increase dementia risk. A Canadian study showed the risk of dementia among users of benzodiazepines was increased by 50% compared to non-users. Benzodiazepines with a long half-life (diazepam, flunitrazepam, nitrazepam) may be most harmful.

A 2015 meta-analysis found a 50% increased risk for the development of dementia among people who have used benzodiazepines, either recently or in the past, compared with never users.

Another meta-analysis conducted in 2016 found the odds for developing dementia in people who used benzodiazepines for more than 30 days was 78% higher among users compared to non-users.

Further meta-analysis in 2018 reinforced the evidence for an association between the use of benzodiazepines and the development of dementia, finding a 38% increased risk.

Deprescribing

Deprescribing strategies will vary with the type of dependence (therapeutic dose, prescribed high dose, multiple benzodiazepines).

After short-term use (less than 4 weeks), benzodiazepines can usually be stopped abruptly. In general, benzodiazepines should be withdrawn over several weeks to months in long-term users. 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. Slower weaning may be necessary if discontinuation symptoms occur.

Withdrawal symptoms may appear in 1–2 days for benzodiazepines with shorter half-lives, but may not appear until 3–7 days for agents with longer half-lives. Acute withdrawal symptoms include anxiety symptoms, hypersensitivity to sound, light, touch and taste, abnormal body sensations and rarely hallucinations, seizures, delirium and psychosis. Protracted benzodiazepine withdrawal symptoms include anxiety, depression, gastrointestinal upset, insomnia, irritability, muscle aches, poor concentration and memory, and restlessness.

Discontinuation is usually beneficial as it is followed by improved psychomotor and cognitive functioning.

Summary

Use of benzodiazepines is associated with an increased risk of dementia, particularly among long-term users. The risk is higher with long-acting benzodiazepines, longer duration of use and higher cumulative doses. In addition to the increased risk of dementia, there is also evidence that benzodiazepines increase the risk of injurious falls, fractures, acute respiratory failure, and delirium, all of which reduce a resident's quality of life. Benzodiazepines should be used in the lowest dose for the shortest time possible, generally no longer than 4 weeks.

Additional information

The Department of Health has developed an infographic which outlines the 6 steps for safe prescribing antipsychotics and benzodiazepines in residential aged care.

https://www.health.gov.au/resources/publications/six-steps-for-safe-prescribing-of-antipsychotics-and-benzodiazepines-in-residential-aged-care

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