

Benzodiazepine Use and Falls in Older Adults

Is It Worth the Risk?

This editorial presents current evidence on benzodiazepine (BZD) use in older adults with particular reference to falls and makes recommendations for research to reduce the use of BZDs. Falls are a significant health concern for older adults (age ≥ 65) worldwide. A fall incident is an indication of the quality of life and quality of care of older adults. Risk factors for falls are often complex; however, studies reveal that BZD use is related to high falls incidents among older adults (Díaz-Gutiérrez et al., 2017). Therefore, avoiding inappropriate use of BZDs may substantially decrease fall-related incidents in older adults.

BACKGROUND

The issue of falling is a universal problem affecting older adults. In a systematic review of falls incidents, statistics showed an estimated 30% of adults age ≥ 65 and 50% age ≥ 85 will have a fall incident annually (Díaz-Gutiérrez et al., 2017). In residential aged care facilities (RACFs), approximately 50% of residents will experience a new fall and 5% to 10% will sustain serious injuries (Hanlon et al., 2017). In 2016, the Health Quality & Safety Commission of New Zealand (2018) reported admission to public hospitals due to fall-related injuries amounted to 12.9 per 1,000 falls ($n = 5,210$) for individuals ages 65 to 74, 36.4 per 1,000 falls ($n = 7,750$) for individuals ages 75 to 84, and those age ≥ 85 were notably higher at 102.6 per 1,000 falls ($n = 8,560$). Furthermore, a retrospective study by Carryer et al. (2017) of 276 older adults residing in 13 different RACFs in central New Zealand reported a total of 36 (13%) fall incidents in the 30-day retrospective period of the study. BZD use is shown to be a significant risk factor for falls in older adults, although a recent study involving 8,270,000 older adults from the United States, Canada, and Australia reported a downward trend in BZD use (Brett et al., 2018). The goal of the current report is to explore how BZD use impacts fall-related incidents in older adults; the interaction between the normal aging process and BZD use; consequences of inappropriate BZD prescribing; and recommendations for the management of falls prevention in clinical practice.

BENZODIAZEPINE USE AND FALL-RELATED INCIDENTS

Several studies have found a positive correlation between BZD use and fall-related incidents among older adults. BZDs are psychoactive drugs with therapeutic effects (e.g., anti-anxiety, anti-epileptic, muscle relaxant) (Díaz-Gutiérrez et al., 2017), but are commonly prescribed to treat insomnia, anxiety, and agitation (odds ratio [OR] = 4.05; 95% confidence interval [CI] [4.44, 11.43]) in older adults (Gerlach, Maust, Leong, Mavandadi, & Oslin, 2018). A systematic review involving 18 studies from various countries by Yu and Zecevic (2018) on recurrent or two or more falls over 12 months in older adults living in the community reported an increased risk of 1.2 to 3.7 times in older adults taking BZDs. A 1-year study by Blachman, Leipzig, Mazumdar, and Poeran (2017) on fall incidents at Mt. Sinai Hospital in the United States among 490 patients age ≥ 65 recorded a total of 328 falls. The use of high-risk medications within 24 hours before the incident was involved in 62% ($n = 203$) of recorded falls, of which approximately 20% ($n = 41$) received BZDs and 57% of those ($n = 29$) received BZDs above the recommended dose (Blachman et al., 2017). Moreover, a study on the risk of falling and hip fractures by Machado-Duque et al. (2018) among 287 older adults identified BZD use within 1 month prior to a fall resulting in a hip injury (OR = 3.73; 95% CI [1.30, 8.70]). In addition, the relationship of BZD use and falls among older adults revealed a higher risk of falling and fractures within 24 to 120 hours following the start of a BZD regime (Díaz-Gutiérrez et al., 2017). Likewise, the B-PROOF study concerning community-dwelling older adults revealed an increased risk of falling (hazard ratio = 1.32; 95% CI [1.02, 1.71]; $p = 0.034$) related to BZD use in 2,407 older adults within the 2- to 3-year follow-up period (Ham et al., 2014). The cited studies showed the upward trend of fall incidents within 1 year of commencing BZD use among older adults—the incidents are higher at the beginning of BZD treatment, but the risk of fall-related incidents remains throughout the treatment period.

It has been suggested that the use of BZDs in older adults is contraindicated due to harmful side effects and limited therapeutic value. The Beers Criteria[®] (American Geriatrics Society Beers Criteria[®] Update Expert Panel, 2019) identified BZDs as the most inappropriate treatment in older adults and advised against the use of all BZDs among older adults (Brett et al., 2018). In RACFs, an estimated 90% of residents with dementia are inappropriately prescribed BZDs (Westbury et al., 2018). A systematic review by Airagnes, Pelissolo, Lavallée, Flament, and Limosin (2016) stated that BZD prescriptions were inappropriate in two thirds of cases, with long-term BZD use being the most frequent issue. Findings also included overdosage, underdiagnosis, and guidelines not being followed. Treating sleep problems with BZDs is a common misuse among older adults because of their short-term effectivity (Canady, 2018) and resulting low quality of sleep (Gerlach et al., 2018). In addition, BZD use increases in prevalence with age. The risk of falls for adults age ≥ 85 taking >180 doses per year increases by 30% (nine times) compared to a 20% increase in older adults ages 65 to 75. Among those ages 65 to 85, 31% were reported to be chronic BZD users (Bachhuber, Hennessy, Cunningham, & Starrels, 2016).

The repercussions of inappropriate BZD use according to Picton, Marino, and Nealy (2018) are due to the tranquilizing effect of gamma-aminobutyric acid (GABA) on the central nervous system (CNS). BZD intensifies the sedative effect of GABA leading to slow or diminished function of the CNS (Airagnes et al., 2016). CNS depression includes symptoms such as gait and balance disturbances, tiredness and weakness, disorientation, giddiness, and light-headedness (Picton et al., 2018)—all symptoms that have been identified in previous studies as risk factors for falls primarily in older adults.

INTERACTION BETWEEN THE NORMAL AGING PROCESS AND BENZODIAZEPINE USE

The normal aging process that takes place in the body changes how BZDs are used, distributed, and eliminated by the body. According to studies, there is an increased susceptibility of older adults to the numerous harmful effects of BZDs, which are heightened by age-related factors (Aspinall et al., 2019). According to Picton et al. (2018), elimination half-lives of BZDs last longer in older adults. Two age-related factors causing prolonged elimination have been identified (Adis Medical Writers, 2019): (a) increase in total amount of body fat that leads to accumulation of BZDs in blood circulation; and (b) inefficient hepatic clearance of BZDs secondary to liver atrophy and decreased circulation in the liver. The delay in elimination results in BZD build up and intolerance (Aspinall et al., 2019). As a consequence of the normal aging process,

BZDs are not adequately used or efficiently eliminated from the body, making older adults increasingly vulnerable to BZD-related harm and falls-related incidents.

CONSEQUENCES OF INAPPROPRIATE BENZODIAZEPINE PRESCRIBING

Falls affect a majority of the older adult population. Several studies have provided evidence supporting the ongoing impact of BZDs on fall-related incidents. Age-related changes in the body interfere with the metabolism of BZDs, resulting in accumulation and residual effects of BZDs. Moreover, BZDs are psychoactive drugs commonly used as anxiolytic, sedative, or hypnotic medications in older adults. BZDs are not recommended but widely used among older adults for several indications but most commonly for sleep disturbances. Unfortunately, this means that BZDs are often prescribed for extended periods against the Beers Criteria and other medication guidelines. Likewise, inappropriate practices in prescribing BZDs predispose older adults to the risk of fall incidents. However, BZDs are probably useful as a short-term treatment for acute anxiety and insomnia. Therefore, clinicians prescribing BZDs should consider the benefit/risk due to their influence on increased fall-related incidents in older adults.

RECOMMENDATIONS FOR THE MANAGEMENT OF FALLS PREVENTION

Unlike age-related factors, which are non-modifiable, BZD use is a modifiable risk factor and clinicians may be able to prevent BZD-related fall incidents. The continued administration of BZDs to older adults in the midst of compelling evidence regarding dangers for older adults raises the question of research needed to change the course of practice. Priorities for further research include adequately powered, high-quality, randomized controlled trials comparing pharmacological interventions to facilitate BZD discontinuation in chronic BZD users. These trials need to be conducted with minimal bias, be independent of industry involvement, and include adverse effects, along with patient-centered and long-term clinical outcomes (Baandrup et al., 2018). Randomized controlled trials in participants newly prescribed BZDs need to take the “new user” effect into consideration and outline clearly in the patient information sheet what to expect and what routine tasks to avoid (Díaz-Gutiérrez et al., 2017). As insomnia is one of the common reasons for long-term BZD prescription, further research also needs to investigate efficacy of nonpharmacological options for improved somnolence, particularly in older adults (Donnelly, Bracchi, Hewitt, Routledge, & Carter, 2017). Although considerable research has been conducted on optimum sleep hygiene practices, few studies involve the

very old, the medically compromised, and those with dementia. In addition, there is a need for more rigorous research on nonpharmacological approaches to treating both short- and long-term anxiety and agitation in these populations. A plethora of interventions have been developed and found effective for reducing the use of antipsychotic medications by older adults and may be studied for efficacy in reducing BZD use. Studying interventions such as audit and feedback reports, educational interventions, screens for BZD use among those at risk for falls, benefit/risk checklists, and titration down and withdrawal protocols are needed.

REFERENCES

- Adis Medical Writers. (2019). Take a multifaceted stepwise approach when deprescribing benzodiazepines in older patients. *Drugs & Therapy Perspectives*, 35, 72-76. doi:10.1007/s40267-018-0578-z
- Airagnes, G., Pelissolo, A., Lavallée, M., Flament, M., & Limosin, F. (2016). Benzodiazepine misuse in the elderly: Risk factors, consequences, and management. *Current Psychiatry Reports*, 18, 89. doi:10.1007/s11920-016-0727-9
- American Geriatrics Society Beers Criteria® Update Expert Panel. (2019). American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society*, 67, 674-694. doi:10.1111/jgs.15767
- Aspinall, S.L., Springer, S.P., Zhao, X., Cunningham, F.E., Thorpe, C.T., Semla, T.P.,...Hanlon, J.T. (2019). Central nervous system medication burden and risk of recurrent serious falls and hip fractures in veterans affairs nursing home residents. *Journal of the American Geriatrics Society*, 67, 74-80. doi:10.1111/jgs.15603
- Baandrup, L., Ebdrup, B., Rasmussen, J., Lindschou, J., Gluud, C., & Glenthøj, B. (2018). Pharmacological interventions for benzodiazepine discontinuation in chronic benzodiazepine users. *Cochrane Database of Systematic Reviews*, 3, CD011481. doi:10.1002/14651858.CD011481.pub2
- Bachhuber, M.A., Hennessy, S., Cunningham, C.O., & Starrels, J.L. (2016). Increasing benzodiazepine prescriptions and overdose mortality in the United States, 1996-2013. *American Journal of Public Health*, 106, 686-688. doi:10.2105/AJPH.2016.303061
- Blachman, N.L., Leipzig, R.M., Mazumdar, M., & Poeran, J. (2017). High-risk medications in hospitalized elderly adults: Are we making it easy to do the wrong thing? *Journal of the American Geriatrics Society*, 65, 603-607. doi:10.1111/jgs.14703
- Brett, J., Maust, D.T., Bouck, Z., Ignacio, R.V., Mecredy, G., Kerr, E.A.,... Pearson, S.A., (2018). Benzodiazepine use in older adults in the United States, Ontario, and Australia from 2010 to 2016. *Journal of the American Geriatrics Society*, 66, 1180-1185. doi:10.1111/jgs.15292
- Canady, V.A. (2018). New research examines use, misuse of benzodiazepines. *Mental Health Weekly*, 28(48), 4-5. doi:10.1002/mhw.31714
- Carryer, J., Weststrate, J., Yeung, P., Rodgers, V., Towers, A., & Jones, M. (2017). Prevalence of key care indicators of pressure injuries, incontinence, malnutrition, and falls among older adults living in nursing homes in New Zealand. *Research in Nursing & Health*, 40, 555-563. doi:10.1002/nur.21835
- Díaz-Gutiérrez, M.J., Martínez-Cengotitabengoa, M., Sáez de Adana, E., Cano, A.I., Martínez-Cengotitabengoa, M.T., Besga, A.,...González-Pinto, A. (2017). Relationship between the use of benzodiazepines and falls in older adults: A systematic review. *Maturitas*, 101, 17-22. doi:10.1016/j.maturitas.2017.04.002
- Donnelly, K., Bracchi, R., Hewitt, J., Routledge, P.A., & Carter, B. (2017). Benzodiazepines, Z-drugs and the risk of hip fracture: A systematic review and meta-analysis. *PLoS One*, 12, e0174730. doi:10.1371/journal.pone.0174730
- Gerlach, L.B., Maust, D.T., Leong, S.H., Mavandadi, S., & Oslin, D.W. (2018). Factors associated with long-term benzodiazepine use among older adults. *JAMA Internal Medicine*, 178, 1560-1562. doi:10.1001/jamainternmed.2018.2413
- Ham, A.C., Swart, K.M., Enneman, A.W., van Dijk, S.C., Oliari Araghi, S., van Wijngaarden, J.P.,...van der Velde, N. (2014). Medication-related fall incidents in an older, ambulant population: The B-PROOF study. *Drugs and Aging*, 31, 917-927. doi:10.1007/s40266-014-0225-x
- Hanlon, J.T., Zhao, X., Naples, J.G., Aspinall, S.L., Perera, S., Nace, D.A.,... Thorpe, C.T. (2017). Central nervous system medication burden and serious falls in older nursing home residents. *Journal of the American Geriatrics Society*, 65, 1183-1189. doi:10.1111/jgs.14759
- Health Quality & Safety Commission New Zealand. (2018). *Falls in people aged 50 and over*. Retrieved from <https://www.hqsc.govt.nz/our-programmes/health-quality-evaluation/projects/atlas-of-healthcare-variation/falls/>
- Machado-Duque, M.E., Castaño-Montoya, J.P., Medina-Morales, D.A., Castro-Rodriguez, A., Gonzalez-Montoya, A., & Machado-Alba, J.E. (2018). Association between the use of benzodiazepines and opioids with the risk of falls and hip fractures in older adults. *International Psychogeriatrics*, 30, 941-946. doi:10.1017/S1041610217002745
- Picton, J.D., Marino, A.B., & Nealy, K.L. (2018). Benzodiazepine use and cognitive decline in the elderly. *American Journal of Health-System Pharmacy*, 75, e6-e12. doi:10.2146/ajhp160381
- Westbury, J.L., Gee, P., Ling, T., Brown, D.T., Franks, K.H., Bindoff, I.,... Peterson, G.M. (2018). RedUSE: Reducing antipsychotic and benzodiazepine prescribing in residential aged care facilities. *Medical Journal of Australia*, 208, 398-403.
- Yu, M., & Zecevic, A. (2018). Medications and polypharmacy influence on recurrent fallers in community: A systematic review. *Canadian Geriatrics Journal*, 21, 14-25. doi:10.5770/cgj.21.268

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