

Editors: **Michael Woodward**, Director, Aged and Residential Care Services, **Stephen Campbell**, Consultant Geriatrician, **Rohan Elliott**, Clinical Pharmacist, **Graeme Vernon**, Drug Information Pharmacist, **Francine Tanner**, Clinical Pharmacist, Austin Health; **Robyn Saunders**, Consultant Pharmacist, Victoria.

Medications and Falls in Older People

Henry Zeimer

ABSTRACT

Falls are a major cause of morbidity in older people. Although in most cases falls are multifactorial in aetiology, medications are one of the most easily reversible risk factors that need to be considered in the falls assessment process. There is strong evidence that sedatives, particularly benzodiazepines (short-acting and long-acting), are associated with falls with odds ratios in the range of 1.3 to 1.5. Although antipsychotics (typical and atypical) are associated with a similar falls risk, most of the data are from nursing home studies. Antidepressants consistently increase falls risk, with a similar risk from the selective serotonin reuptake inhibitors compared to tricyclic antidepressants. The evidence for an association with falls risk and anticonvulsants, narcotic analgesics, and cardiovascular medications is less strong due to fewer studies published on these drug classes. Medication review is an integral component of the comprehensive falls assessment process in older people.

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INTRODUCTION

Falls are a major cause of morbidity in older people. Thirty per cent of people over the age of 65 years who live in the community fall each year, and frail and institutionalised older people experience a higher percentage of falls.¹ Falls result in hospitalisation due to injury and fracture, as well as other less apparent sequelae, such as the post-fall syndrome of immobility, anxiety and depression.

Before reviewing the association between medications and falls, two important points need to be made:

- falls are usually multifactorial in aetiology, and only occasionally a single intervention can reduce falls rates significantly; and
- data on the relationship between medications and falls are almost entirely derived from observational studies, which have their inherent limitations and biases. Only one double-blind, randomised controlled trial has been published looking at psychotropic medications and falls.

However, medication review is an integral component of the comprehensive falls risk assessment of patients and is a recommendation in the consensus guidelines for the prevention of falls in the elderly.² Medications are also one of the simplest and most easily reversible risk factors in the falls assessment process.

POLYPHARMACY

Polypharmacy is known to be associated with adverse outcomes in several areas of geriatric medicine. Falls are one such adverse outcome. Several studies have confirmed that

the more medications used by a patient, regardless of the class of medication, the greater the risk of falling.³⁻⁵ In a large Dutch study of community-dwelling elderly, use of four or more medications was associated with an odds ratio of 1.3 (95% CI 1.0–1.7) for having a fall.⁴ Other studies have shown that using two or more psychotropic medications in combination is associated with an increased risk of falls compared to the use of a single psychotropic medication.^{6,7}

PSYCHOTROPIC MEDICATIONS

Many studies have grouped all psychotropic medications (neuroleptics, antidepressants, hypnotics, sedatives, and sometimes anticonvulsants) into one group and analysed the effect of the group on falls risk. This, of course, makes the interpretation of results difficult and impossible to draw conclusions about the individual drug class and the risk of falls. In the only double-blind, randomised controlled trial published in this area, Campbell et al. undertook a pilot study of 93 elderly patients living in the community in Dunedin, New Zealand, who were current users of psychotropic medications.⁸ They grouped all psychotropic medications together (major tranquillisers, antidepressants, benzodiazepines) and in a unique study design, crushed these medications and packed them into plain gelatin capsules with matching control capsules containing placebo, in order to be able to withdraw medications with the patient remaining blinded. The trial showed that psychotropic medication withdrawal was associated with a significant (66%) reduction in falls over an average of 44 weeks (hazard ratio 0.34; 95% CI 0.16–0.74) after adjusting for history of falls in the previous year and total number of medications taken.

In a Dutch study of community-dwelling older people with a history of falls, the authors grouped psychotropic medications with other medications considered to increase falls risk, such as antihypertensives, antiarrhythmics, antihistamines, anticholinergics, hypoglycaemic drugs and analgesics.⁹ In this non-randomised study of 139 patients, the medications were withdrawn or the dosages reduced in 54% of patients. In the group where such modifications were possible, there was a significant reduction in the adjusted mean number of falls compared to the group without modification to falls risk increasing medications (0.3 vs 3.6; $p = 0.025$) during two months of follow-up. On subanalysis, there was a greater lowering of the hazard ratio in patients who had cardiovascular medications withdrawn compared to those who had psychotropic medications withdrawn (hazard ratio 0.35 compared to 0.56) but the small sample size in each subgroup may have influenced the results.

Sedatives

Older people may be at a greater risk of the adverse effects of sedatives, such as benzodiazepines, because of their altered pharmacokinetic status compared to younger people, such

Henry Zeimer, FRACP, Geriatrician, Aged Care Services, Austin Health, Heidelberg West, Victoria

Address for correspondence: Dr Henry Zeimer, Aged Care Services, Austin Health, PO Box 5444, Heidelberg West Vic. 3081, Australia
 E-mail: henry.zeimer@austin.org.au

as reduced clearance of the sedative or of an active metabolite. There is also some evidence of altered pharmacodynamic status in older people, such as increased sensitivity to peak drug effects.¹⁰ Benzodiazepines may directly increase the risk of falls by causing sedation, dizziness, impairment of motor coordination and slowed corrective responses. Benzodiazepines have demonstrated impairment of function in tests of body sway, reaction time and proprioception.¹¹

It should be noted that many studies looking at the relationship between falls and sedatives included data on chloral hydrate and barbiturates, which are no longer available in many countries. Sedative use, and benzodiazepines in particular, have consistently been associated with falls in published studies. In an early study by Tinetti et al. of community-dwelling older people, there was a highly significant odds ratio of 28.3 for falls in users of sedatives but the study only controlled for the presence of depression and dementia, and not other confounders, such as comorbidity or overall medication use.¹² In the landmark 1999 meta-analysis by Leipzig et al., sedative or hypnotic use had an adjusted odds ratio of 1.54 (95% CI 1.40–1.70) for falls, and for all benzodiazepines use the adjusted odds ratio was 1.48 (95% CI 1.23–1.77).¹³ Odds ratios of a similar magnitude have also been observed in more recent studies. In one of the largest epidemiological studies on falls, Ensrud et al. prospectively examined elderly community-dwelling women who participated in the Study of Osteoporotic Fractures.⁶ Their findings were an odds ratio of 1.34 (95% CI 1.09–1.63) for at least one fall and an odds ratio of 1.51 (95% CI 1.14–2.01) for frequent falls in benzodiazepine users compared to non-users. These odds ratios were adjusted for potential confounders.

A further question is whether short-acting benzodiazepines (elimination half-life less than 24 hours), such as lorazepam, alprazolam and temazepam, have a lower falls risk than long-acting benzodiazepines (elimination half-life greater than 24 hours.), such as diazepam and clonazepam. In a large Canadian database study, there was a relative risk of 1.7 for hip fracture in users of long-acting benzodiazepines compared to non-users, while there was no significant increased hip fracture risk in users of short-acting benzodiazepines.¹⁴ However, another study has shown similar falls risk with the use of short-acting benzodiazepines.¹⁵ In the meta-analysis by Leipzig et al., the pooled odds ratios were 1.44 for short-acting and 1.32 for long-acting benzodiazepines, and no difference in risk was observed in the study by Ensrud et al.^{6,13}

A short-acting non-benzodiazepine imidazopyridine sedative, zolpidem, was marketed in Australia in 1996 as a safer alternative to traditional benzodiazepine use in older people. However, using a Medicaid database in the US, Wang et al. observed that zolpidem use was associated with a significantly increased risk of hip fracture (adjusted odds ratio 1.95; 95% CI 1.09–3.51), which is similar to the increased risk with other psychotropic medications.¹⁶ A limitation of this study is confounding by indication, i.e. patients at a higher risk of falls may have been preferentially prescribed zolpidem as it was perceived to be safer, which cannot be adjusted for. Of even more concern are bizarre sleep-related events, such as sleep walking, that have been reported to the Adverse Drug Reactions Advisory Committee.¹⁷ Such adverse effects would most likely increase falls risk in the elderly, and apart from the association with hip fractures according to Wang et al., no published study has directly linked zolpidem to falls.

Antipsychotics and Neuroleptics

Antipsychotics predispose to falls due to sedation, psychomotor slowing, extrapyramidal effects, and for some, orthostasis. Most of the available data are from studies of institutionalised elderly, as antipsychotic use is more common in this group, with only a few published studies looking at the effect of antipsychotics on falls risk in the community.

In an Australian nursing home study, Yip and Cumming found an adjusted odds ratio of 4.4 (95% CI 1.2–16.5) for falls among antipsychotics users compared to non-users.¹⁸ A large Canadian nursing home study looking at admission to hospital with injurious falls from antipsychotic use found a weak but significant association with an adjusted odds ratio of 1.31 (95% CI 1.06–1.60).¹⁹ A Brazilian study of elderly community-dwelling women, found an adjusted falls odds ratio of 2.04 (95% CI 1.05–3.99) for users of psychoactive drugs, which included antidepressants together with antipsychotics.²⁰ Leipzig et al. in their meta-analysis, similarly grouped these two classes of medications to show an adjusted odds ratio of 1.69 (95% CI 1.29–2.22) for falls.¹³ This meta-analysis included institutionalised as well as community-dwelling elderly.¹³ Cumming calculated that approximately 33% of falls in nursing homes and 13% of falls in the community were related to the use of psychotropics.²¹

Recent research has focused on the risk of falls and the use of the newer atypical antipsychotics. The atypical antipsychotics have been promoted as having a more favourable adverse effect profile, in particular less extrapyramidal and anticholinergic effects. The evidence on whether this translates into lower falls risk is conflicting and once again confounded by indication, as in the case of zolpidem, may be impacting on the data. In a post-hoc analysis of data from a large randomised placebo-controlled trial in nursing home patients with behavioural and psychiatric symptoms of dementia, patients treated with risperidone had no reported increased risk of falls compared to those treated with placebo.²² Surprisingly, patients treated with risperidone 1 mg daily had a statistically significant lower incidence of falls, but a non-significant trend of a higher incidence of falls with risperidone 2 mg daily. In another Australian study of older people in aged-care facilities (nursing homes and hostels) in the North Sydney Health Area, olanzapine was associated with a significantly greater risk of falling (adjusted odds ratio 1.74; 95% CI 1.04–2.90), while the associations with risperidone (adjusted odds ratio 1.32; 95% CI 0.57–3.06) and typical antipsychotics (adjusted odds ratio 1.35; 95% CI 0.87–2.09) were not statistically significant compared to non-users.²³ Liperoti et al. used a Medicaid database in the US to assess hip fracture risk among nursing home residents using antipsychotics.⁷ The adjusted odds ratios for typical and atypical antipsychotics were virtually the same (1.37; 95% CI 1.11–1.69 and 1.35; 95% CI 1.06–1.71 respectively). Overall, there is emerging evidence that the atypical antipsychotics confer a similar risk of falling as the older typical antipsychotics.

Antidepressants

Antidepressants may predispose to falls due to effects on sedation, psychomotor function, and orthostasis. In a large Canadian case-controlled study for injurious falls in community-dwelling elderly, antidepressants as a group had an adjusted falls odds ratio of 1.46 (95% CI 1.21–1.78).²⁴ In Leipzig et al.'s meta-analysis, the adjusted odds ratio for falling in users of tricyclic antidepressants was 1.35, which is similar to the findings in the Australian nursing study with an adjusted odds ratio of 1.45 (95% CI 1.09–1.93).^{13,23}

The focus of recent research on antidepressants, similar to the antipsychotics, has been on the falls risk associated with the use of selective serotonin reuptake inhibitors as compared to the risk to users of tricyclic antidepressants. Selective serotonin reuptake inhibitors are considered to be largely free of the adverse effects thought to predispose to falls, and therefore a safer option in older people. One of the first to test this hypothesis was Liu et al., who studied community-dwelling older people in Canada and assessed hip fracture rates by using an administrative healthcare database, found an adjusted odds ratio for hip fracture of 2.4 for selective serotonin reuptake inhibitor users, adjusted odds ratio of 2.2 for secondary amine tricyclics and an adjusted odds ratio of 1.5 for tertiary amine tricyclics.²⁵ These findings were confirmed by Thapa et al. who in a large Tennessee nursing home study, found that users of tricyclic antidepressants had an adjusted odds ratio of 2.0 (95% CI 1.8–2.2) for falling, while users of selective serotonin reuptake inhibitors had an adjusted odds ratio of 1.8 (95% CI 1.6–2.0).²⁶ In the Ensrud et al. study, the adjusted odds ratio for falls in selective serotonin reuptake inhibitor users was nearly double to that of tricyclic antidepressant users (2.61; 95% CI 1.51–4.50 and 1.32; 95% CI 0.90–1.94 respectively).⁶ Once again, confounding by indication may be influencing the data, but current evidence suggests that selective serotonin reuptake inhibitors do not offer an advantage over tricyclic antidepressants in terms of falls and risk of hip fracture.

Anticonvulsants

Less data are available for anticonvulsants and their relationship with falls, mainly due to lower usage rates in older people compared to psychotropic medications and sedatives. Anticonvulsants may increase the risk of falls due to central nervous system effects such as sedation, dizziness and impaired postural control. Ensrud et al. found that anticonvulsant use was a strong risk factor for falls (adjusted odds ratio 1.75; 95% CI 1.13–2.71), and this was similarly found in the Canadian study of injurious falls among community-dwellers (adjusted odds ratio 1.51; 95% CI 1.11–2.06).^{6,24} Both studies adjusted for comorbidities, such as seizure disorders. The evidence of an increased falls risk with anticonvulsants should be kept in mind in the current climate of the increased use of these drugs as mood stabilisers in the treatment of behavioural disturbance in dementia.

Narcotic Analgesics

Although narcotic analgesics may increase falls risk by causing sedation, dizziness and psychomotor impairment, limited data are available. In the Ensrud et al. study, narcotic use increased the risk of falls with a crude odds ratio of 1.44 (95% CI 1.17–1.77) but after adjustment for multiple factors related to narcotic use and falling, no difference was found in falls risk between narcotic analgesic users and non-users.⁶ There were similar findings in the meta-analysis by Leipzig et al. as well as a non-significant increased odds ratio for non-steroidal anti-inflammatory drug use of 1.16, all probably due to the limited powering of the studies due to small numbers of users.³

CARDIOVASCULAR MEDICATIONS

Generally speaking, the quality and quantity of research into the association between falls and cardiovascular medication is poor. For instance, some studies include diuretics in the antihypertensive category and others do not. Drugs which cause postural hypotension have traditionally been considered an important risk factor for falls. However, there is little

evidence in the literature to support this association. In the landmark Systolic Hypertension in the Elderly Program trial, there was no difference in the rates of falls between the treated and placebo groups.²⁷ In the meta-analysis by Leipzig et al., only type 1A antiarrhythmics (quinidine, procainamide), digoxin and thiazide diuretic usage were associated with falls (adjusted odds ratio 1.59, 1.22 and 1.06 respectively).³ The general opinion is that cardiovascular medications, particularly digoxin and diuretics, have a weak association with falls.

OTHER MEDICATIONS

Medications that impair neuromuscular function, such as corticosteroids, baclofen and colchicine, could be expected to be associated with falls. However, no evidence in the literature supports this, and further targeted studies are needed to assess this possible risk.

CONCLUSION

There is strong evidence in the literature that benzodiazepines, antipsychotics, and antidepressants are independent risk factors for falls. This reinforces the status of medication review as an integral component of the comprehensive falls risk assessment of patients. Short-acting benzodiazepines seem to have a similar falls risk as long-acting benzodiazepines, and newer drugs, such as atypical antipsychotics and selective serotonin reuptake inhibitors confer a similar falls risk as the more established and conventional therapies in these therapeutic areas.

Competing interests: None declared

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A series of questions that can assist you with evaluating your learning outcomes can be found on the SHPA web site. Answers to these questions can be lodged at <www.shpa.org.au/docs/cpd.html> until June 2009.

In **shpacpd** this is considered an Activity Group 2 activity: Improving Knowledge and Skills with assessment. The number of hours will be dependent on the time you have taken to read the article, complete the multiple choice questions and submit the answers.

Learning objectives are as follows:

1. Understand the association between medications and falls risk.
2. Review medications as part of the falls risk assessment for older patients

Pharmacist competency units addressed include:

Competency Unit 3.1: Participate in therapeutic decision making.

Competency Unit 3.2: Provide ongoing pharmaceutical management.

Competency Unit 3.3: Promote rational drug use.

Competency Unit 4.2: Evaluate prescribed medicines.