Medication and falls: in older people

Falls in older people result in considerable morbidity and mortality. Since many factors contribute to falls, the interventions to minimise them need to be multifactorial as well. Medication-associated falls are not uncommon and are a potentially modifiable risk factor. **Drs Narasimhan Pradeep Kumar and Rosalind Gait** look at the common drugs used in the elderly and their part in contributing to falls.

Injuries due to falls represent an important public health concern in terms of morbidity, mortality and cost to health and social services. About 30 per cent of people over 65 living in the community have a fall at least once each year and this figure is higher in institutional care. One-fifth of these incidents require medical attention. This, in turn, can result in significant morbidity and healthcare costs, restrictions on the patient’s activity level, a fear of subsequent falls and – in the worst case scenario – it can lead to institutionalisation.

It is estimated that about 40–60 per cent of falls lead to injuries, with 30–50 per cent being minor and five per cent being fractures. Up to one per cent of falls in older people are said to result in a hip fracture. In one study of 204 community dwelling people who had experienced more than one fall in the previous year with consequences, the results were:

> physical injury (68.1 per cent);
> health service use (23.5 per cent);
> treatment (17.2 per cent);
> decline in functional status (35.3 per cent);
> decline in social activity (16.7 per cent); and
> decline in physical activity (15.2 per cent).

The main contributory factors associated with functional decline were being female, increased medication use and depressive symptoms.

There are a number of risk factors that have been identified. The Effective Health Care Bulletin placed the causes into five major categories:

- environmental (eg, loose carpets, poor lighting, unsafe stairs);
- medical conditions and changes associated with ageing (poor vision, cognitive impairment);
- nutritional (eg, calcium and vitamin D deficiency);
- lack of exercise; and
- medication related.

The majority of non-syncopal falls do not have well-defined aetiologies and are often felt to be the result of multiple interacting factors. The contributing factors have also been described as ‘intrinsic’ (ie, age-related changes and health status-related factors) and extrinsic (eg, the physical environment surrounding the patient).

The use of drugs in this population is often unavoidable and may be considered as either an intrinsic or an extrinsic factor. The role of medications in contributing to falls has received much attention over the past two decades, as medication exposure is potentially modifiable as a strategy to their prevention. Two landmark case-control studies by Ray et al. suggested that use of long-elimination half-life hypnotic anxiolytic agents in general – and use of long-elimination half-life...
benzodiazepines in particular – increase the risk of hip fractures in elderly patients.

Current National Institute for Clinical Health and Excellence (NICE) guidelines recommend a medication review be an integral part of the initial multifactorial assessment in those who fall. Indeed modifications to be considered include the following:

- primary care physicians should review the need for medications on a regular basis;
- rescheduling the taking of medications to minimise any cumulative effects;
- close monitoring of a patient when new medications are commenced.

The management of medicines is a fundamental component of each of the National Services Framework (NSF) standards. The NSF standard on falls points out that polypharmacy is a risk factor. In patients taking medications known to contribute to falls, medication review can play an important part in falls prevention. The majority of older people take medicines, making this a significant issue for the NSF.

**Evidence implicating medications as a risk factor**

The evidence for drug-related falls comes from numerous small-scale studies, meta-analyses, systematic reviews and community-based case-control/cohort studies. There are no randomised control trials to produce evidence, as this would be unethical to carry out.

A meta-analysis by Leipzig et al pooling the results of 40 studies carried out between 1966–1996 indexed under ‘accidents/accidental falls’ and ‘aged/age factors’ revealed a small – but consistent – association between the most classes of psychotropic drugs and falls.

The pooled odds ratio for one or more falls was odds ratio (OR)1.73 for any psychotropic use, OR1.50 for neuroleptic use, OR1.54 for sedative/hypnotic use, OR1.66 for any antidepressant use, OR1.51 for only tricyclic antidepressant (TCA) use and OR1.48 for benzodiazepine use, with no difference between short and long-acting formulas. The evidence used in this meta-analysis was based solely on observational data and most of the studies evaluated did not take into account confounding factors at the time of fall. Subsequent studies have found confounders to provide a significant contribution to falls, thus this factor is a significant limitation in Leipzig’s meta-analysis.

Neutel et al produced figures in keeping with those by Leipzig while examining drug use and falls in an institutionalised population. The relationship between benzodiazepines and analgesics were statistically significant, but only when unadjusted for confounders. They found that residents starting a new (defined as a new prescription of the medication, or an increase in dose) benzodiazepine or antipsychotic were greatly at risk of having a fall and patients starting a ‘new’ drug of any class were at nearly twice as much at risk of having a fall within two days. Residents taking multiple drugs were also at particular risk of falling when compared with those taking less than five medications.

Narcotics, anticonvulsants and antidepressants were associated with a significant increased risk of an injurious fall, even after accounting for underlying medical conditions and confounders in one large community-based case-control study. This used 2,278 individuals presenting to any of six regional emergency departments in Alberta, Canada, classified by ICD-9 criteria as having an ‘injurious fall’. The strengths of the study included the selection bias being minimal, as all cases from the database were included and all individuals over 65 years of age residing in that area have premium-free health insurance. The limitations were that only falls related to emergency and hospital treatment were included and that non-prescription medications, alcohol or illicit drug use could not be accounted for. However, the statistically significant, positive association with the aforementioned medication classes adds strongly to the existing evidence base.

Other studies have examined associations between certain medications and hip fractures. A French study failed to show an association between benzodiazepine use and hip fracture when reviewing 245 institutionalised and community-dwelling persons admitted to hospital with hip fracture resulting from a fall. Use of the medication was assessed by a patient questionnaire, medical records and plasma assay. Hip fracture was associated with the use of two or more benzodiazepines as determined by the questionnaire and medical records, but not from plasma samples, therefore showing long-life benzodiazepines or increased doses are not risk factors. They did, however, confirm an increased
risk from TCAs but as this was not the main objective of their study, this relationship may be tenuous.

Wagner\textsuperscript{14} found an increased incidence of hip fracture in people over 65 years of age in 24 per cent of those exposed to benzodiazepines compared with those without exposure. This was after adjustment for confounding factors. They also found the incidence rate to be significantly higher within the first two weeks of starting a benzodiazepine, with the risk declining as time went on. This data adds strength to studies previously reported\textsuperscript{15–17}. Another finding in this large study controlling for multiple confounders was that an increased risk of hip fracture was associated with the use of short half-life high potency benzodiazepines but not low potency long half-life or mixed benzodiazepine exposure.

This is important as short half-life preparations are often considered to be the best choice of drug in this class for elderly patients. Evidence for this from previous studies is inconsistent\textsuperscript{18}. The publication by Wagner should be interpreted with the following potential limitations in mind:

> since exposure to benzodiazepines was inferred from pharmacy dispensing claims, it is therefore impossible to tell whether increased risk of fracture in the first two weeks was due to an increased compliance in this time period; and

> whether patients were actually taking their medications when the hip fracture occurred.

However, other studies were unable to confirm an association between benzodiazepines or anticonvulsants and falls/hip fracture\textsuperscript{18,19}.

Other classes of medications have also been investigated. Leipzig \textit{et al.}, published a second meta-analysis reviewing the role of cardiac and analgesic medications as an aetiological factor\textsuperscript{20}. Methodology and data sources are the same as for their previously mentioned study. Very few of the sources had adjusted for confounders, which are a possible limitation of their findings. However, out of 14 medication groups analysed, only the use of diuretics, digoxin and type 1A antiarrhythmics were associated with one or more falls. The pooled odds ratios for these classes were: diuretics OR1.08; digoxin OR1.22; type 1A antiarrhythmics OR1.59. They also found the use of more than three medications associated with an increased risk of recurrent falls. It is interesting to note that Pierfitte \textit{et al.}\textsuperscript{21} confirmed a protective effect from diuretics – as did Jones \textit{et al.}\textsuperscript{23} – although that was not the main objective of their study.

### Drug-related orthostatic hypotension

Diuretics can induce falls by causing hypovolemia, dehydration and subsequent orthostatic hypotension. TCAs, by virtue of

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**References**

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their anticholinergic and sedative properties, can potentially precipitate falls. The falls may be related to the underlying medical condition aggravated by these effects.

The role of orthostatic hypotension in this situation is debatable. Orthostatic hypotension does not appear to predict falls and this is due to a number of reasons. First, there is a large day-to-day variability in postural blood pressure readings and a frequent lack of associated symptoms. It is also difficult to ascertain whether patients were actually taking the medication thought to be responsible for falls secondary to postural hypotension at or around the time of postural hypotension.

**Methodological issues**

Having discussed the various studies, let us concentrate on some of the methodological issues in many of these studies. There appears to be lack of clarity in the way all the co-morbid conditions were recorded. The use of non-prescription drugs is difficult to assess or ascertain. Many studies were small scale and had a small sample size. There is also less clarity whether the medications were actually taken around the time of falls. Some were community-based studies, some were institution-based cohort case-controlled studies but there were no randomised controlled trials. There were innumerable confounding factors to adjust as well as a lack of an exact unit of reference in many studies (ie, did they take total falls or fallers as the outcome of interest). It is only fair to say the recall for falls in the older adult can be very misleading and a gross underestimate.

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