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The risk of falls and fractures associated with persistent use of psychotropic medications in elderly people

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ABSTRACT

The aim of this study was to examine the effect of psychotropic medications (antipsychotics, antidepressants, anxiolytics, hypnotics and sedatives) on the risk of falls and fractures in a cohort of elderly people in South Australia. A retrospective cohort study was undertaken using the wave 1 (1992) and wave 3 (1994) data of the Australian Longitudinal Study of Ageing (ALSA). Persistent use of psychotropic medicines was defined as use of one or more psychotropic medications at both wave 1 and wave 3. A comprehensive list of potential confounding variables was individually entered into regression models to examine effects on risk ratios. The results showed that the use of psychotropic medications was associated with an increased risk of falls in females (IRR = 1.47, 95% CI = 1.31–1.64) but not in males (IRR = 1.03, 95% CI = 0.85–1.26). The use of psychotropic medications was also associated with an increased risk of a fracture in females (RR 2.54; CI 1.57–4.11; $p < 0.0001$) but not in males (RR = 0.66; $p = 0.584$; CI 0.15–2.86). In both analyses, the body mass index (BMI) was determined to be the only confounding variable. After adjusting for BMI, the IRR in females decreased to 1.22 (95% CI 1.02–1.45; $p < 0.015$) for falls and the RR decreased to 1.92 ($p < 0.015$, CI 1.13–3.24) for fractures.

1. Introduction

Falls are common among older people and often result in fractures or other serious injuries. In Australia, around a third of people aged 65 years and over fall each year, with 10% having recurrent falls and over 30% experiencing injuries requiring medical attention (NARI, 2004). In 2003–2004, 60,497 fall injury incidents led to hospitalization among Australian people aged 65 years and older, corresponding to an age-standardized rate of 2.3% incidents per year (Bradley and Harrison, 2007). The rates of fall injury incidents were higher in the older age groups and in females. Two-thirds of the fall injury incidents were fractures and one third of these were hip or thigh fractures (Bradley and Harrison, 2007). The costs related to fall injuries are expected to rise steeply over the next 50 years as a result of the increase in the elderly population (NPHP, 2005a). The development of policies for fall prevention in the elderly population is an important priority of the National Injury Prevention and Safety Promotion Plan 2004–2014 and the National Falls Prevention for Older People Initiative (NPHP, 2005a,b).

Several predisposing factors have been shown to increase the risk of fall including arthritis, depressive symptoms, impairment in vision, cognition, psychological well-being, balance, gait or muscle strength (Tinetti, 2003; NARI, 2004; Anstey et al., 2006, 2008). Increased risk of falls has also been associated with use of psychotropic medicines. A systematic review of 40 studies showed that the pooled odds ratio for falls was 1.73 (95% CI 1.52–1.97) for any use of a psychotropic medicine (Leipzig et al., 1999). Another systematic review found that the risk of fractures among psychotropic drug users was moderate, ranging from a risk ratio (RR) of 1.15 (95% CI 0.94–1.39) for the hypnotics to 1.59 (95% CI 1.27–1.98) for the antipsychotics (Takkouche et al., 2007). Many of the studies reviewed had several limitations. Most did not evaluate confounders such as cognitive impairment. Most fall studies did not differentiate injurious from noninjurious falls.

This study examined in detail the effect of psychotropic medications (antipsychotics, antidepressants, anxiolytics, hypnotics and sedatives) on the risk of falls and fractures in a cohort of elderly people in South Australia taking into account potential important confounding variables. The latter were identified through a comprehensive search of previous studies and reviews on risk factors for falls and fractures and included so that the unique effect of psychotropic medication could be estimated independently of the contribution from other sources.

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2. Methods

The study utilized data from the ALSA. ALSA is a South Australian cohort study. The baseline data collection began in 1992 and enrolled 2087 people aged 65 years or over living in the Adelaide metropolitan area (Luszcz et al., 2007). Participants were followed-up across 8 waves over a 13-year period. Only data from waves 1 (1992) and 3 (1994) were used in this study because they involved full face-to-face interviews and clinical assessments and had the highest participation rates. Data collected included self-reported medical conditions, medication use, health service utilization, physical and psychological health, clinical measures and demographic information. Respondents were asked to report the names of all medicines that they had taken or were supposed to have taken in the previous 2 weeks.

Medications were classified according to the 2006 Anatomical Therapeutic Chemical (ATC) Classification system (World Health Organization 2003). Psychotropic medications included antipsychotics (N05A), antidepressants (N06A), anxiolytics (N05B) and hypnotics and sedatives (N05C).

The main study factor was persistent use of psychotropic medications. Persistent use was defined as use of one or more psychotropic medications at both wave 1 and wave 3. No use was defined as absence of use of any psychotropic medication at either wave 1 or wave 3. Subjects who used a psychotropic medication in either wave 1 or wave 3, but not in both, were excluded from the study.

The outcome variables were the number of falls in the 12 months preceding the wave 3 interview and one or more fractures caused by a fall at ground level or a spontaneous fracture in the 2 years preceding the wave 3 interview.

Variables available in the ALSA dataset which had been reported in the literature to alter the risk of falls or fractures were selected. These included age, gender, style of accommodation (community or residential aged care), body mass index (BMI, classified as underweight, average weight, overweight and obese), dizziness (yes or no), vision trouble (not at all or a little, moderately, a lot), abnormal gait (yes or no), mobility (good, average or poor), smoking (yes or no), alcohol intake (never, monthly or less, 2–4 times a month, 2–3 times a week, 4 or more times a week), cognitive function (impaired or normal), depressive symptoms (yes or no) and a number of self-reported medical conditions (arthritis, glaucoma, fractured hip, osteoporosis, Parkinson's disease, anemia, gout, corns and bunions, stroke/transient ischemic attack). Cognitive function was assessed by the Mini-Mental State Examination (MMSE) with a score of 24 or less indicating cognitive impairment. Depressive symptomatology was assessed using the Centre for Epidemiological Studies-Depression Scale (CES-D) with a score of 16 or more indicating depression. Medications other than psychotropic medicines which have been reported to alter the risk of falls and fractures were also examined. This included oral corticosteroids, proton pump inhibitors, beta-2 agonists (systemic and inhaled), thiazide diuretics, calcium, vitamin D, bisphosphonates, beta-blockers and hormone replacement therapy (HRT). Potential confounding variables were individually entered into the regression models to examine their effect on risk ratios. Confounding variables that were found to increase the risk ratio (RR) or incidence rate ratio (IRR) by 15% or more were included in the final analysis.

The Statistical Package for the Social Sciences (version 14, SPSS, Chicago, IL) was used to generate descriptive statistics including frequencies and cross-tabulations. Regression analyses were conducted using SAS version 9.1 (SAS Institute, Cary, NC, USA). The relationship between persistent use of psychotropic medicines and the number of falls was examined using a Poisson regression model stratified by gender and adjusted for confounding variables. Results were reported as IRRs. The relationship between persistent use of psychotropic medicines and fracture risk was examined using a log binomial generalized linear model stratified by gender and adjusted for confounding variables, and reported as RRs. Stratification by gender was undertaken as we hypothesized that gender was likely to be an effect modifier.

3. Results

A total of 1492 people were included in the study with 49.8% males. There were 1167 non-users and 325 persistent users of psychotropic medicines. This included 43 (13%) persistent users of antipsychotics (mostly prochlorperazine), 101 (31%) persistent users of anxiolytics (mostly diazepam and oxazepam), 135 (12%) persistent users of hypnotics (mostly nitrazepam and temazepam) and 105 (32%) persistent users of antidepressants (mostly tricyclic antidepressants).

Characteristics of people are presented in Table 1. Compared to non-users, persistent users of psychotropic medicines were more likely to be female (61.5% vs. 46.6%), older (78.5 years vs. 77.1 years), living in residential aged care (9.2% vs. 2.6%), experiencing dizziness (41.5% vs. 20.1%), poor mobility (23.7% vs. 12.5%), cognitive impairment (17.2% vs. 11.6%), and reporting arthritis (63.4% vs. 49.4%), cataract (53.4% vs. 23.2%), history of stroke or transient ischemic attack (16.6% vs. 8.6%).

A total of 540 people (36.2%) fell at least once in the 12 months preceding the wave 3 interview. The mean number of falls was 2.5 ± 6.3 ($\pm$S.D.) in non-users vs. 3.4 ± 9.9 in persistent users. Gender was found to be a strong effect modifier with a significantly increased risk for female persistent users of psychotropic medications (IRR = 1.77; 95% CI = 1.54–2.05; $p < 0.0001$) but not for male users (IRR = 1.03; 95% CI = 0.85–1.26; $p = 0.72$). BMI was found to be the only confounding variable. After adjusting for BMI, the IRR in the female group decreased to 1.22 (95% CI = 1.02–1.45; $p < 0.015$). Females in the underweight BMI group and the obese BMI group were both at higher risk of frequent falling than those in the normal and overweight categories (Table 2).

The number of people who reported sustaining a fracture as a result of a fall at ground level or a spontaneous break was higher among persistent users (9.5%) than in non-users (3.9%) of psychotropic medications. Gender was found to be a strong effect modifier with a significant increased risk in female users (RR = 2.54; CI = 1.57–4.11; $p < 0.0001$) but not in male users (RR = 0.66; $p = 0.584$; CI = 0.15–2.86). BMI was again found to be the only confounding variable. After adjusting for BMI, the RR in females decreased to 1.92 ($p < 0.015$, CI = 1.13–3.24). The highest fracture risk was observed in females with an underweight BMI compared to normal, overweight and obese females (Table 2).

4. Discussion

Our results show that the persistent use of psychotropic medicines is associated with a significantly increased risk of falls and fractures in elderly women. This effect of psychotropic medicines is consistent with the results of previous studies (Leipzig et al., 1999; Takkouche et al., 2007). It may be partially mediated through the psychomotor effects of psychotropic medicines such as dizziness and postural disturbances, given that persistent users of psychotropic medicines in our study were more likely to suffer from dizziness than non-users (41.5% vs. 20.1%). However, the risk of falls and fractures was significantly increased in women but not in men. Studies on risk of fall-related injuries among older adults generally agree that the risk is higher in females than in males and that may be explained by other fracture-related factors such as osteoporosis that is more frequent in women than in men (Bradley and Harrison, 2007). Previous reports