Psychotropic Medications and Risk for Falls Among Community-Dwelling Frail Older People: An Observational Study

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Background. Injuries due to falls are one of the most important public health concerns for all ages, but especially for frail elderly people. Although a small number of falls have a single cause, the majority have many different causes resulting from the interactions between intrinsic or extrinsic risk factors.

Methods. We conducted an observational study on data from a large population of community-dwelling elderly people to test the hypothesis that the current use of different classes of psychotropic medications, including antipsychotic agents, benzodiazepines, nonbenzodiazepine sedative-hypnotics, and antidepressants, increases the risk for falls. We analyzed data from a large collaborative observational study group, the Italian Silver Network Home Care project, that collected data on patients admitted to home care programs (n = 2854).

Results. After adjusting for all potential confounders, users of any psychotropic drugs had an increased risk of fall of nearly 47% (adjusted odds ratio [OR], 1.47; 95% confidence interval [CI], 1.24–1.74). Similarly, compared with nonusers, users of atypical antipsychotic drugs also had an increased risk of falling at least once (OR, 1.45; 95% CI, 1.00–2.11). Among benzodiazepine users, patients taking agents with long elimination half-life (OR, 1.45; 95% CI, 1.00–2.19) and patients taking benzodiazepines with short elimination half-life (OR, 1.32; 95% CI, 1.02–1.72) had an increased risk of falls. Patients taking antidepressants did not show a higher risk of falling compared to nonusers (OR, 0.92; 95% CI, 0.83–1.41).

Conclusions. Our data suggest that, among psychotropic medications, antipsychotic agents and benzodiazepines are associated with an increased risk of falls. Our findings do not support the hypothesis that preferential prescribing of short-acting benzodiazepines instead of long-acting agents or atypical antipsychotic medications instead of typical agents will substantially decrease fall risk associated with the use of these classes of drugs.

Falls and their related injuries represent one of the major health service problems among the elderly population. Falls are responsible for considerable immobility, morbidity, and mortality among elderly people (1,2). In the United States and other Western countries, it has been estimated that 35%–40% of community-dwelling older people fall each year, and half of these people have more than one fall. For those individuals older than 75 years, the rates are higher (3). In addition to causing pain and distress, falls among older people are so common that they constitute a major part of health care costs. According to recent studies, about 6% of all medical expenditures for elderly persons in the United States are due to fall-related injuries (4). Hospitalization is needed in 5% of elderly people who fall (5,6).

Although some falls have a single cause, the majority have many different causes resulting from the interactions between intrinsic (e.g., functional impairment or balance disorders) or extrinsic risk factors (e.g., adverse drug reaction or environmental hazard) (3,7,8). Several studies (9–11) have documented that there is a relation between falling and the number of drugs used. However, the risks associated with the individual classes of medications have been more variable. The use of psychotropic drugs, such as benzodiazepines, antidepressants, neuroleptics, and anticonvulsants, has been previously identified as a risk factor for falls (9–11). Older people are more vulnerable to the neurological side effects of these medications because of the changes in their pharmacokinetics and pharmacodynamics related to aging (12). However, not all these medications follow the same metabolic pathway in the human body. The association between newer psychotropic medications (such as short-acting benzodiazepines, atypical antipsychotic agents, or selective serotonin-reuptake inhibitors [SSRIs]) and risk of falls among community-dwelling frail elderly people is still unclear (13).

We conducted an observational study on data from a large population of community-dwelling elderly people to test the hypothesis that the current use of different classes of psychotropic medications, including antipsychotic agents, benzodiazepines, nonbenzodiazepine sedative-hypnotics, and antidepressants, increases the risks for falls.
METHODS

Participants

This study used data from the database of the national home care program named Silver Network Home Care project in Italy (14). The database has been described in detail elsewhere (14) and is briefly summarized here. This is a population-based, longitudinal, multilinked database that comprises: a) data collected with Minimum Data Set for Home Care (MDS-HC) (12) on patients in more than 20 home health agencies in Italy, and b) data on all the medications used by each patient at the time of the MDS-HC assessment. Drugs were coded using the Anatomical Therapeutic Chemical (ATC) codes.

The study population consisted of all patients admitted to home care programs in 22 home health agencies from 2000 through 2002 who participated in the national Silver Network Home Care project (n = 2914). Sixty patients (2.1%) were considered not eligible for the study due to comatose status (n = 2), paraplegia (n = 16), or terminal illness (n = 42). As a result, the final analysis sample consisted of 2854 patients.

MDS-HC Assessment Data

The MDS-HC assessment form (15) contains over 350 data elements including sociodemographic variables, numerous clinical items about both physical and cognitive status, as well as all clinical diagnoses. The MDS-HC form also includes information about an extensive array of signs, symptoms, syndromes, and treatments being provided (16). Among others, two summary scales based on MDS-HC items are designed to describe the performance in personal Activities of Daily Living (ADLs), and the level of cognitive function (Cognitive Performance Scale; CPS) (17). The MDS items have been found to have excellent interrater and test–retest reliability when completed by nurses performing usual assessment duties (average weighted Kappa = 0.8) (17,18). Data elements contained in the Silver Network Home Care database used in this study have been previously validated (14), making it a reliable research tool for pharmacoepidemiology (19,20).

Assessment of Falls

A multidisciplinary team of professionals (general practitioner, nurses, and geriatrician) evaluated fall history during the MDS-HC assessment. The assessors were instructed to ask simple and direct questions about whether the patients experienced falls. According to the MDS-HC manual (15), the “fall event” was considered to be a sudden loss of balance causing the contact of any part of the body above the feet with the floor; the event had to occur within 90 days of assessment. Independent, dual assessment of falls in a diverse sample of nursing home patients during the testing and revision of the MDS showed that the interrater reliability for fall assessment was excellent (weighted kappa correlation coefficient = 0.90) (18).

Use of Psychotropic Medications

Information on patients’ use of four mutually exclusive categories of psychotropic drugs (antipsychotics, antidepressants, benzodiazepines, and nonbenzodiazepine sedative-hypnotics), collected directly by general practitioners, were considered in the analysis.

Antipsychotic agents were further classified as typical or atypical. Typical antipsychotic drugs included promazine, perphenazine, chlorpromazine, thioridazine, fluphenazine, and haloperidol; atypical antipsychotic medications included clozapine, risperidone, olanzapine, and quetiapine.

Antidepressants were classified as tricyclic agents (amitriptyline, imipramine, clomipramine, desipramine, nortriptyline, and trimipramine), SSRIs (citalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline), and serotonin antagonist and reuptake inhibitors (SARIs; trazodone).

Benzodiazepines were classified into two different groups according to their metabolic pathway. The short elimination half-life agents (<24 hours) were alprazolam, bromazepam, lorazepam, brotizolam, etizolam, estazolam, triazolam, and temazepam; the long-acting benzodiazepines (>24 hours) included chlordiazepoxide, delorazepam, diazepam, flurazepam, ketazolam, prazepam, quazepam, lorzetamazep, and oxazepam. Nonbenzodiazepine sedative-hypnotic agents included zopiclone, zolpidem, and zaleplon.

Statistical Analysis

Data were analyzed first to obtain descriptive statistics. Continuous variables are presented as mean values ± standard deviation. Differences in sociodemographic, functional, and clinical characteristics between patients who did and did not fall were analyzed in different ways. Quantitative outcomes were tested using Student’s t test after a pretest for homogeneity of variance. The Mann–Whitney U test was used for cases in which the normality assumption was not reasonable. Categorical variables were analyzed by using Fisher’s exact test.

We estimated the relationship between each group of psychotropic medications and risk of fall by deriving odds ratios (ORs) from multiple logistic regression models in which the dependent variable of interest was at least one fall in the last 90 days. For all of the analyses, the reference group for drug exposure consisted of patients who were not using psychotropic medications. Age, sex, comorbidity, number of medications, depression, and indices of functional ability (ADL score) and cognitive performance (CPS score) were considered to be potential confounders. Furthermore, conditions associated with a higher falling risk (foot problems, wandering, gait problems, and fear of falling) were considered in the analysis. Variables showing significant differences (p < .05) between the control group and the group with positive anamnesis for falls were included in the final logistic regression model. From this final model, we derived ORs and corresponding 95% confidence intervals (CIs). Statistical analyses were performed using SPSS software (SPSS, Chicago, IL).

RESULTS

The principal characteristics of the study population are shown in Table 1. Patients were Caucasian, predominantly female (58%), and had a mean age of 77.2 ± 12.1 years. More than 60% of the individuals were aged 75 years or older. Overall, patients had moderate to severe impairment in basic ADLs; similarly, cognitive function was compromised...
in a large number of patients (more than 30% showed a CPS score more than 2, indicating moderate to severe cognitive impairment).

A 37% falls prevalence was found within 90 days of the patient assessment through the MDS-HC instrument. Patients with a positive anamnesis for falls were older than patients included in the control group (78.8 years vs 76.2 years, respectively; \( p < .001 \)). They also had a higher dependency in ADLs (ADL score 4.7 vs 4.3, respectively; \( p < .001 \)), but a lower CPS score (4.4 \pm 2.2 vs 4.7 \pm 2.5, \( p < .001 \)).

The relationship between antipsychotic drug use and the increased risk of falls in elderly persons may be related to the underlying medical condition for which the drug was prescribed or to the side effect of the drug on gait and balance.

### DISCUSSION

The major finding of the present study is that current use of antipsychotic agents or benzodiazepines was associated with an increased risk of falls in our cohort of older community-dwelling patients. In contrast, we found no evidence of an association between risk of falls and current use of antidepressants and nonbenzodiazepine sedative-hypnotic drugs. Our findings indicate that the increase in fall risk of patients taking antipsychotic drugs is not substantially reduced by the use of the newer atypical medications such as clozapine, risperidone, olanzapine, and quetiapine. Similarly, the present data suggest that the preferential use of benzodiazepines with short elimination half-life is unlikely to reduce fall risk among older persons taking benzodiazepines. Finally, an interesting finding was the strong association between falls and depression, but not antidepressants.

After adjusting for all potential confounders, we found that users of any of psychotropic drugs had an increased risk of falls of nearly 47% (adjusted OR, 1.47; 95% CI, 1.24–1.74). Table 2 shows the association between current use of psychotropic medications and risk of falling. Compared with nonusers, users of typical antipsychotic drugs had an increased risk of falling (adjusted OR, 1.49; 95% CI, 1.10–2.51); similarly, users of atypical antipsychotic drugs had an increased risk of falling (adjusted OR, 1.45; 95% CI, 1.00–2.11). Among benzodiazepine users, those patients taking agents with long elimination half-life had an increased risk of falling (adjusted OR, 1.45; 95% CI, 1.00–2.19); similarly, patients taking benzodiazepines with short elimination half-life had an increased risk for falling (adjusted OR, 1.32; 95% CI, 1.02–1.72).
postural stability (21–23). Many studies (11,24) have documented that patients taking antipsychotic medications have balance problems, gait instability, and impaired performance on reaction time and other sensorimotor functions. In particular, antipsychotic drugs are well known to produce rigidity and extrapyramidal symptoms (25). In this respect, it is important to underline that, although our results are in contrast with many studies demonstrating that the clearest advantage of new atypical antipsychotic drugs is the reduced risk of extrapyramidal side effects (26,27), they are in accordance with the recent meta-analysis showing that such medications are not associated with the onset of significantly fewer extrapyramidal symptoms (28).

The use of benzodiazepines has been also identified as one of the most important risk factor for falls among elderly adults (29–31). Ataxia, drowsiness, dizziness, postural disturbances, and impaired motor coordination (common adverse effects of benzodiazepines) increase the risk of falling (32). Furthermore, older people are more vulnerable to the psychomotor effects of benzodiazepines because of the changes in their pharmacokinetics and pharmacodynamics related to aging (30). Although some authors have demonstrated that the use of long half-life benzodiazepines is associated with increased risk of hip fracture (29,31), another found no increased risk (33). For example, Danjou and colleagues (34) demonstrated that benzodiazepines with a short half-life (e.g., alprazolam) and those with a long half-life (e.g., diazepam) impair the psychomotor performance to the same degree. In contrast, in another study (35), quazepam, a long-acting benzodiazepine, had a more prolonged effect on functional performance than did a short half-life agent (alprazolam). In this respect, it is important to emphasize that our results indicate that the risk for falls may be only slightly lower among persons taking benzodiazepines with short elimination half-life than among those persons taking long-acting agents. It is interesting that this finding is similar to that presented in a recent meta-analysis (9) demonstrating that the use of benzodiazepines increased the risk of falling in older persons independently of drug elimination half-life.

Some limitations of our study need to be recognized. First, the association between specific psychotropic medications and falls may simply reflect an intrinsic excess risk of the patients receiving them. However, because of the use of the MDS-HC, a multidimensional assessment instrument, the present study could comprehensively investigate the different domains of elderly status influencing the risk of falling. For this reason, and to permit an analysis considering the largest number of potential confounders, we incorporated in our model a whole series of variables, including measures of cognitive performance, functional status, and comorbid conditions, and these did not affect the association. Nevertheless, residual confounding is always possible. Second, we did not distinguish between different doses of psychotropic agents and the risk of falls. Although this warrants additional studies, we were interested in characterizing the impact of psychotropic medications use itself on the risk of falling. Finally, a more critical consideration is that the patients studied were only those considered to be eligible for home care programs, indicating that a health problem existed (36). In this respect, we are not authorized to extend the results to all community-dwelling elderly individuals.

Despite these methodological problems, our data suggest that, among psychotropic medications, antipsychotic agents and benzodiazepines are associated with an increased risk of falls. These data do not support the hypothesis that preferential prescribing of short-acting benzodiazepines instead of long-acting agents, or atypical antipsychotic medications instead of typical agents, will substantially decrease fall risk associated with the use of these classes of drugs. In conclusion, minimizing the use of these central nervous system active medications may decrease the risk for falling. In the future, to provide more definitive information, clinical trials testing the effects of psychotropic medications should include data on the risk of falls.

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