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Original article

Impact of different drug classes on clinical severity of falls in an elderly population: Epidemiological survey in a trauma center

Francesca Montali, PhD [a], Giovanna Campaniello, MD [a], Mario Benatti, MD [b], Gianni Rastelli, MD [c], Mario Pedrazzoni, MD [d], Gianfranco Cervellin, MD [b,*]

[a] Clinical Governance, Risk Management, Quality and Accreditation Unit, Academic Hospital of Parma, Parma, Italy
[b] Emergency Department, Academic Hospital of Parma, Parma, Italy
[c] Emergency Department, Hospital of Vaio, Fidenza, Italy
[d] Department of Internal Medicine, University of Parma, Parma, Italy

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ABSTRACT

Purpose: Certain classes of drugs have been associated with the risk of falls in elderly individuals. The aim of this study was to evaluate the impact of several classes of drugs on fall-related injuries in individuals aged 65 years or older.

Methods: Data on all the emergency department (ED) visits for trivial falls during the year 2013 were retrieved from the database of the Academic Hospital of Parma. The individual reports of the visits were analyzed to evaluate where and how the patient fell, the drugs currently taken, the type, and severity of injury.

Results: A total of 2533 visits for trivial falls in patients aged 65 years or older were analyzed. We found a significant positive correlation between age and total number of drugs ($r = 0.063$; $p < 0.03$), but no correlation between the number of ED visits for trivial falls and the number of drugs ($r = 0.001$; $p < 0.984$). Anticoagulants [odds ratio (OR), 1.59; 95% confidence interval (CI), 1.22–2.07], antiplatelets (OR, 1.41; 95% CI, 1.12–1.79), and narcotic analgesics (OR, 2.38; 95% CI, 1.23–4.62) were predictors of hospital admission. Antiplatelets (OR, 2.02; 95% CI, 1.56–2.62), anticoagulants (OR, 1.89; 95% CI, 1.141–2.55), antihypertensive (OR, 1.44; 95% CI, 1.08–1.93), and psychotropic drugs (OR, 1.93; 95% CI, 1.09–3.44) were predictors of traumatic brain injury. Other classes of drugs were not related to any of the considered outcomes.

Conclusions: To reduce the risk of falling in elderly patients, a major focus should be placed on optimization of antihypertensives, narcotic analgesics, and psychotropic drugs administration. The risk-to-benefit ratio of anticoagulants and antiplatelet drugs should be individually tailored, to minimize the risk of adverse outcome of falls.

1. Introduction

Falls are a major public health concern. It has been estimated that more than 400,000 fatal falls occur each year worldwide, which makes them the second leading cause of death due to accidental injury, only preceded by road traffic collisions.[1] Even when nonlethal, falls are associated with negative health outcomes, leading to 20–30% of mild to severe injuries, from soft-tissue injuries to fractures.[2,3] Each fall also carries several negative psychosocial consequences such as reduced physical activity,[4] at least partially due to the fear of falling,[2,3] thus resulting in a global impairment of the quality of life.[5] As such, even when nonfatal in the short term, falls are often followed by functional limitations, high health-care costs, along with high mortality on the medium term.[6,7]

Many people have an increased risk of fall with aging, and this is attributable to a variety of reasons, including impaired vision, dizziness, musculoskeletal diseases, malnutrition, gait problems, parkinsonism, and cognitive impairment.[8–11] Environmental

* Corresponding author. U.O. Pronto Soccorso e Medicina d'Urgenza, Azienda Ospedaliero-Universitaria di Parma, Via Gramsci, 14, Parma 43126, Italy.
E-mail address: gcervellin@ao.pr.it (G. Cervellin).

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barriers are also responsible for a considerable burden of falls, often interacting with increased individual susceptibility.[8] Notably, the underlying mechanisms leading to fall remain largely unrecognized.[12] Moreover, there is a large overlap between syncope and falls, which makes an etiological diagnosis even more difficult.[13]

Despite a number of methodological difficulties in establishing these relationships, certain classes of drugs have been associated with the risk of falls,[14,15] especially narcotic analgesics,[16,17] psychotropic drugs,[18–22] antihypertensives,[23] antidiabetics,[24] and polypharmacy (i.e., more than four medications).[25,26] Falls in patients taking anticoagulant drugs have also been associated with a greater mortality,[27] especially when associated with other fall-risk medications.[28]

Based on the aforementioned data, the Swedish National Board of Health and Welfare has produced a "fall-risk-increasing drugs" list, as well as a list of drugs causing or worsening orthostatic blood pressure. The two lists of drugs, obviously, partially overlap.[29] This tool can help in decision making when prescribing drugs in frail elderly individuals.

The purpose of this study was to evaluate the impact of several classes of drugs on the type and severity of falls injuries in patients aged 65 years or older admitted to a large emergency department (ED) of a level 2 trauma center in northern Italy.

2. Materials and methods

Data on all the ED visits during the year 2013 for domestic or trivial falls were retrieved from the database of the ED of the Academic Hospital of Parma, with exclusion of injuries related to sports, car accidents, and all high-energy trauma. We considered the falls as "trivial" if they were not associated with high-energy features, such as accidents, hit pedestrians, and fall from 1.5 m or more.

Furthermore, we identified all falls that occurred in hospitalized patients using the incident-reporting database, and selected data regarding patients admitted for a previous fall in the same year.

The Academic Hospital of Parma is a 1250-bed teaching general hospital, located in the Province of Parma (approximately 447,000 inhabitants). The hospital is a Level 2 trauma center, and a referral center for stroke and myocardial infarction. According to our study design, only patients aged 65 years or older were included in this analysis. The individual reports of the visits were analyzed separately to evaluate where and how the patient fell, the drugs currently taken, the type of injury, the need for hospitalization, and the ward of admission (i.e., medicine/geriatrics, orthopedics, neurosurgery).

In a first step, with the aim of searching for the impact of polypharmacy on falls, we have classified the patients according to the number of drugs currently taken. The second step was to separately analyze the influence of different classes of drugs commonly believed to be a potential concurrent cause of falls, that is, diuretics and antihypertensives, psychotropic drugs, antidiabetic agents, anticonvulsants, antiarrhythmics, and narcotic analgesics. Anticoagulants and antiplatelet agents were separately considered, due to their correlation with the clinical outcomes rather than the falls themselves. All drugs not belonging to the aforementioned classes were classified as "miscellaneous agents."

2.1. Statistical analysis

The characteristics of the patients including age, sex, number of visits to ED for fall during the study period, type of injury, and number of drugs identified in patient's history were descriptively expressed as frequencies, percentages, and mean ± standard deviation (SD). The statistical analysis included Mann–Whitney test, χ^2 test, and Pearson correlation coefficient. The distribution of the falls rate was analyzed with Pearson χ^2 statistic. In particular, the associations between sex (dichotomous variable), severity of injury, and number of drugs taken (continuous variables) have been compared through the Mann–Whitney test. The associations between the continuous variables such as age, severity of injury, and number of drugs taken have been verified through the Pearson correlation test.

Besides, the associations between dichotomous variables (consumption of four or more drugs) and the presence/absence of severe outcome (hospital admission, brain injury, and hip fracture) have been verified through the χ^2 test.

For the purposes of this study, the injuries were classified into a simplified model as follows: (1) hip fractures; (2) traumatic brain injury; (3) others, including minor fractures, contusions, and skin abrasions and lacerations. To determine whether the assumption of certain drugs was significantly associated with the risk of hip fractures, brain injuries, major trauma, and hospital admission, a logistic regression analysis was performed to calculate the adjusted odds ratios (ORs) and the 95% confidence intervals (CIs). For each of the considered outcomes (i.e., hospital admission, traumatic brain injury, and hip fracture), a multiple logistic regression analysis was performed, including all drugs categories [antihypertensive, diuretics, psychotropic drugs, antiplatelets, anticoagulants, antiarrhythmic drugs, proton-pump inhibitors (PPIs), statins, antidiabetic agents, thyroid drugs, nitro derivatives, osteoporosis medications, narcotic analgesics, anticonvulsants, and miscellaneous agents]. Subsequently, the ORs were adjusted for age and sex.

All statistical analyses were performed with SPSS software (version 17.0; SPSS Inc., Chicago, IL, USA) and Analyse-it (Analyse-it Software Ltd, Leeds, UK). A p value less than 0.05 was considered statistically significant.

3. Results

A total of 93,029 ED visits were recorded during the year 2013. During the study period, 2533 visits were related to trivial falls in 2377 patients aged 65 years or older (i.e., 2.7% of the total visits), occurring at home or in nursing home. During the same period, 2229 patients (87.4%) visited the ED for a fall only once, whereas 139 patients visited two times (5.5%), eight patients three times (0.3%), and one patient four times. Accordingly, the ED recorded 2533 visits for the 2377 patients. For 1280 cases, a thorough drug therapy history was available. The mean age of the eligible patients was 81.2 ± 8.02 years. Overall, female patients accounted for 1843 visits (72.8%) and male patients accounted for 690 visits (27.2%), respectively. In both patient groups, the absolute number of visits for falls increased with the age, peaking in the 80–84-year age group and then progressively decreasing in older ages. Nevertheless, when the number of falls was related to the actual number of residents by age groups, female patients displayed a continuous increase [Pearson χ^2 statistic 825; degrees of freedom (DF) = 8; $p < 0.001$ for trend], peaking at age over 100 years; male patients also displayed a continuous increase, but the peak was reached between 95 and 99 years (Pearson χ^2 statistic 716; DF = 8; $p < 0.001$ for trend).

A total number of 756 (i.e., 28.1%) patients needed hospitalization, 463 of whom were admitted to the orthopedic ward due to fractures, and 277 to the medical wards (including geriatrics, cardiology, and neurology) due to nonsurgical brain injury, abdominal or chest trauma, or comorbidity. Ten patients were admitted to the neurosurgical unit for acute subdural hematoma; two patients to the maxillofacial surgery unit for severe facial injuries, two patients to the thoracic surgery unit for severe chest trauma, two to the

intensive care unit for multiple severe injuries. Eight patients (1.1%) fell once more during the hospital stay.

Because of the greater prevalence of falls among women, the need for hospitalization was overall higher in the female group (505 vs. 251).

Overall, more than half ($n = 1458$; 61.3%) of the patients in ED for a trivial fall reported a severe injury (i.e., a fracture, a brain injury, a chest trauma, a multiple trauma). Among these 19.1% ($n = 453$) and 15.6% ($n = 371$) had a traumatic brain injury and a femur neck fracture, respectively (Table 1). Only one patient died while in ED. Female sex was associated with more severe fall-related injuries ($\chi^2 = 13.653$; $p < 0.0001$). Age also has shown to be a significant risk factor for severe injury, with a significant positive correlation between age and severity of injury (Pearson $r = 0.128$; $p < 0.001$).

The drug therapy of the 1280 patients for whom a thorough history was available is shown in Table 2. The patients were taking an average of 3.3 drugs (range, 1–14; SD = 2.6), and only 17.4% of the total patients were taking four or more different drugs. In Table 3, the drugs detected upon evaluating the history of patients are classified as follows: antihypertensives (41.4%), antiplatelets (21.1%), psychotropic drugs (15.8%), anticoagulant drugs (12.2%), PPIs (9.5%), statins (5.7%), antidiabetic agents (4.6%), thyroid/antithyroid drugs (3.1%), nitroderivatives (2.5%), osteoporosis medications (1.9%), narcotic analgesics (1.6%), anticonvulsants (1.4%), and miscellaneous agents (13.9%).

The total number of drugs was similar in both men and women (Mann–Whitney $U = 130{,}497.5$; $p = 0.348$). At variance, we found a significant positive correlation between age and total number of drugs (Pearson $r = 0.063$; $p < 0.03$). However, we found no correlation between the number of ED visits for trivial falls and the number of drugs in history (Pearson $r = 0.001$; $p = 0.984$). The χ^2 test indicated that the cutoff of four drugs was not related to any severe outcome considered (hospital admission, brain injury, and hip fracture).

Multiple logistic regression analysis showed a significant correlation between some drug groups and fall-related outcomes. Three drug classes were identified as predictors of hospital admission in the logistic regression analysis: anticoagulants (OR, 1.59; 95% CI, 1.22–2.07), antiplatelets (OR, 1.41; 95% CI, 1.12–1.79), and narcotic analgesics (OR, 2.38; 95% CI, 1.23–4.62; Table 4).

Four drug classes were identified as predictors of traumatic brain injury in the logistic regression analysis: antiplatelets (OR, 2.02; 95% CI, 1.56–2.62), anticoagulants (OR, 1.89; 95% CI, 1.141–2.55), antihypertensive (OR, 1.44; 95% CI, 1.08–1.93), and psychotropic drugs (OR, 1.93; 95% CI, 1.09–3.44; Table 5).

No drug was found to be a significant predictor of hip fracture. Statins, PPIs, antiarrhythmics, antidiabetic agents, thyroid drugs, nitroderivatives, and anticonvulsants were not related to any of the considered outcomes.

4. Discussion

Certain classes of drugs have been associated with the risk of falls in the elderly patients. The aim of this study was to evaluate the impact of several classes of drugs on falls injuries in patients aged 65 years or older. A total of 2533 visits for trivial falls in patients aged 65 years or older were analyzed, and a significant positive correlation between age and total number of drugs, but no correlation between the number of ED visits for trivial falls and the number of drugs was found. Anticoagulants, antiplatelets, and narcotic analgesics were predictors of hospital admission, whereas antiplatelets, anticoagulants, antihypertensive, and psychotropic drugs were predictors of traumatic brain injury. Other classes of drugs were not related to any of the considered outcomes.

Several factors have been associated with the risk of falling in elderly patients. Gait instability has been identified as a relatively consistent risk factor for falls,[30] and inactivity and comorbidity are strong predictors for falls in older individuals compared with active, ostensibly healthy age-matched controls.[31] Some underlying

Table 1
Demographic characteristics and types of fall-related injuries.

Demographic characteristics and type of injury	*N*	%
Female patients	1843	72.8
Male patients	690	27.2
Traumatic brain injury	453	19.1
Hip fracture	371	15.6
Others	1896	79.8
Needing hospital admission	756	28.1
Total patients	2377	100.0

Table 2
Total number of medications assumed by people aged 65 years and older.

Drugs currently taken by patients	*N*	%
1	458	18.1
2	135	5.3
3	129	5.1
4	131	5.2
5	94	3.7
6	64	2.5
7	57	2.3
8	31	1.2
9	34	1.3
10	11	0.4
11	10	0.4
12	5	0.2
13	2	0.1
14	2	0.1
Unquantified drug therapy	117	4.6
Drug therapy not detected	1253	49.5
Total	2533	100.0

Table 3
Classes of drugs taken by the patients.

Drugs	*N*	% [a]
Antihypertensives		
ACE inhibitors	326	12.9
Diuretics	264	10.4
Beta-blockers	194	7.7
Calcium-channel blockers	145	5.7
Other antihypertensive	119	4.7
Psychotropic drugs		
Antidepressants	178	7.0
Benzodiazepines	149	5.9
Antipsychotics	74	2.9
Antiplatelets drugs		
Aspirin	436	17.2
Clopidogrel	84	3.3
Other antiplatelets	16	0.6
Anticoagulant drugs		
Oral anticoagulants (VKA)	275	10.9
Enoxaparin	32	1.3
Antiarrhythmics	55	2.2
Proton-pump inhibitors	240	9.5
Statins	144	5.7
Antidiabetic agents	117	4.6
Thyroid drugs	79	3.1
Nitroderivatives	63	2.5
Osteoporosis medications	49	1.9
Narcotic analgesics	40	1.6
Anticonvulsants	36	1.4
Miscellaneous agents	353	13.9
Total [a]	2533	100

ACE = angiotensin-converting enzyme; VKA = vitamin K antagonists.
[a] 2533 refers to the number of patients, not to the number of falls-related visits.

Table 4
Relation between drugs use and hospital admission.

Outcome: Hospital admissions						
Drugs use, *N* (%)		Falls leading to hospital admission ($n = 712$)	Falls not leading to hospital admission ($n = 1821$)	*p*	Adjusted OR	95% CI
		N (%)	*N* (%)			
Anticoagulants	Yes	116 (16.3)	191 (10.5)	0.001	1.592	1.224–2.070
	No	596 (83.7)	1630 (89.5)			
Antiplatelets drugs	Yes	178 (25.0)	335 (18.4)	0.004	1.411	1.115–1.786
	No	534 (75.0)	1486 (81.6)			
Narcotic analgesics	Yes	21 (2.9)	19 (1.0)	0.010	2.379	1.225–4.618
	No	691 (97.1)	1802 (99)			

CI = confidence interval; OR = odds ratio.

medical conditions, such as stroke and arthritis, are also recognized risk factors for falls.[32–34]

The results of our study show that falls represent an important cause of morbidity in elderly patients in a medium-size province in northern Italy, representing up to 2.7% of the whole ED workload, and up to 13.3% of the visits for patients aged 65 or older.

Older people not only consume more medication than younger ones, but also represent a group at higher risk of adverse effects, including falls. Indeed, several drugs clearly associated with risk of falling (i.e., psychotropic drugs, antihypertensive drugs, narcotic analgesics, or multiple medications)[23,35–37] require a more rational approach in their use.

Overall, a weaker association was found between falls and antihypertensive drugs, and this is clearly attributable due to the different characteristics of the medications.[38,39] In fact, loop diuretics are associated with a higher risk,[40,41] thiazide diuretics with a lower risk,[38] and angiotensin-system-blocking medication may even be protective.[42] In some studies, a peak of risk has been observed in the 1st week of therapy.[43,44] In our study we were not able to establish when the therapies were initiated, and this may represent a limitation.

One more limitation of this study is the lack of data regarding comorbidities. Unfortunately, these data were not fully available in the ED database, and we think that this should be an aim of further research.

Some explicit criteria have been identified to help determine the inappropriate use of medication in elderly patients.[45] A group of French researchers also showed that the use of inappropriate medications was associated with an increased risk of falling in elderly persons, in particular long-acting benzodiazepines, other psychotropics, and medications with anticholinergic properties.[46] In a large Irish ED, a significant prevalence of potentially inappropriate prescription was observed in older fallers, and no substantial improvements in prescription occurred in the 12 months after the falls, suggesting the need for focused intervention studies.[47]

Notably, a Finnish study demonstrated that a one-time counseling by a geriatrician had positive effects in decreasing the number of regular users of benzodiazepines and related drugs, which persisted for the total 12-month intervention period.[48] Similarly, a Dutch study showed that withdrawal of fall-risk-increasing drugs was effective as a single intervention for falls prevention in a geriatric outpatient setting.[49]

It is noteworthy that falls and fractures have shown to increase anxiety and depression in elderly patients, thus leading to further prescription of benzodiazepines and antidepressants, and creating a vicious circle toward an even greater risk of falls and fractures.[50]

In contrast to previous studies,[25,26] we failed to find a significant correlation between the number of ED visits for trivial falls and the number of drugs in history. Moreover, the cutoff of four drugs seems to be unrelated with any severe outcome considered (i.e., hospital admission, brain injury, and hip fracture) in our study population. Similarly, we found no correlation between PPI and risk of falling or fall-related injuries, which is at odds with the recent findings of Lewis et al.[51]

By contrast, and quite surprisingly considering the high prevalence of fractures, only 46 of our patients were taking drugs for osteoporosis (i.e., calcium, vitamin D, and bisphosphonates). This is noteworthy, as it has been demonstrated that fallers have lower vitamin D values than nonfallers, and this may help identify those patients who would potentially benefit from vitamin D supplementation.[52]

Considering the social and economic burden of such a high rate of hospitalization for falls, preventive strategies should be planned to improve gait ability through exercise programs, general and bone health through adequate dietary programs and drug delivery. In particular, a major focus should be placed on optimization of antihypertensives, narcotic analgesics, and psychotropic drugs administration, to minimize the risk of falls. Moreover, the risk-to-benefit ratio of anticoagulants and antiplatelet drugs should be

Table 5
Relation between drugs use and traumatic brain injuries.

Outcome: Traumatic brain injuries						
Drugs, *N* (%)		Brain injury ($n = 453$)	Other ($n = 2080$)	*p*	Adjusted OR	95% CI
		N	*N*			
Antiplatelets drugs	Yes	143 (31.6)	370 (17.8)	0.000	1.941	1.498–2.516
	No	310 (68.4)	1710 (82.2)			
Anticoagulants	Yes	76 (16.8)	231 (11.1)	0.000	1.794	1.329–2.421
	No	377 (83.2)	1849 (88.9)			
Antihypertensive	Yes	147 (32.5)	423 (20.3)	0.011	1.453	1.088–1.942
	No	306 (67.5)	1657 (79.7)			
Psychotropic drugs	Yes	81 (17.9)	226 (10.9)	0.041	1.404	1.014–1.942
	No	372 (82.1)	1854 (89.1)			

CI = confidence interval; OR = odds ratio.

individually tailored to optimize the advantages of the therapeutic choices.

Conflicts of interest

All authors have no actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations within 3 years of beginning the submitted work that could inappropriately influence, or be perceived to influence, their work.

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