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Original Study

Psychotropic Medications and Falls in Nursing Homes: A Cross-Sectional Study

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A B S T R A C T

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Background: Psychotropic medications are very frequently used in nursing homes and have been associated with falls. Little is known on the potential differences between types and subtypes of these medications, and also regarding different prescription patterns.

Methods: Data from 4502 residents living in 41 nursing homes belonging to a Spanish private chain were collected during a study period of 1 month and analyzed. Frequency of injurious and noninjurious falls were investigated for the following groups of psychotropic medications: typical neuroleptics; atypical neuroleptics; antidepressants; short and middle half-life benzodiazepines (BZD); long half-life BZD; BZD (of any type) administered only if needed; other hypnotic, sedative or anxiolytic drugs; cholinesterase inhibitors, and memantine. OR (95% CI) were calculated using regression analysis adjusted for age, sex, number of medications, physical restraint, and cognitive performance.

Results: Mean age (SD) was 84.3 (8.6) and 73.4% of the subjects were female. Psychotropic medication was prescribed to 2987 residents (66.3%), and there were 490 falls. Total falls were associated with use of atypical neuroleptics (OR 1.50, CI 1.17–1.94), antidepressants (OR 1.36, CI 1.03–1.78), short and middle half-life BZD (OR 1.27, CI 1.00–1.60), long half-life BZD (OR 1.65, CI 1.14–2.38), cholinesterase inhibitors (OR 1.42, CI 1.05–1.92), and memantine (OR 1.90, CI 1.32–2.74). Injurious falls were associated with typical neuroleptics (OR 1.77, CI 0.99–3.17), atypical neuroleptics (OR 1.64, CI 1.11–2.44), and long half-life BZD (OR 2.57, CI 1.56–4.25). The use of 2 or more psychotropics in combination was also associated with a significant increase of total falls and injurious falls.

Conclusions: Psychotropic medications were highly prescribed in the studied sample and were associated with falls. The most unsafe profile was detected for long half-life BZD, neuroleptics, and psychotropics in combination.

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An increasing proportion of the oldest-old is living in institutions. In that setting, people with functional dependence and cognitive impairment are certainly overrepresented.^{1,2} In addition, behavioral disturbance is particularly prevalent in nursing homes. In Spain, a recent study estimated an 84.4% prevalence of neuropsychiatric symptoms in institutionalized people with dementia.³ Not surprisingly, psychotropic medications are frequently prescribed in the institutions, all too frequently.⁴

Use of neuroleptics, benzodiazepines (BZD), and other psychotropic medications has been highly criticized because of

inappropriate prescription, inadequate risk-benefit balance, and lack of regular evaluation of convenience of use, all in the context of an unsafe risk profile.^{5,6} Among the adverse drug events of psychotropics, falls are particularly feared.^{7,8} Indeed, falls are a major predictor of functional dependence and suffering in the elderly, clearly raising the personal and societal costs of aging.⁹ Hence, any effort to prevent falls in nursing homes should bring important benefits for both the individual and society as a whole.

Balance and gait depends on the conjunction of several body systems and organs, with the nervous system involved at all levels.¹⁰ A large number of factors determine falls in old people, which could be classified as medical, neurologic, psychiatric, sensorial, psychosocial, environmental, organizational, and drug-related factors. A previous history of falls, gait dysfunction, pain, cognitive impairment, and use of neuroleptics, antidepressants, or BZD have all been associated with increased risk of falls in geriatric care settings.^{11,12}

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Although psychotropic medication is a well-known risk factor of falling in nursing homes,¹³ the effect of different groups, subgroups, and combination of that medication has not been sufficiently investigated. Since many potential causes of falls converge in the nursing home (very old age, physical frailty, polimedication, activity restriction, and dementia, among other causes) studies in that setting are particularly needed. To avoid falling and other adverse events, antidepressants are usually preferred to neuroleptics and BZD. A smaller risk of parkinsonism is also documented for atypical vs typical neuroleptics,¹⁴ and short and medium half-life BZD are usually preferred to long-acting BZD. However, the potential consequences of those preferences and distinctions related to fall risk have not been specifically investigated.

Cholinesterase inhibitors (CEI) and memantine are dementia-specific medications that were marketed in the last 2 decades. On the basis of some positive effects on behavior and mood, these drugs have been proposed to replace traditional psychotropics.¹⁵ In a recent study, donepezil was associated with less risk of falling in patients with Parkinson's disease for whom frequent falls were previously reported.¹⁶ However, CEI may provoke symptomatic bradycardia and syncope, thus, increasing risk of injurious falls.^{17,18}

The present study focused on the relationship between falls and use of psychotropic drugs in the nursing home setting. We aimed at describing the frequency, kind, and pattern of prescription in a large sample of institutionalized people. Main psychotropic groups and also some subgroups of interest were previously identified and extracted from a database of 41 nursing homes and their potential associations with falls were investigated. Cognitive deterioration and number of concomitant medications were controlled and injurious falls were specifically analyzed.

Methods

Setting and General Procedure

This was a cross-sectional study conducted at Sanitas Residencial, a Spanish chain of 41 nursing homes belonging to Bupa. Figures of this article refer to the early stage of a corporate project to eliminate restraints and promote person centered care culture and procedures. Data from the period of September 1 to September 30, 2011 were collected on October 4, 2011, described, and analyzed. Medical status data were recorded in the corporate nursing home software/database (ResiPlus v3.0.11, Informática, Spain) by Sanitas' medical doctors and nurses in charge of the residents (in Spain each nursing home has at least 1 medical doctor hired to treat or coordinate medical treatment of the home's residents). Each nursing home's dataset was later extracted and consolidated by an IT engineer at the chain's central offices. Data were reviewed for potential artifacts and errors by the IT engineer, the chain's head of care management (D.V.), and the principal investigator (J.O.). Data were exported from MS Access to MS Excel and from there into SPSS v.10.0 (SPSS Inc, Chicago, IL). Approval from the local ethics committee was obtained.

Study Variables

Psychotropic medications were divided into the following groups: typical neuroleptics; atypical neuroleptics; antidepressants; short and middle half-life BZD; long half-life BZD; BZD (of any type) administered only if needed; other hypnotic, sedative or anxiolytic drugs; CEI, and memantine. In addition, groups of subjects were created according to the number of prescribed psychotropic medications.

Falls were coded only if they happened and, when present, injurious falls were defined as including at least 1 of the following

consequences: hip or other fractures, head trauma, skin erosion, bruise, bleeding wound, hematoma, and oedema. In absence of any of these previous items, falls were accounted for as noninjurious.

Daily use of physical restraint was coded as present (ie, any of 9 different kinds of restraints) or absent. Bed rails were not considered restraints.

Cognitive status was documented using the last available 'Mini-examen Cognoscitivo' (MEC),¹⁹ which was conducted once a year. The MEC is a Spanish adaptation of the Mini-Mental State Test.²⁰ A cutoff of 23/24 was used to determine if the resident had dementia or not.

Statistical Analyses

The χ^2 and Student *t* tests were used to compare characteristics between residents who fell and those who did not fall and also to compare characteristics between those who suffered injurious falls and those with noninjurious falls. Associations of psychotropic medications with falls were further verified by means of logistic regression. Beta coefficients (β) and ORs were calculated using models adjusted for age, sex, number of medications (psychotropics excluded), physical restraint, and cognitive performance. The regression analyses were conducted for any fall (ie, injurious or noninjurious fall) and for injurious falls separately.

Results

Data were obtained from 4502 residents. Mean age was 84.3 (SD 8.6, range 28–106) and 73.4% of the subjects were female. Mean number of prescribed medications (psychotropics excluded) was 6.6 (SD 4.1, range 0–26). Physical restraint was used in 834 of the residents (18.5%) and dementia was present in 61.6% of the subjects (the MEC was not available, and therefore dementia status could not be estimated, for 543 subjects). During the observation period, 46 subjects (1%) died.

A total of 2987 residents were prescribed at least 1 psychotropic medication during the observation period (33.7% none, 33.2% 1, 21.8% 2, and 11.3% 3 or more psychotropics). The frequency of prescription of the different types of psychotropic medication is shown in Figure 1. The most frequently prescribed psychotropics were BZD, which were prescribed to 40.4% of residents. These medications were prescribed either on a daily basis (37.1% of the total sample) or if needed (3.2% of the subjects). In most cases, short- or medium-acting BZD were used (short- or medium acting BZD, 81.8%; long-acting BZD, 13.5%; both, 4.6%).

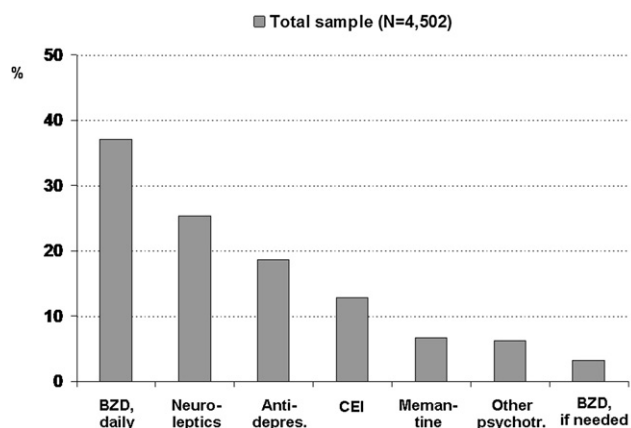


Fig. 1. Frequency of prescription of psychotropic medications. BZD, benzodiazepines; CEI, cholinesterase inhibitors.

Neuroleptics were the second most frequently prescribed psychotropic, being prescribed to 25.4% of the total sample on a daily basis. In most cases, atypical neuroleptics were used (atypical neuroleptics, 75.3%; typical neuroleptics, 17.1%; both, 7.6%). The remaining groups of studied medications were less frequently prescribed: antidepressants (18.6%), CEI (12.8%), memantine (6.7%), and other hypnotic, sedative, or anxiolytic drugs (6.2%).

Overall frequency of psychotropic prescription did not differ between subjects with or without dementia (68.3% vs 66.6%, $P = .248$). However, dementia was a major determinant of the kind of psychotropic prescribed. Subjects with dementia received neuroleptics more frequently, as well as CEI and memantine, whereas subjects without dementia received BZD and antidepressants more frequently (all $P < .0005$). Differences in prescription between subjects with and without dementia are represented in Figure 2.

During the observation period 394 (8.8%) residents experienced at least 1 fall (83.8% 1 fall, 11.9% 2 falls, 4.3% 3–6 falls). There was a total of 490 falls of which 156 (31.8%) were injurious falls (275 residents had 334 noninjurious falls and 146 residents had 156 injurious falls). Injurious falls were due to fracture (8 falls hip fracture, 5 falls other fracture), head trauma (5 falls), or other consequence (138 falls). Dementia was a determinant of falling, with 9.7% of subjects with dementia experiencing at least 1 fall, vs 7.5% of subjects without dementia ($P = .018$). Injurious falls were more frequent among subjects with dementia, but this difference did not reach statistical significance (3.7% vs 2.6%, $P = .078$). The clinical characteristics and medications according to fall status are presented on Table 1. Besides more frequent dementia, subjects who fell received more number of medications and were more frequently prescribed neuroleptics, antidepressants, BZD, CEI, and memantine compared with those subjects who did not fall. From among the analyzed groups of psychotropics, only the categories of 'BZD, if needed' and 'other sedatives, hypnotics, or anxiolytics' were not associated with falls. However, when injurious and noninjurious falls were compared, there was only a trend of more frequent use of long-acting BZD in those people who suffered injurious fall (14.4% vs 8.5%, $P = .066$) (Table 1).

Adjusted OR of any (ie, injurious or noninjurious) fall and of injurious fall according to psychotropic categories are given on Table 2. Significantly increased OR were obtained for atypical neuroleptics (OR 1.50 [CI 1.17–1.94] for any fall and OR 1.64 [CI 1.11–2.44] for injurious fall), long half-life BZD (OR 1.65 [CI 1.14–2.38] for any fall and OR 2.57 [CI 1.56–4.24] for injurious fall), short and

medium half-life BZD (OR 1.27 [CI 1.00–1.60] for any fall), antidepressants (OR 1.36 [CI 1.03–1.78] for any fall), CEI (OR 1.42 [CI 1.05–1.92] for any fall), and memantine (OR 1.90 [CI 1.32–2.74] for any fall). The prescription of 2 or more psychotropics in combination was also associated with an increased frequency of falls (any fall and injurious fall) (Table 2).

Discussion

The frequency and pattern of prescription of psychotropic medications was described in a large sample of institutionalized older people and the associations between different types of psychotropics, patterns of prescription, and falls were analyzed. As expected for nursing homes, the sample was very old, and dementia was very prevalent.²¹ Also expectedly, falls were more frequently observed in people with dementia.^{12,22}

Prescription of psychotropic medication was high regarding BZD and neuroleptics, but it was low regarding CEI and memantine (Figure 1). BZD were particularly frequent in nondemented subjects (47.4%), whereas neuroleptics were more frequently prescribed for demented subjects (30.9%). CEI and memantine were lowly prescribed, even in the subgroup of residents with dementia (17.6% and 10.5% of prescription of CEI and memantine, respectively) (Figure 2). While neuroleptics bear important risk of adverse outcomes including cognitive deterioration, parkinsonism, metabolic syndrome, and vascular disease,²³ CEI and memantine may improve cognition, psychotic symptoms and agitation with a more favorable risk profile.¹⁵ Hence, CEI and memantine could have been underused in the studied sample. Whether that underuse was due to lack of training, logistical prescription difficulties, or both, cannot be inferred from our data (in Spain, these drugs need specialist's prescription for state reimbursement).

Unexpectedly, age was not associated with falls in the present investigation. The lack of association between falls and age could be due to the very small proportion of young people, but also to the fact that in our sample higher age was associated with higher use of restraints (data not shown). Regrettably, as it was confirmed in the present study (Table 1), Spain is still amongst the countries with the highest prevalence of use of physical restraints.²⁴

In the present study, neuroleptics were associated with falls in both the unadjusted and adjusted analyses (Tables 1 and 2). The frequency of falls in the typical and atypical neuroleptic subgroups was comparable, with lack of statistical significance of typical neuroleptics for injurious falls clearly because of a small sample size (Table 2). This was unexpected because higher risk of parkinsonism was reported with typical neuroleptics.¹⁴ Hence, other common adverse effects (eg, cardiovascular effect and sedation) should be responsible for falls and fall complications in old people taking neuroleptics.

BZD were also associated with falls (Table 1) and that was particularly the case for long-acting BZD, which were associated with injurious falls in the multivariate analysis (Table 2). This finding supports the common practice recommendation of avoiding long-acting BZD in old persons. We also found a trend of injurious falls in those who received BZD only if needed (OR 1.86, CI 95% 0.89–3.92, $P = 0.101$) (Table 2) with lack of statistical significance possibly due to the small number of subjects receiving this pattern of BZD prescription only (it might have happened that some proportion of subjects who received daily BZD were also prescribed BZD if needed, but that situation was not specifically coded). Nevertheless, in light of these results, caution should also be advised regarding the use of BZD on an 'if needed' basis. Fluctuations in arousal attributable to occasional use of BZD could be particularly relevant for incidence of injurious falls and this possibility deserves further research.

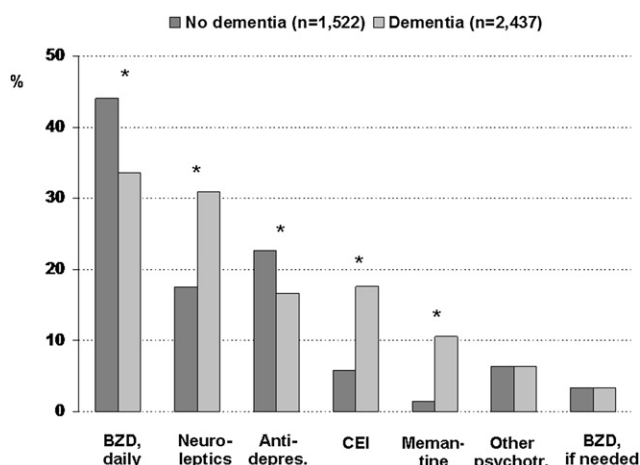


Fig. 2. Frequency of prescription of psychotropic medications by dementia status. BZD, benzodiazepines; CEI, cholinesterase inhibitors. * $p < 0.0005$.

Table 1
Clinical Characteristics and Medications According to Fall Status

	No Fall (n = 4108)	Fall (any type) (n = 394)	P	Noninjurious Fall (n = 248)	Injurious Fall* (n=146)	P
Age	84.3 (8.7)	84.5 (7.5)	.628	84.5 (7.6)	84.3 (7.2)	.785
Female sex	73.7	71.2	.287	70.9	71.7	.854
Medications (n) [†]	6.5 (7.0)	7.0 (4.3)	.038	6.9 (4.2)	7.2 (4.5)	.542
Physical restraint	18.5	18.3	.893	19.4	16.4	.469
Dementia	61.0	67.4	.018	66.5	69.0	.633
Neuroleptics, typical	6.0	9.4	.007	8.5	11.0	.413
Neuroleptics, atypical	20.3	28.9	.000	27.4	31.5	.388
Antidepressants	18.2	23.1	.017	23.4	22.6	.858
BZD, short and middle half-life	34.4	39.8	.031	40.7	38.4	.643
BZD, long half-life	7.0	10.7	.008	8.5	14.4	.066
BZD, if needed	3.1	4.1	.323	2.8	6.2	.105
Other hypnotics, sedatives, or anxiolytics	6.3	5.6	.572	6.0	4.8	.601
CEI	12.4	16.8	.013	16.1	17.8	.666
Memantine	6.3	11.2	.000	12.1	9.6	.445
Number of psychotropics			.000			.715
0	34.3	26.9		28.2	24.7	
1	33.8	27.4		27.0	28.1	
2	21.6	24.6		23.0	27.4	
≥3	10.4	21.1		21.8	19.9	

BZD, benzodiazepines; CEI, cholinesterase inhibitors.

Values represent % except for age and number of medications, expressed as mean (SD).

*Twenty-six subjects who had both noninjurious and injurious falls were included in the group of injurious falls.

[†]Psychotropics excluded.

Memantine and CEI were associated with noninjurious falls, and a trend for the occurrence of injurious fall was observed in the subjects who received CEI (OR 1.41, CI 95% 0.88–2.26, $P = .149$) (Table 2). In a very large cohort study on community dwelling people with dementia, adjusted OR of 1.81 (CI 95% 1.57–2.10) and 1.21 (CI 95% 1.03–1.43) were reported, respectively, for syncope and hip fracture, in those subjects who received CEI.¹⁷ In a meta-analysis of randomized controlled trials on both institutionalized and community dwelling people with dementia, CEI were not associated with fall risk (OR 0.88, CI 95% 0.74–1.04), but increased risk was reported for syncope (OR 1.53, CI 95% 1.02–2.30) and fracture (OR 1.39, CI 95% 0.75–2.56). Higher surveillance of patients in a research context could explain, at least in part, these divergences in results. In the same meta-analysis of randomized controlled trials, memantine was not associated with falls nor with any other adverse outcome and it was even protective for fracture (OR 0.21, CI 95% 0.05–0.87).¹⁸ Our data, however, do not support a protective effect of memantine on fractures (Table 2). In fact, the frequency of fall complicated with

fracture was higher when memantine was used (1.0% vs 0.2%, $P = .06$, *post-hoc* analysis).

Injurious and noninjurious falls increased when 2 or more psychotropic medications were used in combination and differences in OR became larger as the number of combined psychotropics increased (Table 2). These results suggest a synergistic effect that could be explained on the basis of the variety of putative mechanisms involved (unspecific sedation, cardiovascular effects, metabolic interactions, etc). As the only exception to a widespread unsafe profile regarding falls, the category of 'other hypnotics, sedatives, or anxiolytics' displayed a safe profile (Tables 1 and 2). Although drugs should not be prioritized over care and environmental modifications, this category that was mostly composed of BZD-related and antihistaminic medications deserves more research.

The present study had several limitations. Measures of gait and balance, evaluation of visual acuity, and data regarding other physical and medical conditions usually associated with falls were not available.²⁵ Another important limitation is that causality between drugs

Table 2
ORs of any Fall and Injurious Fall According to Psychotropic Medications

	Fall (any type)		P	Injurious fall		P
	β	OR (CI 95%)		β	OR (CI 95%)	
Typical neuroleptics	0.33	1.40 (0.93–2.09)	.106	0.57	1.77 (0.99–3.17)	.055
Atypical neuroleptics	0.41	1.50 (1.17–1.94)	.002	0.50	1.64 (1.11–2.44)	.013
Antidepressants	0.31	1.36 (1.03–1.78)	.028	0.25	1.29 (0.83–1.99)	.255
BZD, short and middle half-life	0.24	1.27 (1.00–1.60)	.046	0.16	1.18 (0.81–1.70)	.392
BZD, long half-life	0.50	1.65 (1.14–2.38)	.007	0.94	2.57 (1.56–4.24)	.000
BZD, if needed	0.09	1.09 (0.61–1.96)	.776	0.62	1.86 (0.89–3.92)	.101
Other hypnotics, sedatives, or anxiolytics	–0.30	0.75 (0.45–1.22)	.244	–0.61	0.54 (0.22–1.34)	.186
CEI	0.350	1.42 (1.05–1.92)	.022	0.35	1.41 (0.88–2.26)	.149
Memantine	0.64	1.90 (1.32–2.74)	.001	0.25	1.29(0.69–2.41)	.425
Number of psychotropics						
0	–	1 (reference)	–	–	1 (reference)	–
1	0.03	1.03 (0.76–1.40)	.835	.13	1.14 (0.69–1.87)	.618
2	0.35	1.42 (1.03–1.96)	.032	.53	1.70 (1.02–2.84)	.041
≥3	0.93	2.53 (1.80–3.56)	.000	.89	2.44 (1.41–4.25)	.002

BZD, benzodiazepines; CEI, cholinesterase inhibitors.

OR and β coefficients were calculated by logistic regression (models adjusted for age, sex, number of medications (psychotropics excluded), physical restraint, and cognitive performance).

and falls cannot be established, given the cross-sectional design. Moreover, use of neuroleptics and long-acting BZD could be the consequence of some previous conditions (eg, agitation, cognitive deterioration) that provoked falls. Longitudinal studies should definitely settle this issue, but evidence in this regard is very scarce so far with only 1 study demonstrating reduction of falls after weaning off neuroleptics.⁸ Another important limitation of the present study, also derived from its cross-sectional nature, was that a more sensible analysis including time of exposure to medications could not be performed.

In conclusion, use of psychotropic medications was very frequent in nursing homes and, in most cases, those medications were associated with falls. The use of neuroleptics was clearly inferior to previous studies,²⁶ but BZD were more frequently used, in agreement with a recent study that reported a use of hypnotics and anxiolytics even slightly higher (42.5%) than the use of BZD reported in the present study (37.1%).²⁷ Hence, it could be the case that, after profound knowledge of the deleterious effects of neuroleptics, those medications are being replaced by BZD. However, these medications demonstrated also very important adverse events and might increase dementia risk in the old people.²⁸ The results herein presented were collected in 2011 and belong to a corporate project of Sanitas Residencial to eliminate physical restraints and to reduce and optimize psychotropic medication. Sanitas Residencial is working actively to be able to present in the near future new data with further reduction of psychotropic medications, particularly BZD.

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