Effects of a multifaceted intervention in psychogeriatric patients: one-year prospective study

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ABSTRACT

Objectives The aetiology of behavioural and psychological symptoms (BPSD) could be related to inadequate treatment in patients with dementia. The aim of this study was to determine how a multifaceted intervention based on a medication review and multidisciplinary follow-up could improve treatment and minimise risk in these patients.

Methods A prospective interventional study was undertaken between July 2015 and July 2016 of patients with dementia admitted to control BPSD. Patients with previous psychiatric illness or palliative care were excluded. Prescription information was obtained from Aegerus and the Catalonia clinical record HC3. The intervention was conducted by a multidisciplinary team. The Medication Appropriateness Index (MAI) was used to assess the intervention.

Results 65 patients (60% women, mean age 84.9±6.7 years) with mild-moderate cognitive impairment (mean 4.5±1.8), moderate-severe functional dependence (mean 43.8±23.9) and a high prevalence of geriatric syndromes and comorbidity were included in the study. 87.7% of the patients were taking ≥5 drugs (mean 9.0±3.1) and 38.5% were taking ≥10. Patients presented with BPSD values of 1.9±0.8 at admission. Common symptoms prompting admission were agitation (47.7%) and irritability (43.1%). A total of 175 drug-related problems (DRPs) were detected (2.97 per patient). Significant differences ($p<0.001$) were found between the MAI score at admission (4±4.6) and post-intervention (0.5±2.6). Most prevalent MAI criteria were related to interactions (40%), dosage (38.5%) and duplication (26.2%). 55 patients (84.6%) were taking anticholinergic drugs at admission (2.6±1.2 anticholinergic drugs per patient), and the post-intervention reduction was significant ($p<0.016$).

Conclusions The balance between effective treatment and safety is complex in these patients. Medication review in interdisciplinary teams is an essential component to optimise interventions and assessment of safety.

INTRODUCTION

Dementia is a multi-aetiological syndrome which is chronic, irreversible and with a slow evolution. It is a syndrome that affects memory, thinking, behaviour and the ability to perform everyday activities. The number of people living with dementia worldwide is currently estimated at 35.6 million. According to the World Health Organization, this number will double by 2030 and more than triple by 2050, and it has been declared a public health priority.[1]

Cognitive impairment in patients with dementia is usually associated with behavioural and psychological symptoms (BPSD). The prevalence[2] of these neuropsychiatric disturbances is more than 80% and it is one of the leading causes of premature admission to institutions.[3]

BPSD includes heterogeneous symptoms such as delusions, hallucinations, agitation/aggression, depression, apathy, euphoria, anxiety, disinhibition, irritability, aberrant motor behaviour, night-time behaviour disturbances, and appetite and eating abnormalities. The first options for treatment are non-pharmacological strategies[4] but, once they fail, psychotropic drugs are prescribed.

Inadequate drug treatment is recognised as a risk for geriatric patients and has been widely described.[5] This inadequate treatment could be the aetiology behind behavioural symptomatology in patients with dementia. The higher number of comorbidities exposes them to higher risk[6] (duplicate treatments, adverse drug events and interactions), inappropriate prescriptions[7] and even further impairment of the BPSD and dementia. The management of psychotropic medication is complex and has been associated with a high incidence of side effects, especially in long-term use.[8–12] Older patients are more susceptible to these effects due to decreased hepatic metabolism and renal excretion of drugs, as well as the increased permeability of the blood-brain barrier.[13 14]

There is a lack[15] of evidence for the efficacy and safety of drugs due to the exclusion of this population from clinical trials (typically because of comorbidity and advanced chronic diseases). There is also a limited[16] number of studies examining medicine management[17] interventions for people with dementia and BPSD symptoms. Most interventions to improve psychotropic prescribing only focus on antipsychotic drugs.

The aim of the present study was to determine how multifaceted pharmacist intervention based on medication review and multidisciplinary follow-up could improve the treatment and minimise risk for people with dementia and BPSD symptoms in a psychogeriatric unit.

METHODS

Design, setting and inclusion/exclusion criteria

This was a one-year prospective interventional study performed in a long-term care psychogeriatric unit (21 beds) in an intermediate care hospital (HSS Mutuam Güell, 165 beds) in Barcelona, Spain.

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The study was conducted from July 2015 to July 2016. All patients admitted to the ward were eligible for enrolment. Patients who met any of the following criteria were excluded from the study: patients without cognitive impairment, length of stay <7 days, palliative or previous psychiatric pathology. During this period a pharmacist and a specialist doctor in the unit collected and carried out the intervention.

Instruments used

Tests used to assess functional and cognitive impairment were:

- Barthel Index: a scale that measures disability or dependence in activities of daily living. The main goal of the Barthel Index is to establish the degree of independence, physical or verbal, however minor and for whatever reason. Values range between 0 and 100, with the lowest score indicating a higher dependency.[18]
- Global Deterioration Scale (GDS), which provides caregivers with an overview of the stages of cognitive function for those suffering from a primary degenerative dementia such as Alzheimer's disease. It is divided into seven stages: stages 1–3 are pre-dementia stages and stages 4–7 are dementia stages.[19]
- Neuropsychiatric Inventory Questionnaire (NPI-Q) to assess BPSD symptoms[20]: this is a 12-item questionnaire; each NPI domain is scored for frequency on a 4-point scale ranging from 0 (absent) to 3 (severe).

Tools used to assess the improvement of the treatment after pharmacist intervention:

- Improvement in the appropriateness of drug treatments was evaluated using the Medication Appropriateness Index (MAI).[21] MAI criteria consists of 10 questions, which are graded according to the suitability of the medication (a higher score indicates worse status) and different aspects related to prescription (indication, efficacy, safety and cost). MAI is the main variable to assess the result of the intervention.
- Anticholinergic burden was evaluated using the Drug Burden Index (DBI).[22] The anticholinergic burden is defined as the cumulative effect of taking one or more drugs that are capable of producing adverse anticholinergic effects.[23] High scores have been associated with an increased risk of adverse events (including falls, delirium and cognitive disorders). The DBI scale measure of the anticholinergic effect is based on the calculation of a mathematical formula that takes into account the prescribed dose and the minimum effective dose of the drug.

Procedure and data collection

A programme was implemented to improve drug treatments in psychogeriatric patients through a multidisciplinary team consisting of a pharmacist and a geriatrician, based on medication reviews and follow-up.

Information was obtained from sources such as electronic prescriptions and electronic medical records in HSS (Aegerus), medical records at admission and at discharge of different healthcare levels and the Catalonian Healthcare System electronic record (HC3).

The variables included were: (i) demographics: age, gender and place of patient origin at admission, length of stay, destination at discharge; (ii) pharmacological: number and type of drugs, dosage, frequency, route of administration, and prescription start dates (if possible); (iii) clinical: diagnosis (ICD-10 International Classification of Diseases, 10th Revision), dementia type, geriatric syndromes (falls, dysphagia, pain, ulcers, constipation, dyspnoea, hearing loss, visual impairment, malnutrition, insomnia, depressive-anxiety syndrome and incontinence), cognitive assessment (according to the GDS-FAST scale, functional assessment (according to Barthel Index) and NPI (Neuropsychiatric Inventory). Polypharmacy was defined as ≥5 drugs prescribed.[24] Inadequate drug treatment was defined as medication which is prescribed with an unclear evidence-based indication, whose risk outweighs the benefits, is not well tolerated in most patients and is cost ineffective.[5]

Demographic and pharmacological data were obtained from electronic medical records and HC3 by the pharmacist. Clinical

Table 1 Baseline diagnoses (ICD-10 International Classification of Diseases, 10th Revision)

Variable	Results	
Number of patients	**65**	
	Qualitative	**Quantitative**
Age		84.9 years (SD 6.7)
Gender	Women 39 (60%); men 26 (40%)	
Place of origin	Home 36 (55.4%); acute hospital 27 (41.5%); intermediate care 2 (3.1%)	
Length of stay (days)		58.5 (mean)
Geriatric syndromes	Falls, 47 (72.3%); previous fractures, 12 (18.5%) Dysphagia, 21 (32.3%) Pain, 15 (23.1%) Ulcers, 16 (24.6%) Dyspnoea, 3 (4.6%) Hearing loss, 10 (15.4%) Constipation, 44 (67.7%) Visual impairment, 21 (32.3%) Malnutrition, 6 (9.2%) Insomnia, 22 (33.8%) Depression/anxiety, 21 (32.3%) Incontinence, 44 (67.7%)	
Type of dementia	Alzheimer, 20 (30.8%) Vascular, 5 (7.7%) Mixed, 3 (4.6%) Diagnosis not completed, 28 (43.1%) Lewy body, 5 (7.7%) Others, 4 (6.2%)	
Functional abilities (Barthel Index)	Some dependence or independence (BI 80–100), 6 (9.2%) Slight dependence (BI 60–75), 16 (24.6%) Moderate dependence (BI 40–55), 18 (27.7%) Severe dependence (BI 20–35), 12 (18.5%) Total dependence (BI 0–15), 13 (20%)	
Cognitive function (GDS-R)	Incipient (GDS 3), 16 (24.6%) Mild (4), 18 (28%) Moderate (5), 16 (25%) Severe (6), 13 (20%) Very severe (7), 2 (3%)	
Discharge destination	Home, 26 (40%) Nursing home, 27 (41.5%) Change ward, 1 (1.5%) Acute hospital, 2 (3.1%) Psychiatric hospital, 1 (1.5%) Death, 8 (12.3%)	

Table 2 Baseline characteristics of the study patients

Diagnosis	Results
Diseases of the circulatory system	54 (83.1%)
Endocrine, nutritional and metabolic diseases	39 (60%)
Diseases of the genitourinary system	21 (32.3%)
Diseases of the musculoskeletal system and connective tissue	19 (29.2%)
Diseases of the nervous system	18 (27.7%)
Neoplasms	11 (16.9%)
Injury, poisoning and certain other consequences of external causes	17 (26.2%)
Diseases of the digestive system	15 (23.1%)
Diseases of the eye and adnexa	11 (16.9%)
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	10 (15.4%)
Mental and behavioural disorders	10 (15.4%)
Symptoms, signs and abnormal clinical and laboratory findings not elsewhere classified	9 (13.8%)
Diseases of the respiratory system	8 (12.3%)
Diseases of the ear and mastoid process	5 (7.7%)
Certain infectious and parasitic diseases	3 (4.6%)
Diseases of the skin and subcutaneous tissue	1 (1.5%)

Table 3 Distribution of behavioural and psychological symptoms

	N	%
Agitation	31	47.7
Irritability	28	43.1
Sleep disturbances	21	32.3
Anxiety	10	15.4
Appetite changes	10	15.4
Dysphoria/depression	6	9.2
Aberrant motor behaviour	5	7.7
Delusions	4	6.2
Hallucinations	4	6.2
Apathy	2	3.1
Disinhibition	2	3.1
Euphoria	0	0.0

date registration and tests for functional, cognitive assessment and NPI were performed by the physician.

The pharmacist performed a review of the medication and the drug-related problems (DRPs) detected and recommendations for their solution were communicated to the physician via email, telephone and a weekly meeting. A further review of the treatments was performed at the weekly meetings between the pharmacist and the physician in charge of the patients and any DRPs found were evaluated and the outcomes and evolution of the patients were discussed.

All data, such as the interventions/recommendations related to the DRP, its outcomes and general information, were recorded in a database using Microsoft Excel 2010 and Power Pivot.

From the prescription we recorded the DRP using the classification of the American Society of Health-System Pharmacists (ASHP). The Anatomical Therapeutic Chemical Code (ATC) classification system was used for the qualitative classification of drugs.

To assess the result of the intervention, MAI was used to evaluate improvement in the appropriateness of drug treatments. The pharmacist obtained a score before and after the intervention based on the treatments the patient was taking on admission and discharge. A decrease in the initial score was considered positive.

The Drug Burden Index (DBI) was used for anticholinergic burden. The pharmacist obtained a score before and after the intervention based on the treatments the patient was taking on admission and discharge through the DBI. The score allows us to classify these treatments according to the risk.

Statistical analysis

SPSS software (IBM-SPSS 25.0 version) was used for the statistical analysis. Granmo (version 7.12 April 2012) was used to calculate the sample size based on the main variable to assess intervention MAI. Accepting an alpha risk of 0.05 and a beta risk of 0.2 in a one-sided test, 58 subjects are necessary to recognise a difference greater than or equal to 0.7 units as statistically significant. The SD is assumed to be 2.03 (data from previous studies in geriatric patients in HSS Mutuam Güell). A drop-out rate of 10% was anticipated.

The Kolmogorov–Smirnov test was used to assess the normal distribution of the sample for comparison of the quantitative variables. The Student's t-test was used for all comparisons before and after the intervention.

All quantitative variables were summarised as mean (SD). Qualitative variables were summarised as the frequency and percentage for each value.

RESULTS

General characteristics

Between July 2015 and July 2016, 65 patients met the inclusion criteria for the study (60% women, mean (SD) age 84.9 (6.7) years); 49 were excluded.

Baseline characteristics showed mild-moderate cognitive impairment 4.5 (SD1.8), moderate-severe functional dependence 43.8 (SD23.9) and a high prevalence of geriatric syndromes: incontinence in 44 patients (67.7%), constipation in 44 (67.7%), falls in 47 (72.3%) and previous fractures in 12 (18.5%). The most prevalent type of dementia was Alzheimer's disease in 20 patients (30.8%), but the cognitive impairment study was not completed for 28 (43.1%) patients (table 1).

Statistically significant differences were observed in the length of stay (mean 58.5 days) with regard to gender: a mean of 60.0 days in women versus a mean of 84.3 days in men (p=0.034). Cognitive and functional characteristics were similar in both groups. There were also no differences in the number of drugs with regard to gender.

The most common patient diagnoses included diseases of the circulatory system (54, 83.1%) and endocrine, nutritional and metabolic disease (39, 60%) (table 2). The comorbidity mean was 4.8±1.6; a total of 64.6% of patients had >4 chronic diseases.

87.7% of the patients were taking ≥5 drugs (mean (SD) 9.0 (3.1) drugs per patient) and 38.5% were taking ≥10. We observed at admission that, according to the N-ATC classification, N05A (antipsychotics) were the most frequent (51, 78.5% of patients), followed by N05C (hypnotics and sedatives)/N05B (anxiolytics) (31, 47.7%), N06A (antidepressants) (35, 53.9%), N02 (analgesics) (43, 66.2%), N06D (anti-dementia drugs) (24, 30.9%), N03A (antiepilepticdrugs) (8, 12.3%) and N04 (anti-Parkinson drugs) (3, 4.6%).

Table 4 Intervention characteristics, drug-related problem (ASHP Classification), ATC code (Anatomical Therapeutic Chemical (ATC) Classification System)

Characteristics	Interventions	
Number of interventions	175 (90.8% of patients)	
Gender	Women, 104 (59.4%); 38 patients	
	Men, 71 (40.6%); 21 patients	
Point of the intervention	Admission, 98 (56%)	
	Hospitalisation, 77 (44%)	
Accepted	152 (86.9%)	
Drug-related problem	Actual and potential adverse drug events	33 (19%)
	Medication prescribed inappropriately for a particular condition	29 (17%)
	Therapeutic duplication	18 (10%)
	Inappropriate dose	17 (10%)
	Medication with no indication	15 (9%)
	Condition for which no drug is prescribed	14 (8%)
	Length	14 (8%)
	Schedule	13 (7%)
	Failure to receive the full benefit of prescribed therapy	8 (5%)
	Actual and potential drug-drug that are clinically significant	6 (3%)
	Drug-disease that are clinically significant	4 (2%)
	Lack of understanding of the medication	2 (1%)
	Inappropriate dose renal impairment	1 (1%)
	Dosage form	1 (1%)
ATC Code	A - Alimentary tract and metabolism	7 (4%)
	B - Blood and blood forming organs	7 (4%)
	C - Cardiovascular system	15 (9%)
	G - Genitourinary system and sex hormones	3 (2%)
	H - Systemic hormonal preparations, excluding sex hormones and insulin	2 (1%)
	M - Musculoskeletal system	2 (1%)
	N - Nervous system	137 (78%)
	S - Sensory organs	2 (1%)

Table 5 Potentially inappropriate medication by Medication Appropriateness Index (MAI)

MAI criteria		Qualitative values: patients affected (%)
1	Is there an indication for the drug?	20.0
2	Is the medication effective for the condition?	10.8
3	Is the dosage correct?	38.5
4	Are the directions correct?	0.0
5	Are the directions practical?	3.1
6	Are there clinically significant drug–drug interactions?	9.2
7	Are there clinically significant drug–disease/condition interactions?	40.0
8	Is there unnecessary duplication with other drug(s)?	26.2
9	Is the duration of therapy acceptable?	16.9
10		0.0
Total patients affected by some criteria by MAI criteria (%)		90.8
Mean (SD) score at admission 4 (4.6)	Mean (SD) score post-intervention 0.5 (2.6)	p<0.001

Behavioural and psychological symptoms (BPSD)

Patients at admission had BPSD values of 1.9±0.8. The most prevalent symptoms prompting admission were agitation (47.7%) and irritability (43.1%) (table 3). We found significant differences (p=0.017) in NPI scoring in patients with agitation (mean at admission 20.8±8.2) compared with scores for other BPSD (16.7±7.1). We also found differences in the length of stay in patients presenting with sleep disturbances, which was longer for these patients (92.3±71.1 days vs 58.9±37.5 days, p=0.0077). NPI at admission was 18.7±7.9 vs 4.7±5.2, p<0.0001 (table 3, distribution of BPSD per patient).

Drug-related problems (DRPs) and pharmaceutical interventions

A total of 175 DRPs were detected by the pharmacist (2.97 per patient). The physician's acceptance of the interventions/recommendations for solving the DRPs was 86.9%. The most frequent DRPs were those related to dose, schedule and length of treatment (25.7%), adverse drug events (19%) and inappropriate prescription in the elderly (17%). The most prevalent ATC group with DRPs was the nervous system (78%) (table 4). The most prevalent problems in this group involved N05A (antipsychotics) (31% of the interventions for quetiapine and 8% for haloperidol), N06A (antidepressants) (6% citalopram and 4% trazodone) and N05C (hypnotics and sedatives)/N05B (anxiolytics) (8% lorazepam and 6% clometiazol). The most frequent DRPs in this group (N) were inappropriate dose (20%), actual and potential adverse drug events (14%) and medication with no indication (12%), length (11%), schedule (11%) and therapeutic duplication (11%). The most prevalent DRP with quetiapine were dose problems (30.2%), inappropriate length of treatment (14.0%), no indication of quetiapine (14.0%) and schedule (16.3%). Problems in the case of lorazepam were due to adverse events (18.2%), and for haloperidol were mostly related to duplication (36.4%).

There was a mean (SD) of 9.0 (3.1) drugs/patient on admission. After the intervention we found a slight improvement of 9.0 (3.0) drugs/patient, although the difference was not significant (p=0.405).

MAI criteria

There were significant differences (p<0.001) between the mean (SD) MAI scores at admission and post-intervention (4 (4.6) vs 0.5 (2.6)). The most prevalent MAI criteria were related to interactions (40%), dosage (38.5%) and duplication (26.2%) (table 5).

We also found a significant difference (p=0.043) between the mean scores at admission depending on gender (men 2.9, women 4.5).

Anticholinergic burden per DBI

Fifty-five patients (84.6%) were taking anticholinergic drugs at admission, with the mean (SD) number per patient being 2.6 (1.2). The mean (SD) anticholinergic burden per patient was 1.38 (0.7) and the number of patients who presented with an anticholinergic burden >1 (considered high-risk burden limit) was 44 (DBI range 0.3–3).

Statistically significant differences were found between pre- and post-intervention (p<0.016). The post-intervention

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mean (SD) DBI was 1.08 (0.7) and the number of patients with an anticholinergic burden >1 was 30 (DBI range 0.3–2.6).

There were also statistically significant differences between patients who had ≥4 diagnoses (mean DBI 1.1±0.8) and patients with <4 (0.9±0.6) (p=0.0445). According to the NPI, there were 20.1±8.5 >1 DBI high-risk patients and 16.7±6.5 <1 DBI low or no risk patients (p=0.00443).

DISCUSSION

The primary goal of this prospective interventional study was to determine whether multidisciplinary intervention was a useful strategy with which to improve treatment management and minimise risk for people with dementia and BPSD symptoms. A widely employed tool—MAI—was used and improved after the intervention.

There are few studies reported in the literature related to pharmacist interventions evaluating patients with dementia and even fewer in psychogeriatric patients.[16]

The close collaboration of the pharmacist and physician resulted in a high degree of acceptance of the recommendations/interventions suggested by the pharmacist (86.9%).

There was a good correlation between the DRPs found as most prevalent and the MAI results. The study demonstrated the high prevalence of non-adequate prescription in this population, especially psychotropic drugs, as the literature shows that few of the drugs for neuropsychiatric symptoms are fully appropriate.[25] Another significant finding regarding MAI was the difference at admission between women and men, although no reason was found for this difference.

Using MAI criteria, the results showed that the most prevalent problems were those associated with clinically significant drug–disease interactions (40% of patients), dose (38.5% of patients) and duplication of therapies (26.2% of patients), and these were mostly with psychotropic drugs. This confirms a real need to review treatments regularly and systematically. The limited efficiency of the treatments in these patients and increasing the dose or adding the same class of antipsychotic or new psychotropic drugs to the treatment exposes them to a very high risk of adverse events.[26] Adverse effects have been reported in various alerts from the Food and Drug Administration concerning fatal cardiovascular events due to antipsychotics when used in frail patients with high comorbidity and a high prevalence of cardiovascular pathology (in our case 83.1% of patients presented with cardiovascular disease).

Anticholinergic medications are considered inadequate for geriatric patients and especially those with psychogeriatric symptoms.[27] We found a high prevalence of anticholinergic drugs at admission (84.6% of patients), with a mean of 2.14 drugs per patient. We also found a relationship between comorbidity and drugs with a greater anticholinergic effect. Patients with ≥4 comorbidities had higher DBI than those with <4. Those with a high risk of anticholinergic burden also had higher scores in NPI, showing a relationship between a higher risk of anticholinergic effect and an increased risk of adverse events (eg, falls, delirium, cognitive disorders), and even more those patients who can worsen BPSD.[27] The anticholinergic effect should really be considered when prescribing, especially with psychotropic drugs used to treat BPSD. It has been noted that the anticholinergic effect of antipsychotics varies depending on the drug, and it is important to prioritise this when choosing from the different options for these patients and to choose the option with less anticholinergic effect.

We found polypharmacy in 87.7% of the patients and, as expected, we also found a high incidence of comorbidity (4.8±1.6 per patient). The total number of medications prescribed at discharge was not significantly different from at admission. However, there was a significant difference in MAI, suggesting that it may not be polypharmacy alone that causes undesirable clinical outcomes but also the underuse of safer or more effective alternatives, as noted by other authors.[28]

This study population showed a high prevalence of geriatric syndromes, especially falls (72.3%) and previous fractures (18.5%), which is one of the highest risks for frail geriatric patients such as those with dementia, especially where there is a high prevalence of psychotropic drug use in this population. Benzodiazepines and other hypnotics have a dose-dependent correlation with the risk of falling.[29]

Another notable finding was the significant difference in the length of stay between men and women, with men having a longer length of stay, although no significant differences were found in cognitive ability tests. These differences could be associated with cultural characteristics and social resources for their return home.

This study found that, although most patients had a diagnosis of cognitive impairment, not all patients had a complete assessment (43.1%). This led to difficulties in choosing the correct treatment and increased the risk of undertreatment with drugs that could improve behavioural symptomatology and progression of the main pathology. This undertreatment in Alzheimer's is an important concern and has been noted by authors in previous studies.[30]

This study has the limitation of not being able to include the patient's objectives in the review of the medication and in the adjustment to the current situation, mainly due to the cognitive deterioration that prevents direct communication with the patient and consequently the interlocution takes place with the main caregivers.

What this paper adds

What is already known on this subject

- Geriatric patients are a complex group for medicines management, even more so in patients with cognitive impairment. Patients commonly present polypharmacy and multimorbidity.
- The risks associated with the treatments usually outweigh the benefits. There is evidence of a high rate of inadequate prescriptions in this population.
- There is limited evidence of studies examining medicines management in patients with dementia and behavioural and psychological symptoms.

What this study adds

- This research specifically contributes to the literature because only a limited number of studies considering a global approach to medicines management in patients with dementia and targeting patients presenting with behavioural and psychological symptoms have been conducted.
- It adds evidence of medicines management in a multidisciplinary team including a hospital pharmacist.
- This study shows the use of different strategies to follow-up.

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CONCLUSIONS

There is a complex balance between effective treatment and risks of adverse outcomes in psychogeriatric patients. Cognitive impairment and the medication used to treat it are added to other frailties of the geriatric state and, as the study shows, this results in high-risk medication.

The safety strategy in this population should include multidisciplinary team interventions to assess risk and adequate treatment centred on the patient and disease progression. Systematic review of the treatments and their adequacy should be part of regular practice to balance efficiency and risk.

Contributor CM, MH, PM,CF and EM conceived and designed the study. MH and JJ enrolled the patients and made the interventions. CM, MH, LC, PM, CF and EM evaluated the results. LC performed the statistical analysis. CM and MH wrote the manuscript.

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