



ORIGINAL ARTICLE

## Utilisation of atypical antipsychotic drugs in institutionalised elderly persons and prevalence of metabolic alterations

G. Martínez Romero,<sup>a,\*</sup> J.F. Peris Martí,<sup>a</sup> J. Gomar Fayos,<sup>b</sup> M. Navarro Gosalbez,<sup>b</sup>  
I. Quintana Vargas,<sup>a</sup> and J. Muelas Tirado<sup>b</sup>

<sup>a</sup>Servicio de Farmacia, Centro Sociosanitario de La Cañada (Valencia), Valencia, Spain

<sup>b</sup>Servicio de Ordenación y Control del Medicamento, Dirección General de Farmacia y Productos Sanitarios, Conselleria de Sanitat, Valencia, Spain

Received November 12, 2008; accepted October 21, 2009

### KEYWORDS

Atypical  
antipsychotics;  
Elderly;  
Metabolic disorder;  
Drug use;  
Social health centre

### Abstract

**Objectives:** Describe and evaluate the use of atypical antipsychotics on the institutionalized elderly population of the Valencian Community and prevalence of associated metabolic disorders.

**Material and methods:** Multicentre transversal descriptive study on drug use and case-control of the prevalence of disorders of glycaemia, cholesterol and triglycerides. The statistical analysis of metabolic disorders is performed on the difference in prevalence and its statistical significance between control and study groups.

**Results:** Six hundred eighty-one patients were included (study group: 344; control group: 337) from 20 social-health-care centres. 18.5% of the institutionalized patients are being treated with atypical antipsychotics. The most frequent diagnoses are: behavioural disorders associated with dementia (63.6%) and schizophrenia (18.4%). Risperidone is the most frequently used antipsychotic (66.0%). For all the drugs in general the doses used adjusted to those recommended for the elderly patients. The prevalence of disorders in glucose, cholesterol and triglyceride metabolism in the group under study is 23.96% 34.83% and 26.29% respectively, with no statistically significant differences from the control group. The analysis by type of drug did not show significant differences.

**Conclusions:** The results obtained show that use of atypical antipsychotics in elderly patients complies with the established general recommendations. The doses used in elderly patients with behavioural disorders associated with dementia, mostly treated with risperidone, do not have a significant impact on the prevalence of metabolic disorders.

© 2008 SEFH. Published by Elsevier España, S.L. All rights reserved.

\*Corresponding author.

E-mail address: martinez\_gre@va.es (G. Martínez Romero).

**PALABRAS CLAVE**

Antipsicóticos  
atípicos;  
Anciano;  
Alteración  
metabólica;  
Utilización de  
medicamentos;  
Centro sociosanitario

**Utilización de fármacos antipsicóticos atípicos en ancianos institucionalizados y prevalencia de alteraciones metabólicas****Resumen**

**Objetivos:** Describir y evaluar la utilización de antipsicóticos atípicos en la población anciana institucionalizada de la Comunidad Valenciana y la prevalencia de alteraciones metabólicas asociadas.

**Material y métodos:** Estudio multicéntrico, descriptivo y transversal de utilización de medicamentos y caso-control de la prevalencia de las alteraciones de la glucemia, colesterol y triglicéridos. El análisis estadístico de las alteraciones metabólicas se realiza a partir de la diferencia de prevalencia y su significación estadística entre el grupo control y estudio.

**Resultados:** Se incluyen 681 pacientes (grupo estudio: 344; grupo control: 337) de 20 centros sociosanitarios. El 18,5% de los pacientes institucionalizados está en tratamiento con antipsicóticos atípicos. Los diagnósticos más frecuentes son alteraciones de conducta asociada a la demencia (63,6%) y a la esquizofrenia (18,4%). La risperidona es el fármaco antipsicótico más utilizado (66,0%). En general, para todos los fármacos, las dosis utilizadas se ajustan a las recomendadas en el paciente anciano. La prevalencia de alteraciones en el metabolismo de la glucosa, el colesterol y los triglicéridos en el grupo de estudio es del 23,96, el 34,83 y el 26,29%, respectivamente, no encontrándose diferencias estadísticamente significativas con respecto al grupo control. El análisis por tipo de fármaco no muestra diferencias significativas.

**Conclusiones:** Los resultados obtenidos muestran que la utilización de antipsicóticos atípicos en el paciente anciano sigue en líneas generales las recomendaciones establecidas. Las dosis utilizadas en el paciente anciano con alteraciones de conducta asociadas a la demencia, mayoritariamente tratado con risperidona, no tienen un impacto significativo sobre el aumento de la prevalencia de alteraciones metabólicas.

© 2008 SEFH. Publicado por Elsevier España, S.L. Todos los derechos reservados.

**Introduction**

The elderly patient with dementia usually develops behavioural disorders that include more or less severe episodes of psychosis, hallucinations, and both verbal and physical aggressiveness. Non-pharmacological strategies are considered to be the first choice for the treatment of these symptoms,<sup>1</sup> but in many cases these are difficult to implement in clinical practice or prove to be poor, and consequently, drug treatment is required. Typical or conventional antipsychotics, such as haloperidol, reveal discreet efficiency and an unfavourable adverse effect profile in the treatment of behavioural disorders in dementia.<sup>2</sup> Atypical, or second-generation antipsychotics are considered to have a more favourable adverse effect profile<sup>3</sup> and are currently the first choice for treatment of elderly patients.<sup>4</sup> However, there are a number of opinions on the effectiveness and safety of these drugs in elderly patients. A double blind randomized clinical study with 421 patients with Alzheimer and behavioural disorders concluded that the adverse effects of atypical antipsychotics offset their advantages.<sup>5</sup> In 1994,<sup>6</sup> the first case of hyperglycaemia in a patient treated with clozapine was reported, and since then, a high prevalence of this condition has been observed in schizophrenic patients treated with atypical antipsychotics. The diagnosis of diabetes, in most cases, is associated with weight gain and changes in lipid metabolism. Other atypical antipsychotics such as olanzapine and risperidone have also been associated with weight gain

problems, lipid metabolism disorders, and diabetes, all metabolic disorders.<sup>7</sup> It has been postulated that antagonism of the serotonin receptor 5HT<sub>1A</sub> that these drugs cause could inhibit insulin secretion and contribute to these adverse metabolic effects.<sup>8</sup> In May of 2004, the Spanish Agency for Drug and Health Products, along with the European Medicines Agency, published a note on the publication of studies indicating a significant increase in mortality and cerebrovascular accidents in patients treated with atypical antipsychotics for behavioural disorders associated with dementia. In April, 2005, the Food and Drug Administration published a report on the use of atypical antipsychotics in patients with dementia, associating it with an increased risk of death compared with placebo treatments.<sup>9</sup> With this background information, along with the scarcity of published studies in the field of institutionalized elderly patients with dementia under treatment with atypical antipsychotics, we set out to perform a study with the objectives of describing and evaluating the use of this type of medication and the prevalence of associated metabolic disorders.

**Methods and materials****Study population and study design**

We performed a multicentre transversal descriptive study on drug use and a case-control study for the analysis of

prevalence of metabolic disorders in institutionalized patients in public social health centres in the Valencian community.

## Patients

The study was performed on a group of patients institutionalized in the participating centres currently under treatment with atypical antipsychotics (risperidone, olanzapine, quetiapine, ziprasidone, or aripiprazole) and who had at least one available lab analysis of at least three months after starting antipsychotic treatment.

The control group was made up of a similar number of patients randomly selected from among those who did not receive antipsychotic treatment in the last 12 months and with current available test results. A similar number of patients were selected from each centre for the study group.

The information for each patient was supplied by the centres using a form designed for the study that included:

- Anthropometric data: age, weight, height, and body mass index (BMI).
- Pharmacological data: drug, documented indication in the clinical history and current dose (mg/day). Only taken for the study group (patients under treatment with atypical antipsychotics).
- Concomitant drugs and pathologies related to altered metabolism. The drugs included were diuretics, typical antipsychotics, beta-blockers, corticosteroids, and/or antidepressants. The concomitant pathologies included were renal failure, hepatic failure, hypothyroidism, and hypertension.
- Analyses of baseline glycaemia, total cholesterol, and triglycerides. The patient's final available analysis is selected, as long as it came 3 months prior to the initiation of treatment with antipsychotic drugs.
- Pharmacological treatment to correct metabolic disorders: statin, fibrate, insulin, or oral antidiabetics.

The information was obtained from the clinical histories for the patient at the centre and from the pharmacological management program at the pharmacy.

## Data analysis

**Drug use study.** For the study of the use of atypical antipsychotics in elderly institutionalized patients, we studied the following variables:

- Documented diagnoses that motivated the prescription.
- Overall percentage of use for each active ingredient according to the indications.
- Global mean dose (mg/day), 95% confidence interval (mg/day) and range (mg/day) by indication for each drug.
- Need for concomitant treatment using drugs for the correction of metabolic abnormalities.

**Prevalence of metabolic disorders.** This case-control study was performed in order to evaluate whether or not patients in the group with treatment by atypical antipsychotics presented a significantly higher prevalence

of metabolic disorders than the patients in the control group (without treatment by this type of drugs). The metabolic disorders and their definitions for our study were the following:

- **Altered glucose metabolism.** This is defined using the criteria from the American Diabetes Association.<sup>10</sup> A patient was considered to be presenting a glucose metabolic disorder when the baseline glycaemia level was  $\geq 110$  mg/dl and/or the patient was under treatment by some antidiabetic medication (insulin and/or oral antidiabetics).
- **Altered cholesterol and triglyceride metabolism.** This was defined using the criteria established by the National Cholesterol Education Program Adult Treatment Panel III.<sup>11</sup> A patient was considered to be presenting altered cholesterol metabolism when tests showed levels of 200 mg/dl or higher and/or was under treatment by some type of lipid-lowering drug (statin and/or fibrate or resin). In the case of triglycerides, we considered there to be an altered metabolic state when tests showed levels of 150 mg/dl or higher and/or the patient was under treatment by some type of lipid-lowering drug (statin and/or fibrate or resin).

For the analysis of the prevalence of metabolic disorders, we examined whether the patients from the study and control groups were comparable as far as the aforementioned concomitant pharmacological, anthropometric, and pathological data. Thus, in the case of significant differences existing in the prevalence of metabolic disorders, a possible association with the antipsychotic treatment could be assumed.

## Statistical analysis

The comparison of the continuous variables (age, weight, height, and BMI among control and study groups) was performed using the Student's T parametric test for independent samples. We applied Levene's test in order to test for equal variance. The normality of the distribution was assessed using the Kolmogorov-Smirnov test.

For the comparison of categorical variables corresponding to the prevalence of concomitant drugs and pathologies, we used the chi-squared test. For the analysis of metabolic disorders, we used the !CSP® V2000 macro by SPSS, which calculates the difference in prevalence and its statistical significance (with 95% confidence interval) between the control and study groups.

The statistical analysis of the data was performed using SPSS software version 11.0.1. We considered the test results to be statistically significant when *P* was equal to or less than .05.

## Results

We selected a total of 681 institutionalized patients from 20 different social health centres in the Valencian Community, 344 of which made up the study group for treatment with atypical antipsychotics and 337 formed the control group (no atypical antipsychotic treatment). Figure 1 demonstrates the inclusion process of the study patients.

Anthropometric and clinical characteristics of patients from both groups are shown in Table 1. The two groups showed statistically significant differences in the following variables: age (79.5 years in the study group versus 82.4 years in the control group), the percentage of patients with no pertinent pathologies (63.8% in the study group in front of 45.1% in the control group), the percentage of patients diagnosed with hypertension; (25.9% in the study group, 40.9% in the control group), the presence of two or more pathologies related to metabolic disorders (3.8% in the study group, 7.4% in the control group), the percentage of patients treated with diuretic medications (16.9% in the study group, 27.3% in the control group), and the percentage of patients without concomitant treatment with drugs related to metabolic disorders (57.0% in the study group, 42.1% in the control group).

### Drug use study

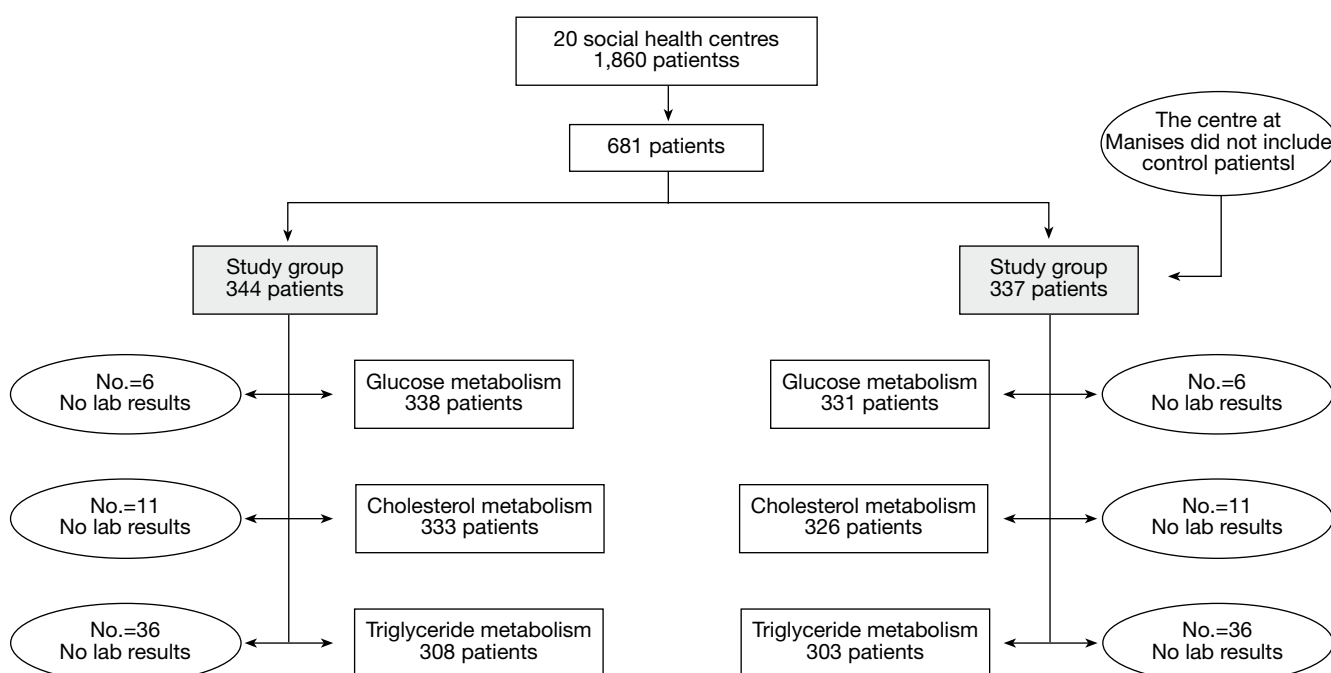
18.5% (n=344) of the institutionalized patients at the centres included in this study were under treatment from one or more antipsychotics at the time. The analysis of diagnoses that motivated the prescription of atypical antipsychotics that was obtained from the review of patient clinical histories demonstrated that these drugs were used mostly to treat behavioural disorders associated with dementia (63.56%), followed by schizophrenia (18.37%). To a lesser degree, they were also used to treat bipolar disorder (4.66%), psychosis (4.66%), and obsessive-compulsive disorder (0.3%). Additionally, in 8.45% of patients, no indication for the

use of antipsychotic medication was present in the clinical history.

As far as active ingredients and their frequency of use is concerned, the most commonly used components were risperidone (65.99%) followed by quetiapine (16.28%), olanzapine (13.66%), and, to a lesser degree, ziprasidone (0.9%). The concomitant use of two or more drugs was present in 3.2% of patients. The prevalence of use according to the documented indications in the medical histories is shown in Table 2. The global analysis of regimens used for each antipsychotic drug according to the indications is summarized in Table 3. Due to the minimal use of ziprasidone (n=3), this has not been listed on the table, nor is it evaluated in the analysis of metabolic disorder prevalence.

### Analysis of metabolic disorder prevalence

The global analysis of prevalence of disorders in glucose, cholesterol, and triglyceride metabolism in both patient groups showed no statistically significant differences. The results are shown in Table 4. The individual analysis by type of drug, as compared to the control group, showed no statistically significant differences in any of the studied parameters. The results from this analysis are summarized in Table 5. The comparison between the three antipsychotic drugs used in the study showed a higher prevalence of disorders in triglyceride metabolism from patients treated with olanzapine as compared to those treated with risperidone (38.29% vs 23.76%; chi-squared: 4.1354;  $P=.042$ ). The rest of the comparisons showed no significant differences.



**Figure** Inclusion process for patients in the study.

**Table 1** Anthropometric and clinical characteristics

	Control	Study	P
<i>Anthropometric characteristics</i>			
n	337	344	
Age (range)	82.4 (45.5-101.1)	79.5 (45.5-98.2)	< .0001
Weight (95% CI)	63.4 (61.8-65.1)	62.5 (61.5-64.7)	> .05
Height (95% CI)	154.9 (153.7-155.9)	155.6 (154.5-156.7)	> .05
BMI (95% CI)	26.45 (25.8-27.0)	26.1 (25.4-26.7)	> .05
<i>Concomitant pathologies</i>			
No pertinent pathologies (%)	152 (45.1)	219 (63.8)	< .00005
Renal failure (%)	15 (4.5)	8 (2.3)	> .05
Hepatic failure (%)	4 (1.3)	6 (1.7)	> .05
Hypothyroidism (%)	3 (0.9)	8 (2.3)	> .05
Hypertension (%)	138 (40.9)	89 (25.9)	= .00003
Two or more associated pathologies (%)	25 (7.4)	13 (3.8)	= .039
<i>Concomitant drugs</i>			
No pertinent medications (%)	142 (42.1)	196 (57.0)	= .00011
Diuretics (%)	92 (27.3)	58 (16.9)	= .001
Typical antipsychotics (%)	20 (5.9)	20 (5.8)	> .05
Beta blockers (%)	5 (1.5)	2 (0.6)	> .05
Corticosteroids (%)	3 (0.9)	1 (0.3)	> .05
Antidepressants (%)	36 (10.7)	35 (10.2)	> .05
Two or more drugs (%)	39 (11.6)	32 (9.3)	> .05

BMI indicates body mass index; CI: confidence interval.

**Table 2** Antipsychotic drug use according to indication

Indication	Antipsychotic drug					Total
	Risperidone	Quetiapine	Olanzapine	Ziprasidone	Two or more	
Behavioural disorder. Dementia (%)	146 (67.0)	39 (17.9)	26 (11.9)	3 (0.9)	5 (2.3)	219
Schizophrenia (%)	41 (65.1)	7 (11.1)	9 (14.3)	1 (1.6)	5 (7.9)	63
Bipolar disorder (%)	8 (50.0)	3 (18.8)	5 (31.3)	–	–	16
Psychosis	8 (50.0)	4 (25.0)	4 (25.0)	–	–	16
Obsessive-compulsive disorder (%)	–	–	1 (100.0)	–	–	1
Not specified (%)	23 (79.3)	3 (10.3)	2 (6.9)	–	1 (3.4)	29
						344

The comparison of drug use profiles for correcting metabolic disorders (statins, fibrates, oral antidiabetics, and/or insulin) between both patient groups shows a significantly higher use of oral antidiabetics in the control group (11.30% vs 6.70%; chi-squared: 4.3484;  $P=.037$ ). No statistically significant differences were found with the rest of the correcting drugs (Table 6).

## Discussion

This study is aimed to describe the drug use profile for atypical antipsychotics in the elderly institutionalized

population, evaluating the prevalence of glucose, cholesterol, and triglyceride metabolism disorders. In order to ensure that the results are representative of this population, we attempted to include the maximum number of patients possible through participation of a high number of social health centres in the Valencian Community. For the drug use study, we decided to use a transversal study design, and a case-control prevalence study design for the evaluation of metabolic disorders. A cohort study for this evaluation was rejected due to the impossibility of including enough patients with initiation of antipsychotic treatment at the centre.

Upon analysis of the clinical and anthropometric characteristics of each group of patients, we detected

**Table 3** Global analysis of antipsychotic drug regimens according to indications

	Mean dose, mg/day	95% CI, mg/day	Dose range, mg/day
<i>Risperidone</i>			
Risperidone (n=218)	1.79	1.59-1.98	0.5-12
<i>According to diagnosis</i>			
Behavioural disorder. Alzheimer	1.45	1.30-1.60	0.5-6.0
Schizophrenia	2.88	2.19-3.54	0.5-12.0
Bipolar disorder	2.68	0.47-4.90	1.0-9.0
Psychosis	2.54	0.62-4.46	0.5-6
<i>Olanzapine</i>			
Olanzapine (n=44)	6.12	5.23-7.00	2.5-15
<i>According to diagnosis</i>			
Behavioural disorder. Alzheimer	5.76	4.49-7.03	2.5-12.5
Schizophrenia	6.94	5.10-8.81	5.0-10.0
Bipolar disorder	8.50	3.30-13.69	5.0-15.0
Psychosis	4.37	2.38-6.36	2.5-5
<i>Quetiapine</i>			
Quetiapine (n=46)	176.33	128.5-224.1	25-1200
<i>According to diagnosis</i>			
Behavioural disorder. Alzheimer	134.61	106.44-162.78	25-400
Schizophrenia	457.14	132.9-781.31	100-1200
Bipolar disorder	200	–	–
Psychosis	125	–	–

CI indicates confidence interval.

**Table 4** Global analysis of the metabolic disorder prevalence in the study and control groups

	Study group	Control group	Totally
<i>Glucose metabolism</i>			
Metabolic disorder	81	84	165
No disorder	257	247	504
Total	338	331	669
Altered patients, % (95% CI)	23.96 (19.51 to 28.88)	25.37 (20.77 to 30.42)	24.66 (21.44 to 28.11)
Difference in prevalence, % (95% CI)	–1.41 (–7.9 to 5.1)		
Odds prevalence ratio (95%CI)	0.92 (0.65 to 1.31)		
Chi-squared	0.1797	P=.67160	
<i>Cholesterol metabolism</i>			
Metabolic disorder	116	106	222
No disorder	217	220	437
Total	333	326	659
Altered patients, % (95% CI)	34.83 (29.72 to 40.21)	32.51 (27.45 to 37.89)	33.68 (30.08 to 37.43)
Difference in prevalence, % (95% CI)	2.32 (–4.89 to 9.53)		
Odds prevalence ratio (95%CI)	1.10 (0.80 to 1.53)		
Chi-squared	0.3967	P=.52878	
<i>Triglyceride metabolism</i>			
Metabolic disorder	81	81	162
No disorder	227	222	449
Total	308	303	611
Altered patients, % (95% CI)	26.29 (21.46 to 31.59)	26.73 (21.83 to 32.09)	26.51 (23.05 to 30.20)
Difference in prevalence, % (95% CI)	–0.43 (–7.43 to 6.56)		
Odds prevalence ratio (95% CI)	0.97 (0.68 to 1.40)		
Chi-squared	0.0148	0.90329	

CI indicates confidence interval.

**Table 5** Analysis by drug of the prevalence of metabolic disorders compared to the control group

	Study group, %(95%CI)	Control group, %(95%CI)	Chi-squared (P)
<i>Glucose metabolism disorders</i>			
Risperidone	24.00 (18.57 to 30.12)	25.37 (20.77 to 30.42)	0.1362 (.71205)
Olanzapine	19.15 (9.14 to 33.25)		0.8608 (.35350)
Quetiapine	28.84 (17.12 to 43.07)		0.2821 (.59531)
<i>Cholesterol metabolism disorders</i>			
Risperidone	31.81 (25.71 to 38.41)	32.51 (27.45 to 37.89)	0.0292 (.86426)
Olanzapine	38.29 (24.50 to 53.62)		0.6189 (.43141)
Quetiapine	44.23 (30.46 to 58.67)		2.7380 (.09798)
<i>Triglyceride metabolism disorders</i>			
Risperidone	23.76 (18.07 to 30.24)	26.73 (21.83 to 32.09)	0.5622 (.45337)
Olanzapine	38.63 (24.35 to 54.50)		2.6864 (.10121)
Quetiapine	31.25 (18.65 to 46.25)		0.4255 (.51418)

CI indicates confidence interval.

**Table 6** Drug use profile for metabolic disorders

Treatment	Patient group		
	Control, n (%)	Study, n (%)	Total
No corrective treatment	239 (70.9)	251 (72.9)	490
Statin	29 (8.6)	23 (6.7)	52
Fibrate	–	4 (1.2)	4
OAD	38 (11.3)	23 (6.7)	61
Insulin	19 (5.6)	23 (6.7)	42
Combined treatment (OAD or insulin+statin and/ or fibrate)	12 (3.6)	20 (5.8)	32
Total	337	344	681

CI indicates confidence interval; OAD, oral antidiabetics.

significantly lower ages in the group treated with antipsychotics, probably due to the fact that psychiatric disorders in elderly patients are one of the primary reasons for early institutionalization. However, the mean age in both patient groups was comparable to other studies performed in the elderly.<sup>5</sup>

Regarding weight and BMI, the values were comparable for the two groups, showed a normal distribution, and were similar to those observed in other studies.<sup>12</sup> The prevalence of arterial hypertension was significantly higher in the control group (40.9%) as compared to the study group (25.9%), and both values were significantly lower than those found in the HTA Geriatric Study,<sup>13</sup> which found a prevalence of 62.1% in this field of care. The lower prevalence of patients with hypertension in our population could be explained by the fact that the diagnosis of hypertension in our study was obtained from the information in the clinical history, while this metric was obtained in the previous study from 3 variables (diagnosis in the clinical history, anti-hypertension treatment, and/ or arterial pressure=140/ 90 mm Hg), with the presence of at least one of these factors constituting hypertension. In this sense, in a study carried

out by the La Cañada Pharmacy Department (unpublished) on a cohort of 646 patients at 8 social health centres, the prevalence of patients with hypertension was 46.3% taking into account clinical histories and/ or anti-hypertension treatment as diagnostic criteria. In this sense, the addition of arterial pressure as another criterion yields comparable results to the aforementioned study. The difference between the percentage of hypertensive patients in the study and control groups could be explained by two causes derived from the structure of this health system: the inconsistent and inadequate documentation of the clinical histories in many cases, and the therapeutic and clinical inertia with respect to these patients following admission to the centre, concentrating their treatment on behavioural disorders and cognitive state, while passing on other chronic pathologies such as arterial hypertension to a lower level of diagnostic attention. This greater prevalence of patients diagnosed with arterial hypertension in the control group was accompanied by an increased use of diuretic medications.

Regarding the diagnoses that motivated the prescription of the antipsychotic drugs, we obtained results according to the institutionalized patient profile. For the most part, we



used behavioural disorders associated with dementia (63.6%), and to a lesser degree, but with a significant percentage of cases, for schizophrenia treatment. The results obtained were slightly different regarding those obtained from a health study performed in Santiago de Compostela<sup>14</sup> on elderly patients treated with atypical antipsychotics, 42% of which came with indications from dementia with severe behavioural disorder, 31% with schizophrenia, 24% with moderate-severe manic episodes, and 3% with other severe psychotic conditions. This varying prescription profile could explain the higher prevalence of dementia and associated disorders in patients included in the study, since this disease is one of the primary causes of institutionalization of elderly people.

The most commonly used atypical antipsychotic was risperidone, both globally and as indicated for treatment, which corresponds to the obtained diagnostic profile. Currently, it is the only one of its group with indications for use in the treatment of behavioural disorders associated with dementia, and for the rational use policy in this type of medication stemming from the social health geriatric drug therapy guide.<sup>15</sup> The use profile in behavioural disorders associated with dementia was similar to the results obtained in other studies,<sup>16</sup> with risperidone being the most commonly used drug. The use of quetiapine was slightly higher than olanzapine, since this drug is considered to have the most unfavourable adverse effects in this type of patient, especially at the level of anticholinergic symptoms and metabolic disorders.

The analysis of drug regimens use showed that, in general terms, medication was adjusted to the recommended level for elderly patients, that is, doses lower than 2 mg/ day for risperidone, 10 mg/ day for olanzapine, and between 40% and 50% lower doses than those for regular adults in quetiapine (<200 mg/ day). The magnitude of the dosage was directly related to the most frequent indication (behavioural disorders) and the lower prevalence of patients with schizophrenia, who often receive higher doses. These doses were similar to those used in a study<sup>17</sup> performed on patients institutionalized in elderly residences where the indications for schizophrenia, bipolar disorder, and psychosis provided for mean doses of the three drugs under study were slightly higher than those used for patients with<sup>18</sup> dementia, but still within the recommended dosage for geriatric patients. In a different study with elderly patients, the doses of risperidone and quetiapine were slightly lower than normal, probably due to a more favourable clinical situation for the patients, since it did not include any who required institutionalization.

For the analysis of the relationship between atypical antipsychotic drugs and the appearance of metabolic disorders, a prospective cohort design was first proposed for the identification of incident cases. This was not possible due to the fact that the majority of cases had started before the institutionalization of the patients and no reliable information was available from the clinical histories at the centre. For this reason, the case-control study was used to determine whether or not the prevalence of these disorders in the treatment group was significantly higher than in the control group.

The results obtained do not show significant differences between study and control groups for metabolic disorders.

In the case of glucose metabolism, the total prevalence of patients with disorders according to previously described criteria was around 25% comparable with other studies<sup>19</sup> performed with these types of patients and in accordance with prevalence data from the Spanish Society of Medical Residents and the Andalusian Society of Family and Community Medicine. In the case of cholesterol and triglyceride metabolism, the total prevalence of patients with disorders was around 34% and 26.5% respectively, both of which are comparable to values obtained in other studies with elderly patients from Spain.<sup>20,21</sup>

The analysis performed for each of the antipsychotic drugs showed no significant differences in the prevalence of metabolic disorders between the study and control groups. However, there was a difference between the sample size of patients treated with risperidone (n=218), as compared to olanzapine (n=44) and quetiapine (n=46), which questions the relevance of the results obtained for these two drugs. In this sense, it is difficult to evaluate whether the disorders in cholesterol metabolism in patients treated with quetiapine and triglyceride metabolism disorders in patients treated with olanzapine, which show increased prevalence, could perhaps be statistically significant with larger sample sizes. The concordance with data obtained in other studies<sup>14-16</sup> with similar patient samples minimized the possible influence of the differences found in prevalence of hypertension and treatment with diuretics between the study and control groups on the final results.

In general terms, the data from our study show that the doses used for the treatment of behavioural disorders in dementia patients, significantly lower than those used in schizophrenia patients,<sup>22,23</sup> have no significant impact on the increased prevalence of metabolic disorders, or at least no such relationship has been proved by the design of our study. However, it is important that the patients under treatment by atypical antipsychotics be included in control programs for glycaemia, lipid profile, cardiovascular risk evaluation, and, of course, regular re-evaluation of the need/ adequacy of antipsychotic treatment. However, in order to establish more definitive conclusions on the impact of these types of drugs on glucose, cholesterol, and triglyceride metabolism in elderly patients, studies with prospective and controlled designs must be implemented in different health areas in order to provide better clinical information on patients.

## Conflict of interests

The authors affirm that they have no conflicts of interest.

## Acknowledgements

We would like to thank Patricia Bravo, Vanessa Castro, Elia Fernandez, Patricia Ferrandis, Pilar Martínez, Belen Montañes, Ana Moreno, Vega Ortiz de Urbina and Carmen Saez, pharmacologists from pharmacy departments that comprise the Pharmaceutical Attention Program at Social Health Centres of the Valencian Community, since their interest and important collaboration in the selection of patients and data collection has made this study possible.



## References

1. Sink KM, Holden KF, Yaffe K. Pharmacological treatment of neuropsychiatric symptoms of dementia: a review of the evidence. *JAMA*. 2005;293:596-608.
2. Schneider LS, Pollock VE, Lyness SA. A metaanalysis of controlled trials of neuroleptic treatment in dementia. *J Am Geriatr Soc*. 1990;38:553-63.
3. Jeste DV, Lacro JP, Bailey A, Rockwell E, Harris MJ, Caliguri MP. Lower incidence of tardive dyskinesia with risperidone compared with haloperidol in older patients. *J Am Geriatr Soc*. 1999;47:716-9.
4. Alexopoulos GS, Streim J, Carpenter D, Docherty JP. Using antipsychotic agents in older patients. *J Clin Psychiatry*. 2004;65:5-104.
5. Scheneider LS, Tariot PN, Dagerman KS, Davis SM, Hsiao JK, Ismail MS, et al. Effectiveness of atypical antipsychotic drugs in patients with Alzheimer's disease. *N Engl J Med*. 2006;355:1525-38.
6. Koval MS, Pames LJ, Christie S. Diabetic ketoacidosis associated with clozapine treatment. *Am J Psychiatry*. 1994;151:1520-1.
7. Smith RC, Lindenmayer JP, Bark N, Warner-Cohen J, Vaidyanathaswamy S, Khandat A. Clozapine, risperidone, olanzapine, and conventional antipsychotics drug effects on glucose, lipids, and leptin in schizophrenic patients. *Int Neuropsychopharmacol*. 2005;8:183-94.
8. Bettinger TL, Mendelson SC, Dorson PG, Crismon ML. Olanzapine-induced glucose dysregulation. *Ann Pharmacother*. 2000;34:865-7.
9. US Food and Drug Administration. FDA issues public health advisory for antipsychotic drugs used for treatment of behavioral disorders in elderly patients. FDA Talk Paper T05-13. Rockville, MD: US Food and Drug Administration. 2005 Apr 11 [accessed 25 February, 2008]. Available from: <http://www.fda.gov/bbs/topics/ANSWERS/2005/ANS01350.html>
10. American Diabetes Association. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care*. 1997;20:1183-97.
11. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002;106:3143-421.
12. Scheneider LS, Dagerman K, Insel PS. Efficacy and adverse effects of atypical antipsychotics for dementia: Meta-analysis of randomized, placebo-controlled trials. *Am J Geriatr Psychiatry*. 2006;14:191-210.
13. Martín-Baranera M, Armario-García P, Sánchez-Ferrín P. Prevalencia de hipertensión arterial en ancianos ingresados en centros sociosanitarios y residencias españolas: Estudio Geriatric HTA. *Med Clin*. 2006;127:681-7.
14. Carracedo-Martínez E. Estudio sobre la utilización de antipsicóticos atípicos en población anciana. *FAP*. 2006;4:110-5.
15. Servicio de Coordinación de Centros Propios. Dirección General de Acción Social y Mayores. Conselleria de Bienestar Social. Guía farmacoterapéutica sociosanitaria geriátrica. Valencia, España; 2008.
16. Sudeep G, Bronskill S, Sharon-Lise N, Anderson G, Sykora K, Lam K, et al. Antipsychotic drug use and mortality in older adults with dementia. *Ann Intern Med*. 2007;146:775-86.
17. Redondo Capafons S, Monsó Fernández C, Garriga Biosca MR, Pla Poblador R, Quintana Riera S, Porta Rius G. Utilización de psicofármacos en un centro sociosanitario. *Farm Hosp*. 2006;30:173-6.
18. Sink KM, Holden KF, Yaffe K. Pharmacological treatment of neuropsychiatric symptoms of dementia. *JAMA*. 2005;293:596-608.
19. Trueba J. Diabetes mellitus y calidad de vida en población geriátrica institucionalizada. *Rev Esp Geriatr Gerontol*. 2007;42:16-21.
20. Herrero-Herrero JL, Martín Oterino JA, Sanz Ortega F, Mateos Sánchez A, Polo García JM, García Gómez ML, et al. Población anciana y campañas para la prevención de la hipercolesterolemia en Salamanca. *An Med Interna*. 2001;18:13-9.
21. Sáiz Peña P, María del Carmen N. Estudio epidemiológico del perfil lipídico en población anciana española. Madrid: Doctoral thesis, Universidad Complutense de Madrid; 2004.
22. Lindenmayer JP, Czobor P, Volavka J, Citrome L, Sheitman B, McEvoy JP, et al. Changes in glucose and cholesterol levels in patients with schizophrenia treated with typical or atypical antipsychotics. *Am J Psychiatry*. 2003;160:290-6.
23. Koller E, Cross J, Doraiswamy M, Scheneider B. Risperidone-associated diabetes mellitus: a pharmacovigilance study. *Pharmacotherapy*. 2003;23:735-44.