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Impact of obesity on the use of antipsychotic drugs in the adult population attended in several primary care centers

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Introduction. We describe the association between the obesity and the use of antipsychotic drug (APD) in patients attended by five primary care teams.

Methods. Multicenter-retrospective design, carried out between July 2004 and June 2005, in patients who consumed APD treatment. A Body Mass Index (BMI) >29 kg/m² was considered obesity. The main measurements were: consumption of APD, generals (gender and age), comorbidities and clinical parameters. Regression-logistic analysis and ANCOVA (Bonferroni-adjustment) were applied to correct the model.

Results. From a total of 42,437 attended patients (mean age: 50.9 (SD: 17.8) years; women: 59.9%; with obesity: 27.3% [confidence interval [CI] 95%: 26.9-27.7]), the 1.3% received APD treatment (typical: 48.8%; atypical: 51.2%; p=not significant). In the logistic-model the obesity was related with the ADP use (*odds ratio* [OR]: 1.5, CI: 1.3-1.8), hypertension (OR: 2.4; CI: 2.2-2.5), diabetes (OR: 1.4; CI: 1.3-1.5) and dyslipidemia (OR: 1.3; CI: 1.2-1.4); p=0,000. The adjusted BMI, in presence of APD, was 27.8 kg/m² vs. 27.4 kg/m²; p=0,002.

Conclusions. Obesity was associated with the use of APD and with the presence of hypertension, diabetes and dyslipidemia. Differences could not be observed between the use of typical or atypical APD.

Key words:
Obesity. Antipsychotic use. Primary care.

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Impacto de la obesidad en la utilización de fármacos antipsicóticos en población adulta atendida en varios centros de atención primaria

Introducción. Se describe la asociación de la obesidad con el uso de fármacos antipsicóticos (ATP) en pacientes atendidos por cinco equipos de atención primaria.

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Métodos. Diseño retrospectivo-multicéntrico realizado entre julio de 2004 y junio de 2005 en pacientes en tratamiento con ATP. Se consideró obesidad un índice de masa corporal (IMC) >29 kg/m². Las principales mediciones fueron: consumo de ATP, generales (sexo y edad), comorbilidades y parámetros clínicos. Se efectuó un análisis de regresión logística y ANCOVA (ajuste-Bonferroni) para la corrección del modelo.

Resultados. De 42.437 pacientes atendidos (promedio-edad: 50,9 años [DE: 17,8]; mujeres: 59,9%; con presencia de obesidad el 27,3% [intervalo de confianza [IC] del 95%: 26,9-27,7]); un 1,3% recibían tratamiento ATP (típicos: 48,8%; atípicos: 51,2%; p=no significativo). En el modelo logístico la obesidad se relacionó con el uso de ATP (*odds ratio* [OR]: 1,5; IC: 1,3-1,8), hipertensión (OR: 2,4; IC: 2,2-2,5), diabetes (OR: 1,4; IC: 1,3-1,5) y dislipidemia (OR: 1,3; IC: 1,2-1,4); p=0,000. El IMC corregido en presencia de ATP fue de 27,8 frente a 27,4 kg/m²; p=0,002.

Conclusiones. La obesidad se asoció con el uso de ATP y con la presencia de hipertensión, diabetes y dislipidemia. No se observaron diferencias entre el uso de ATP típicos o atípicos.

Palabras clave:
Obesidad. Uso de antipsicóticos. Atención primaria.

INTRODUCTION

Metabolic alterations such as obesity, diabetes or dyslipidemia increase the risk of suffering cardiovascular events¹. Regarding these, obesity causes an unquestionable repercussion on the health of the population due to its elevated morbidity-mortality^{1,2}. The populational prevalence is found in ranges going from 6% to 20% (Netherlands, USA), with predominance of women and a tendency to increase with age, its maximum being reached between 40 and 50 years. In Spain, the data provided by the Spanish Society for the Study of Obesity (SEEDO)³ or from different studies provide results greater than 14%, with a clear tendency to progressive increase^{3,4}.

The evidence available up to now suggests that the use of antipsychotic drugs (APD) is increasing and that they cause

side effects in the glucose and lipid metabolism, leading to weight gain⁵. These repercussions are more evident in second generation APD (atypical), although the risk level generally varies according to the different active ingredients used^{5,6}. There are clear controversies among the different authors, for example, the effects of clozapine and olanzapine may cause an increase in the cholesterol and triglyceride levels⁶, or a greater risk of suffering diabetes mellitus². The same occurs with subjects treated with risperidone due to its negative effects on glucose and/or lipid metabolism⁷. Multiple etiological factors may be linked to the disease: genetic predisposition, eating habits, psychosocial factors, adipose tissue imbalances, alterations in neurotransmitters that intervene in weight regulation or the association of certain drugs⁴⁻⁷. Unfortunately, the role and importance of each one is often difficult to measure. It is also difficult to distinguish if certain biological alterations have a cause/effect relationship with weight excess⁵. This study aimed to evaluate the association of obesity with the use of typical and atypical APD in adult patients attended by five primary health care teams in a Spanish population setting.

METHODS

A retrospective, multicenter study was conducted based on the medical records of adult patients seen in outpatient regime in the usual clinical practice. The study population was formed by five primary health care teams managed by the Badalona Serveis Assistencials, S.A., in which a population of about 105,300 inhabitants (14.5% over 64 years of age) are assigned. It has reformed organization type, with public management and private suppliers of services contracted by the Catalonia Health Service (CatSalut). The company has personnel, training policy, organizational model and service portfolio similar to that of most of the primary health care centers of Catalonia with a decentralized management model and unique structural services.

All the patients seen between July 1, 2004, and June 30, 2005, age >15 years, who had initiated drug treatment of APD, who were in the chronic prescriptions program and who came regularly to the scheduled appointments to obtain the medical prescriptions (verified registry of daily dose, time interval and duration of each treatment) were included in the treatment. Those patients who did not come to the centers, who were transferred or live outside of the area and those who had incapacitating mental diseases were excluded. Obesity was considered to be the presence of overweightness due to accumulation of fatty tissue, when the body mass index (BMI, kg/m²) was greater than 29 (NCEP criteria⁸). Information was obtained on the prescription of APD drugs (atypical and typical) found in the computerized clinical records according to the recommendations made by the clinician. The different active ingredients were grouped into five categories: a) atypical (amisulpride-clozapine-quetiapine-ziprasidone); b) olanzapine; c) risperidone; d) typical (chlorpromazine, clozapine, flufenazine, levomepromazine, perfenazine, pericia-

zine, pimozide, pipotiazine, tiapride, thioproperazine, thioridazine, zuclopentixole), and e) haloperidol. The episode was defined as a procedure of disease care and was measured according to the International Classification of Primary Care (ICPC: Lamberts-Wood). The following clinical parameters were obtained: systolic blood pressure (SBP, mmHg) and diastolic blood pressure (DBP, mmHg), baseline glycemia (mg/dl), triglycerides (mg/dl), total cholesterol (mg/dl), low density lipoprotein cholesterol fraction (LDLc Friedewald in mg/dl) and high density lipoprotein cholesterol fraction (HDLc) in mg/dl. The data were validated, guaranteeing the confidentiality of the records required by law. A statistical analysis was made with mean, standard deviation (SD) and 95% confidence interval (CI) values. Parametric tests (chi-squared and Student's *t* test) were used for the relationship of variables in the bivariate analysis. Logistic regression analysis was made with a step-by-step procedure for correction of the model. Variables were included based on the significance of the results in the bivariate analysis and their clinical significance (dependent variable-obesity). In addition, a multivariate analysis of the covariance (ANCOVA) was made with estimation of the marginal means using Bonferroni adjustment. The SPSSWIN program version-12 was used, establishing a statistical significance for values of $p < 0.05$.

RESULTS

Information was obtained from 42,437 patients (table 1), with average age of 50.9 (17.8) years and 59.9% women. Demand for attention with obesity in the population attended was 27.3% (CI: 26.9%-27.7%). A total of 1.3% of the patients ($n=551$) received treatment with APD (CI: 0.4%-2.2%). Obesity, associated to the use of APD was 1.8%, with a BMI of 33.8 (3.6); $p=0.000$. There were no significance differences between typical APD (48.8%) and atypical ones (51.2%) or according to active ingredients (p =not significant). The presence of obesity was associated with most of the comorbidities and clinical parameters studied. In the final logistic model, corrected for age and gender, obesity was associated with the use of APD, hypertension, diabetes and dyslipidemia (table 2), $p=0.000$. The clinical parameters were not significant. In the ANCOVA model, the BMI corrected for age and gender for the APD treatment group was 27.8 kg/m² (SE: 0.130), and 27.4 kg/m² (SE: 0.015) in those not taking APD; $p=0.002$ (difference of means: 0.399; CI: 0.142-0.655; F : 9.257).

DISCUSSION

The results manifest that the demand for care for obesity was 27.3%. The results obtained are elevated. One part may be justified because the patients seen are not representatives of the general population and on the other part, it may be due to the fact that young patients make fewer visits to the health care services. However, lack of knowledge about the etiology and the limited therapeutic resources available reduce the therapeutic successes that are often followed by initial

Table 1 General characteristics of the series studied

Variables studied	Absence of obesity (n = 30,843)	Presence of obesity (n = 11,594)	Total of the series (n = 42,437)	p
Subjects under APD treatment (percentage)	n = 344 (1.1)	n = 207 (1.8)	n = 551 (1.3)	0.000
Body mass index (SD) (kg/m ²)	25.0 (3.0)	33.8 (3.6)	27.4 (5.1)	0.000
APD grouping				
Typical*	36.6	38.2	37.2	NS
Haloperidol	11.3	12.1	11.6	NS
Atypical**	6.7	8.7	7.4	NS
Olanzapine	23.3	18.8	21.7	NS
Risperidone	22.1	22.2	22.1	NS
General				
Mean age (SD) (years)	48.2 (18.8)	57.9 (15.5)	50.8 (18.4)	0.000
Gender (women)	52.4	59.9	54.5	0.000
Background or associated comorbidities				
High blood pressure	19.9	47.0	27.3	0.000
Dyslipidemia	22.6	35.9	26.3	0.000
Diabetes mellitus	9.0	19.0	11.7	0.000
Smokers	29.2	18.5	26.3	0.000
Ischemic heart disease	3.5	6.2	4.3	0.000
Cerebrovascular accident	2.0	2.3	2.1	0.042
Cardiovascular events	6.3	9.2	7.1	0.000
Alcoholism	1.9	1.7	1.8	NS
Chronic obstructive pulmonary disease	2.9	4.5	3.4	0.000
Bronchial asthma	3.8	4.7	4.1	0.000
Clinical parameters				
Systolic blood pressure (SD) (mmHg)	127.0 (16.6)	135.2 (16.1)	129.6 (16.9)	0.000
Diastolic blood pressure (SD) (mmHg)	75.1 (9.5)	79.5 (9.4)	76.5 (9.7)	0.000
Baseline glycemia (SD) (mmHg)	95.1 (25.5)	106.6 (32.8)	98.5 (28.4)	0.000
Serum triglycerides (SD) (mmHg)	112.3 (75.2)	140.6 (89.7)	121.5 (81.3)	0.000
Total cholesterol (SD) (mmHg)	204.9 (45.3)	221.4 (42.3)	217.7 (43.6)	0.000
HDLc-cholesterol (SD) (mmHg)	48.3 (13.7)	44.0 (12.0)	46.9 (13.3)	0.000
LDLc-cholesterol (SD) (mmHg)	138.0 (36.1)	143.1 (34.3)	139.6 (35.6)	0.000

Values expressed in percentage or mean (SD: standard deviation); p: statistical significance; N: non-significant; APD: antipsychotics; HDLc: high density lipoproteins-cholesterol; LDLc: low density lipoproteins-cholesterol. *Typical (chlorpromazine, clotiapine, flufenazine, levomepromazine, perfenazine, periciazine, pimozide, pipotiazine, tiapride, thioproperazine, thioridazine, zuclopentixole). **Atypical (amisulpride, clozapine, quetiapine, ziprasidone).

weight recovery. All this favors the idea that the treatment and prevention activities for obesity are not very efficient. This is generating a certain relaxed attitude about this risk factor and resistance towards dedicating too much effort when the interventions of the doctors towards other health problems are more effective. In the logistic model, obesity was associated with the use of APDs and hypertension, diabetes and dyslipidemia were shown as factors independent of weight increase. These results are similar to those described in the literature consulted^{2,5-7}. However, the impact of obesity on health requires a preventive approach and this can only be done through the generalization of the educational activi-

ties⁶. These data manifest the importance of the prevention of weight increase in psychiatry, adequate indication of treatment in each case and the subsequent follow-up of the patients who receive treatment with APD, especially in patients with elevated cardiovascular risk^{6,7}. No differences have been found between the use of typical and atypical APDs with obesity. This finding may be due to a bias in the patient selection, to a statistical artifact or to low statistical power due to limited number of patients in each group⁹. Other limitations make it necessary to be cautious in the generalization of the results. Standing out among these are the observational design itself of the study (lack of external validity, underestima-

Table 2

Final logistic regression and model between the dependent variable, presence of obesity of the series studied

Variables of the model	Beta	p	OR	95% CI
Use of antipsychotics	0.421	0.000	1.5	1.3-1.8
Age	0.132	0.000	1.2	1.1-1.3
Gender (men)	-0.272	0.000	0.8	0.7-0.8
High blood pressure	0.864	0.000	2.4	2.2-2.5
Diabetes mellitus	0.323	0.000	1.4	1.3-1.5
Dyslipidemia	0.272	0.000	1.3	1.2-1.4

p: statistical significance; OR: odds ratio; CI: confidence interval.

tion of the data), the possible variability of the professionals of the centers, coordination of levels (care continuum) and lack of adjustment of the doses prescribed⁵. However, this type of reformed center has a very similar organization model and action protocolization⁹. New research is needed in the future to confirm the consistence of the results and to evaluate the strategies oriented towards reducing the cardiovascular risk factors. Furthermore, it is important to continue advancing in the degree of therapeutic compliance and achievement of the objectives in order to obtain more cost-effective actions⁵. Advances in the knowledge of neurotransmitters and neuropeptides, their adverse reactions or state of the research in the animal modeling are also important aspects for future studies^{5,10}. In conclusion, obesity, an important cardiovascular risk factor, is associated with the use of APD when there are hypertension, diabetes and dyslipidemia. No differences between the use of typical and atypical APD were observed in our sample. New studies under the usual clinical practice situation are needed to reinforce the consistency of the results.

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