Polypharmacy in the antipsychotic prescribing in practices psychiatric out-patient clinic

G. Flórez Menéndez[a], M. Blanco Ramos[b], I. Gómez-Reino Rodríguez[a], P. Gayoso Diz[b] and J. Bobes García[c]

[a] *Psychiatry Service.* [b] *Research Unit. Complejo Hospitalario of Orense.*
[c] *Psychiatry Area. Medical School, Univesity of Oviedo. Spain*

Polifarmacia en la prescripción de antipsicóticos en consultas de psiquiatría

Summary

Introduction. *Due to the lack of scientific studies in the psychopharmacological treatment of psychosis, the references advise against the use of antipsychotic polypharmacy (AP). This study investigates the situation of this matter and its relationship with the introduction of atypical antipsychotics (AA) in our daily out-patient practice.*

Methods. *The study group included 160 patients, with ICD-10 diagnosis of non-affective psychosis and illness evolution of at least two years, whose ages ranged from 18 to 65 years, without mental retardation, who came to the out-patient clinic at least once during the first semester of 2002 and, in order to make a comparison, at least one other time 9 to 12 months before. The retrospective study was done using the clinical records.*

Results. *In both moments studied, more than 50 % of the patients (65 % and 63.4 % respectively) had AA as their only treatment. AP was 25.6 % and 26.9 % respectively, 19.4 % of all patients were always in AP. At the end of the study, patients on AP were being prescribed a higher dose of chlorpromazine equivalents per day ($p < 0.001$) and more anticholinergics ($p < 0.001$).*

Conclusions. *Our results show that in out-patient settings AA have been consolidated as the first treatment option and that AP is a very common and stable phenomenon.*

Key words: *Psychosis. Schizophrenia. Polypharmacy. Antipsychotics.*

Resumen

Introducción. *En el tratamiento psicofarmacológico de las psicosis la bibliografía advierte, debido a la falta de evidencias científicas, contra el uso de la politerapia antipsicótica (PA). En este trabajo estudiamos la situación de esta cuestión en relación con la introducción de los antipsicóticos atípicos (AA) en nuestra práctica ambulatoria.*

Métodos. *El estudio incluye 160 pacientes con diagnósticos CIE-10 de psicosis no afectivas con una evolución de al menos 2 años; edad entre 18 y 65 años; sin retraso mental, y que acudiesen a consultas al menos una vez durante el primer semestre de 2002, y para poder comparar por lo menos otra vez de 9 a 12 meses antes. El estudio, de método retrospectivo, se realizó a través de la revisión de la historia clínica.*

Resultados. *En los dos momentos estudiados más del 50 % de los pacientes (un 65 y 63,4 %, respectivamente) usaban los AA como único tratamiento. La PA representaba un 25,6 y 26,9 %, respectivamente, mientras un 19,4 % de los pacientes estaban siempre en PA. Los pacientes en PA tomaban una mayor dosis de equivalentes de clorpromazina por día ($p < 0,001$) y más anticolinérgicos ($p < 0,001$).*

Conclusiones. *Nuestros resultados indican que los AA se han consolidado como la principal opción terapéutica y que la PA es un fenómeno muy común y estable en las consultas estudiadas.*

Palabras clave: *Psicosis. Esquizofrenia. Politerapia. Antipsicóticos.*

INTRODUCTION

Antipsychotic drugs make up the treatment basis of schizophrenia and other psychotic disorders[1,2]. At present, the new antipsychotics, atypical antipsychotics (AA), are recommended by different experts' committees as first line agents as they have demonstrated high efficacy with a better adverse effects (AE) profile in several studies[3,4].

Although the research studies have been performed under monotherapy conditions and, therefore, the different consensus advocate their use, in recent years, a tendency has been observed in the daily clinical practice consisting in the use of several antipsychotic drugs at the same time, in spite of the absence of scientific data that support the effectiveness and efficiency of this practice[5,6]. To demonstrate this fact, Clark et al.[7] performed a study in which they indicate that the percentage of patients receiving polytherapy in a cohort of 836 patients diagnosed of schizophrenia or schizoaffective disorder had gone from 5.7 % in 1994 to 24.3 % in 1999. In all, it

Correspondence:
Gerardo Flórez Menéndez
Rúa Progreso 41, 9-E
32005 Ourense (Spain)
E-mail: gerardof@wanadoo.es

is estimated that 25 % of the patients diagnosed of schizophrenia in the USA are presently being treated with an antipsychotic polytherapy regime[8]. The main reason used for the use of antipsychotic polytherapy (AP) are those chronic psychotic disorders resistant to monotherapy, a problem that affects 30 %-50 % of the patients diagnosed of schizophrenia[9]. However, only one double blind study that compares efficacy of combining clozapine, the only AA drug that has been demonstrated to be effective in treatment of typical antipsychotics (TA) refractory patients, with sulpiride has been published up to now[10].

The objective of this study is to study the prescription of antipsychotics by the physicians of an area in regards to polypharmacy and the influence that the introduction of the AAs may have on it.

PATIENTS AND METHODS

A retrospective, cross-sectional, epidemiological study of clinical practice was performed in the Psychiatry Service of the Complejo Hospitalario of Orense. All the discharge reports from the Short Hospitalization Psychiatry Unit from January 1996, date it opened, until August 2002, date of the study onset, were reviewed. The following inclusion criteria were applied: patients with ICD-10 diagnosis of non-affective endogenous psychotic disorder (from F20 to F29), including schizoaffective disorder, who came to out-patient visits in Mental Health Units I and II as they were the only ones with a centralized history. Their ages ranged from 8 to 65 years, they had no mental retardation and their psychotic disorder had an evolution of less than two years. Thus, the initial cases with greater diagnostic instability were eliminated. Those patients who presented a single psychotic episode and who only should take the medication for one year were eliminated[11]. A total of 346 valid patients were obtained with these criteria. In a second phase, the centralized history of all these patients was reviewed to verify if they presented any exclusion criteria: not having come to out-patient visits during the first semester of 2002 (moment two-M2) at least once, using the last visit as a reference, or in the case of having done so, not having come to at least one other visit 9 to 12 months before, using the oldest visit as reference (moment one-M1). This requirement was fulfilled by 160 patients (46.24 %) and their data were included in the study. This exceeded the 126 patients, which is the sample size estimated for a 20 % proportion of AP, with a 7 % maximum error permitted and a 95 % safety level (1-α); 104 patients (30.05 %) did not comply with the minimum regime of visits established. There was not sufficient information in the centralized history for 59 patients (17.05 %) to guarantee that they complied with the exclusion criteria; 16 patients (4.62 %) were hospitalized in socio-health care network sites during the period included in the study; three patients (0.86 %) had died and four patients (1.18 %) had been discharged.

Both M1 as well as M2 as well as the prescription of antipsychotic drugs, type of drugs used and global dose were analyzed in the 160 patient included. For the latter, Tandon et al. chlorpromazine equivalent tables[12] were used for the oral medication and that of Yorston and Pinney for the injectable depot medication[13]. Other socio-demographical and clinical data were collected: age, ICD-10 diagnosis (F20: schizophrenia/F21: schizotypal disorder/F22: delusional disorder/F23: acute polymorphic psychotic disorder/F25: schizoaffective disorder/F29: non-specified organic psychotic disorder), gender, years of evolution of the psychotic disorder, number of urgent visits and hospitalizations that each patient presented in the study period and changes in antipsychotic medication, understanding change as the incorporation or elimination of treatment of one or more antipsychotic drugs.

The statistical study was performed with the SPSS 10.0 program. A difference was considered to be significant when the p value was less than 0.05. The usual descriptive statistics was performed: mean and 95 % CI for quantitative variables; frequency and percentage for qualitative variables. For the bivariate analysis, the Student's t test (comparison of means) or the χ^2 (comparison of percentages) were used. In the cases in which the conditions for the application of parametric tests were not fulfilled, non-parametric tests were used. The binary logistic regression was used to study the possible conditioning or explanatory factors of AP. To do so, AP was considered as dependent variable and the following as independent variables: age, years of evolution (on three levels: < 5 years, 5-10 years and > 10 years), hospital admissions, urgent visits and change in antipsychotic medication.

RESULTS

Of the 160 patients, as detailed in table 1, 62.5 % were men. Mean age was 39 years, the most frequent diagnosis was F20 (58.1 %); 73.8 % presented an evolution between 5 and 20 years. Use of antipsychotics in all the study group is considered in tables 2 (M1) and 3 (M2). The marketed AAs during the study period (risperidone, quetiapine, clozapine and olanzapine) are presented individually and the TA are presented as a single group.

Considering the AA together, 104 patients (65 %) were under exclusive treatment with AA in their first visit (M1). Five (4.8 %) of them were taking two AA and 19 (18.3 %) were taking anticholinergics. The mean of the chlorpromazine equivalents (ChEq) per day that were taken was 414.38 (95 % CI 347.42 to 481.33). In M2, 103 patients (64.375 %) were under exclusive treatment with AA; only four (3.9 %) of them were taking two AA and 20 (19.4%) were taking anticholinergics. The mean ChEq per day taken was 440.90 (95 % CI 375.01 to 506.79).

In regards to the use of TA, in M1, 56 patients (35%) took some drug of this type, although not all exclusively, the mean ChEq per day was 673.39 (95 % CI: 605.25 to

TABLE 1. Distribution of the sample based on gender, mean age, diagnosis and years of evolution

N	*Total n = 160*	*Men n = 100 (62.5 %)*	*Women n = 60 (37.5 %)*
Mean age (IC 95%)	39 (37-41) years	37 (34-39) years	43 (41-46) years
Diagnosis			
F20	93 (58.1%)	72 (72%)	21 (35%)
F21	2 (1.3%)	1 (1.0%)	1 (1.7%)
F22	21 (13.1%)	8 (8%)	13 (21.7%)
F23	18 (11.3%)	5 (5%)	13 (21.7%)
F25	17 (10.6%)	8 (8%)	9 (15%)
F29	9 (5.6%)	6 (6%)	3 (5%)
Evolution years			
Less than 5	22 (13.8%)	13 (13%)	9 (15%)
From 5 to 10	62 (38.8%)	40 (40%)	22 (36.7%)
From 10 to 20	56 (35%)	37 (37%)	19 (31.7%)
More than 20	20 (12.5%)	10 (10%)	10 (16.7%)

F20: schizophrenia; F21: schizotypal disorder; F22: delusional disorder; F23: acute polymorphic psychotic disorder; F25: schizoaffective disorder; F29: unspecified non-organic psychotic disorder.

741.53). Of these, 28 (50 %) took anticholinergics. In M2, 57 patients (35.625%) took some drug of this type, although not all exclusively. The mean ChEq taken was 676.91 (95% CI: 609.56 to 744.26). Twenty seven of these patients (47.4%) took anticholinergics.

Both in M1 as well as M2, clozapine was used most in the men ($p = 0.03$ and 0.021 respectively). An increase in the use of TA was also observed with age ($p = 0.003$ and 0.035 respectively) and with the evolution years ($p = 0.005$ and 0.022 respectively). Those patients who were only prescribed AA, both in M1 as well as M2, took fewer anticholinergics ($p < 0.001$) and fewer ChEq per day ($p = 0.01$) than the patients who were prescribed some TA.

The phenomenon of antipsychotic polytherapy (AP) affected 41 patients (25.6%) in M1 and 43 (26.9%) in M2 (figures 1 and 2). No significant differences were found according to age, gender, diagnosis or years of evolution (table 4).

In regards to the distribution of AP based on the antipsychotic, it is observed in both moments that the AAs are mainly used under conditions of antipsychotic monotherapy (AM) and the TA, above all the depots, are mainly used under conditions of AP (figures 1 and 2 and table 5).

In M2, the patients with AP took a mean of 880.29 ChEq per day, while those who were under AM took a mean of 418.85. Of the patients with AP, 53.5% took anticholinergics, while in the AM group, 21.4% took them. A total of 37.20% of the patients in AP took more than ChEq per day versus 5.1% of the patients in AM.

TABLE 2. Use of different antisychotic drugs in moment 1 according to patient variables

Drug	*n*	*Gender*		*Age*		*Evolution years*				*Diagnosis*					
		Men	*Women*	*Less than 39*	*40 or more*	*Less than 5*	*5 to 10*	*10 to 20*	*More than 20*	*F20*	*F21*	*F22*	*F23*	*F25*	*F29*
Risperidone	40 (25 %)	27	13	20	20	4	16	16	4	23		9	3	3	2
A		67.5%	32.5%	50%	50%	10%	40%	40%	10%	57.5%		22.5%	7.5%	7.5%	5%
B		27%	21.7%	22.7%	27.8%	18.2%	25.8%	28.6%	20%	24.7%		42.9%	16.7%	17.6%	22.2%
p		(0.451)		(0.463)		(0.750)				(0.365)					
Quetiapine	12 (7.5%)	6	6	6	6	3	4	4	1	6		3	2		1
A		50%	50%	50%	50%	25%	33.3%	33.3%	8.3%	50%		25%	16.7%		8.3%
B		6%	10%	6.8%	8.4%	13.6%	6.5%	7.1%	5%	6.5%		14.3%	11.1%		7.5%
p		(0.352)		(0.717)		(0.686)				(0.610)					
Clozapine	12 (7.5%)	11	1	7	5	1	4	5	2	11				1	
A		91.7%	8.3%	58.3%	41.7%	8.3%	33.3%	41.7%	16.7%	91.7%				8.3%	
B		11%	1.7%	8%	6.9%	4.5%	6.5%	8.9%	10%	11.8%				5.9%	
p		(0.03)		(0.809)		(0.868)				(0.250)					
Olanzapine	73 (45.6%)	46	27	46	27	11	31	21	10	42	2	9	8	8	4
A		63%	37%	63%	37%	15.1%	42.5%	28.8%	13.7%	57.5%	2.7%	12.3%	11%	11%	5.5%
B		46%	45%	52.3%	37.5%	50%	50%	50%	45.6%	45.2%	100%	42.9%	44.4%	47.1%	44.4%
p		(0.902)		(0.062)		(0.514)				(0.779)					
Typical	56 (35%)	32	24	22	34	2	18	27	9	39		4	3	6	4
A		57.1%	42.9%	39.3%	60.7%	3.6%	32.1%	48.2%	16.1%	69.6%		7.1%	5.4%	10.7%	7.1%
B		32%	42.9%	25%	47.2%	9.1%	29%	45%	35%	41.9%		19%	16.7%	35.3%	44.4%
p		(0.304)		(0.003)		(0.005)				(0.135)					

A: percentage of each variable in regards to the antipsychotic drug; B: percentage of antipsychotic drug use in each variable. The percentages add up to more than 100 due to the polytherapy; *p*: significance level

TABLE 3. Profile of use of the different antipsychotic drugs in moment 2

Drug	*n*	*Gender*		*Age*		*Evolution years*				*Diagnosis*					
		Men	*Women*	*Less than 39*	*40 or more*	*Less than 5*	*5 to 10*	*10 to 20*	*More than 20*	*F20*	*F21*	*F22*	*F23*	*F25*	*F29*
Risperidone	56 (35%)	31	25	30	26	9	20	19	8	32		10	6	5	3
A		55.4%	44.6%	53.6%	46.9%	16%	35.7%	33.9%	14.3%	51.7%		17.9%	10.7%	8.9%	5.4%
B		27%	21.7%	22.7%	27.8%	40.9%	32.3%	28.6%	40%	24.7%		47.6%	33.3%	29.4%	33.3%
p		(0.171)		(0.790)			(0.852)					(0.727)			
Quetiapine	13 (8.1%)	5	8	8	5	3	6	3	1	5		2	4		2
A		38.5%	61.5v%	61.5%	38.5%	23.1%	46.2%	23.1%	7.7%	38.6%		15.4%	30.8%		15.4%
B		5%	13.3%	9.1%	6.9%	13.6%	9.7%	5.4%	5%	5.45%		9.5%	22.2%		22.2%
p		(0.062)		(0.621)			(0.587)					(0.079)			
Clozapine	13 (81%)	12	1	8	5	1	5	5	2	12				1	
A		92.3%	7.7%	61.5%	38.5%	7.7%	38.5%	41.7%	15.4%	92.3%				7.7%	
B		12%	1.7%	9.1%	6.9%	4.5%	8.1%	8.9%	10%	12.9%				5.9%	
p		(0.021)		(0.621)			(0.914)					(0.194)			
Olanzapine	60 (37.5%)	39	21	35	25	6	25	22	7	34	2	9	5	6	4
A		65%	35%	58.3%	41.7%	10%	41.7%	36.7%	11.7%	56.7%	3.3%	15%	8.3%	10%	6.7%
B		39%	35%	39.8%	34.7%	27.3%	40.3%	39.3%	35%	36.6%	100%	42.9%	27.8%	35.3%	44.4%
p		(0.613)		(0.512)			(0.724)					(0.470)			
Typical	57 (35.6%)	38	19	25	32	2	21	25	9	40		4	3	7	3
A		66.7%	31.7%	43.9%	56.1%	3.5%	36.8%	43.9%	15.8%	7.2%		7%	5.3%	12.3%	5.3%
B		38%	31.7%	28.4%	44.4%	9.1%	33.9%	44.6%	35.6%	43%		19%	16.7%	41.2 %	33.3%
p		(0.418)		(0.035)			(0.022)					(0.113)			

A: percentage of each variable in regards to the antipsychotic drug; B: percentage of antipsychotic drug use in each variable. The percentages add up to more than 100 due to the polytherapy; p: significance level

Of the 43 patients who were in AP in M2, 31 (72.1%) were already under it in M1, 12 passed to this condition and 10 abandoned it.

AP significantly ($p < 0.001$) influenced in the global mean of ChEq per day (significant differences were found individually for risperidone, olanzapine and TA) (table 5).

There were also significant differences in the use of anticholinergics ($p < 0.001$) and in the number of patients who took more than 1000 ChEq per day ($p < 0.001$).

The variables that were significantly associated to greater risk of presence of polypharmacy were change of antipsychotic drug (*odds ratio* [OR]: 3.057; 95% CI: 1.339

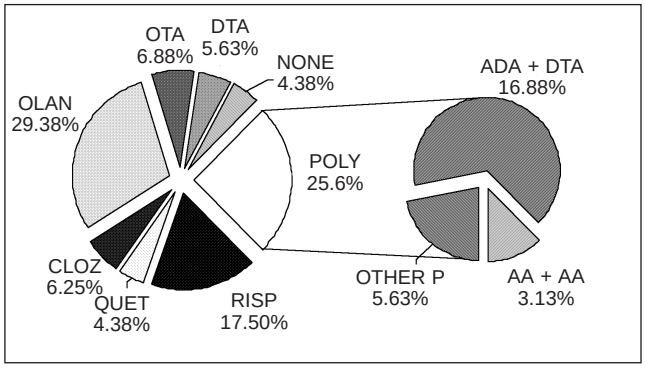

Figure 1. Prescription of antipsychotics in moment 1. NONE: no antipsychotic medication; DTA: depot typical antipsychotic; OAT: oral typical antipsychotic; OLAN: olanzapine; CLOZ: clozapine; QUET: quetiapine; RISP: risperidone; POLY: antipsychotic polytherapy; AA + DTA: atypicals inpolytherapy with depot atypical antipsychotics; AA + AA: atypical antipsychotics in-polytherapy with atypical antipsychotics; OTHER P: other combinations of antipsychotic polytherapy (i.e., more than two antipsychotic drugs).

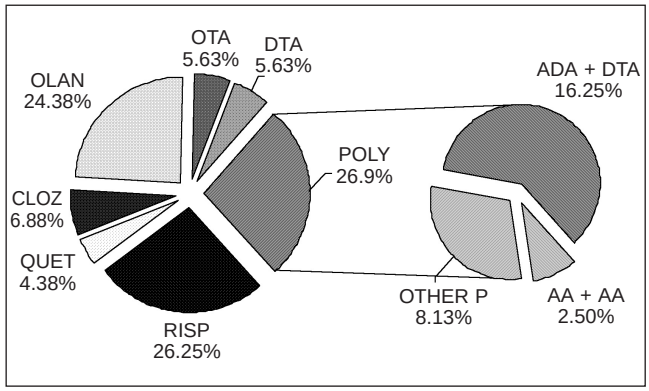

Figura 2. Prescription of antipsychotics in moment 2. DTA: depot typical antipsychotics; OTA: oral typical antipsychotics; OLAN: olanzapine; CLOZ: clozapine; QUET: quetiapine; RISP: risperidone; POLI: antipsychotic polytherapy; AA + DTA: atypical antipsychitics in polytherapy with depot typical antipsychotics; AA + AA: atypical antipsychotics in polytherapy with atypical antipsychotics; OTHER P: other combinations of antipsychotic polytherapy (i.e., more than two antipsychotic drugs).

TABLE 4. Distribution of antipsychotic polytherapy phenomenon based on the variables of gender, mean age, evolution years and diagnosis, both in moment 1 as well as in moment 2

Drug	*n*	*Gender*		*Age*		*Evolution years*				*Diagnosis*					
		Men	*Women*	*Less than 39*	*40 or more*	*Less than 5*	*5 to 10*	*10 to 20*	*More than 20*	*F20*	*F21*	*F22*	*F23*	*F25*	*F29*
Moment one	41 (25.6%)	28	13	19	22	2	14	17	8	28		4	1	4	4
A		68.3%	31.7%	46.3%	53.7%	4.9%	34.1%	41.5%	19.5%	68.3%		9.8%	2.4%	9.8%	9.8%
B		28%	21.7%	21.6%	30.6%	9.1%	22.6%	30.4%	40%	30.1%		47.6%	5.6%	23.5%	44.4%
p		(0.374)		(0.196)			(0.099)					(0.176)			
Moment two	43 (26.9%)	30	13	20	23	1	16	19	7	30		4	1	5	3
A		69.8%	30.2%	46.5%	53.5%	2.3%	37.2%	44.2%	16.3%	69.8%		9.3%	5.6%	11.6%	7%
B		30%	21.7%	22.7%	31.9%	4.5%	25.8%	33.9%	35%	32.3%		19%	5.6%	29.4%	33.3%
p		(0.250)		(0.191)			(0.052)					(0.208)			

A: percentage of each variable in regards to each moment; B: percentage of polytherapy according to moment in each variable; *p*: significance level.

to 6.977) and evolution years (OR: 1.983; 95% CI: 1.055 to 3.727). The OR for the rest of the variables did not reach significant value (table 6).

DISCUSSION

As in the international studies[7,14], the AAs have been established in our setting as the main therapeutic option. In both moments of the study, they were used in AM on more than 50% of the occasions and when they were used in AM, the mean ChEq prescribed per day was adapted to the recommendations made by consensus groups, such as the PORT Committee[11].

AP appears as a stable and concerningly frequent phenomenon in this study, it being even higher among patients with schizophrenia diagnosis who represent the main group of this sample. These results are higher than

TABLE 5. Distribution of antipsychotic polytherapy based on each antipsychotic drug and influence of antipsychotic polytherapy in the potency of dopaminergic blockage (calculated with the chlorpromazine equivalents per day-chlor EQ per day) both in moment 1 as well as in moment 2

Politherapy	*Moment 1 (41 patients in polytherapy)*			*Moment 2 (43 patients in polytherapy)*		
	Monotherapy	*Polytherapy*	*% polytherapy*	*Monotherapy*	*Polytherapy*	*% polytherapy*
Risperidone	28 (70%)	12 (30%)	29.26%	42 (75%)	14 (25%)	32.55%
Chlor EQ per day	495.54	734.58		383.62	744.43	
p	(0.024)			(0.002)		
Quetiapine	7 (58.3%)	5 (41.7%)	12.19%	7 (53.8%)	6 (46.2%)	13.95%
Chlor EQ per day	607.14	1,094		546.88	864	
p	(0.06)			(0.140)		
Clozapine	10 (83.3%)	2 (16.7%)	4.87%	11 (84.6%)	2 (15.4%)	4.65%
Chlor EQ per day	700	1,075		670.45	1075	
p	(0.083)			(0.074)		
Olanzapine	47 (64.4%)	26 (35.6%)	63.41%	39 (65%)	21 (35%)	48.83%
Chlor EQ per day	276.51	955.15		309.33	1017.45	
p	(0.001)			(0.001)		
Typical	20 (35.71%)	36 (64.28%)	87.80%	18 (31.6%)	39 (68.4%)	90.96%
Chlor EQ per day	348	854.17		432	913.38	
p	(0.001)			(0.001)		
Oral	11 (61.11%)	7 (38.89%)	17.07%	9 (45%)	11 (55%)	25.58%
Depot	9 (23.7%)	29 (76.3%)	70.73%	9 (24.3%)	28 (75.7%)	65.11%

p: significance level.

TABLE 6. Binary Logistic regression to study the possible conditioning or explanatory factors of AP

Variables	Odds ratio	*Confidence interval 95%*	*p*
Age	0.995	0.957-1.034	0.792
Change in medication	3.057	1.339-6.977	0.008
Evolution years	1.983	1.055-3.727	0.034
Urgent visits	0.563	0,159-1.993	0.373
Hospitalizations	0.627	0.229-1.715	0.364

p: signifcance level.

those obtained in other studies: 11 % of the Covell et al.[5] sample, 369 psychotic patients, 15 %-17 % of the Weissman[13] study with more than 5,000 psychotic patients or 24.3 % of the 836 patients with schizophrenia diagnosis or schizoaffective disorder of Clark et al.[7].

The low use of clozapine, limited combination of AA and high mean of ChEq per day in AP patients rule out that the high presence of AP in our sample is a reflection of therapeutic strategies aimed at treating the resistant pictures in a sustained way[15-18]. This indication, on the other hand, is not endorsed by the experts' committees[6].

The use of AP temporally has two indications, as commented by Stahl[2]: the first is when one antipsychotic is changed for another due to lack of effectiveness or due to presence of adverse effects. As recommended by the experts' committees[6], the two drugs are administered temporalily to avoid relapse or deterioration. The second indication is when faced with an acute increase of the psychotic symptoms or behavior disorders, above all aggressiveness, a TA, whose greater potential of D2 blockage makes it possible to combat them more quickly, is added. In both situations, experts recommend returning to the antipsychotic monotherapy when the condition has become stabilized[6].

The fact that 31 of the 43 patients who were in antipsychotic polytherapy were already in M1 verifies that these two sporadic uses do not justify the high rates of AP found in the sample.

However, the inadequate use of these indications of AP may explain the high presence of this phenomenon in our sample. It is verified by logistic regression that the «change of antipsychotic» variable decisively influences the AP phenomenon in this study, which verifies, as indicated by Stahl[2], the high risk that one of these transitory AP situations will be chronic, as the psychiatrist fears that going to AM will make the problem controlled by AP reappear. Obviously, the longer the years of evolution, the greater the risk that this change condition will occur and thus, the possibilities of going to AP increases 1.9 with every 5 years of evolution.

New studies are needed to know the effects of the long term AP, to better define the clinical characteristics of the AP patient group and to verify if the use of other non-drug therapeutic forms makes it possible to reduce the AP phenomenon as suggested by some authors[19].

The main limitation of this study is that the sample was obtained from a hospital registry, so that it is possible to speculate that it does not absolutely represent the psychotic patient population that comes as out-patients. Although this is true, it must be remembered, as indicated by Gottesman[20], that most of the persons who suffer a chronic psychotic disorder are hospitalized some time in their life. Considering this and that the hospital registry used includes more than 6 years of hospitalizations, it is possible to assume that this group represents the chronic psychotic population that comes to outpatient visits.

It must also be kept in mind that this is a study that includes a single health care area, and within it, patients seen in two of its mental health units. On the other hand, the study is based on medical prescriptions and not all the patients take, totally or partially, the medication prescribed. This is a situation inherent to the studies that investigate aspects of the clinical practice. However, when incorporating a time framework to the study, it is possible to observe the clinician's response to a low compliance situation (i.e., with changes in the medication or arranging an admission due to relapse) and to study the consequences that this situation has on prescriptions.

Finally, the results presented in regards to ChEq per day would only be comparable to those of the other studies that use the same conversion values, since there is no universal agreement on them.

In summary, although the AAs have been consolidated as the main therapeutic option in the out-patient practice, AP, a phenomenon supported by limited scientific evidence, continues to be very common and stable. Its presence in our area of work seems to respond more to difficulties in the change of antipsychotics than to strategies aimed at treating resistant cases.

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