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Treatment with amisulpride of addicted patients to psychoactive substances and psychotic symptoms

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Introduction. There is ever more available information on the effectiveness of second-generation antipsychotic drugs used in addictive behaviour patients with psychotic symptoms. Due to its characteristics, Amisulpride is a medicine that can be considered as a valid therapeutic option to treat this group of patients.

Objective. To assess the value of Amisulpride to treat patients with addictive behaviours, and the associated morbidity

Method. An experimental, prospective study was conducted. A total of 97 ambulatory patients, who were initiating, or already receiving, treatment at the Addictive Behaviours Unit in Paterna, Valencia (Spain), were selected to take part in the study. Inclusion criteria included female and male patients, diagnosed of misusing any of the following substances: alcohol, heroine, cocaine or cannabis, who having overcome the detoxification phase, presented one or more of the following symptoms: paranoid ideas, hostility, severe irritative or impulsive behaviours, interpersonal sensitivity, and hearing or visual hallucinations. An initial dose of Amisulpride, standardized in two ranges (100-300 mg y \geq 400 mg) was used. It was progressively increased according to the clinical response. Four assessments were conducted at months 0, 3, 6 and 9.

Results. Out of a total of 97 patients, 14 were excluded due to violation of the protocol. Twenty patients dropped out and 63 completed the follow-up period. Mean Amisulpride daily dose was 493.5 ± 197.1 mg. In those patients who completed the treatment, an overall improvement in their psychological distress, a decreased in craving and an improvement in their psychological and social functioning were found.

Conclusion. Treatment with Amisulpride seems to be effective in patients who are on different addictive substances, and its associated morbidity, both at a short and a medium period of time.

Key words:

Amisulpride, psychological distress, social functioning, addictive behaviors

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Tratamiento con amisulpride de pacientes adictos a sustancias psicoactivas y síntomas psicóticos

Introducción. Cada vez disponemos de mayor información sobre la efectividad de los antipsicóticos de segunda generación en pacientes con síntomas psicóticos y trastorno por abuso de sustancias. Amisulpride es un fármaco que por sus características puede considerarse una opción terapéutica válida en el manejo de estos pacientes.

Objetivo. Evaluar la utilidad del Amisulpride en pacientes con Trastorno por Consumo de Sustancias y comorbilidad asociada.

Método. Estudio experimental y prospectivo. Se reclutaron 97 pacientes ambulatorios que iniciaban y/o se encontraban en tratamiento en la Unidad de Conductas Adictivas de Paterna, Valencia (España). Los criterios de inclusión abarcaban a pacientes de ambos sexos con diagnóstico de dependencia, según DSM-IV-TR, a una de las siguientes sustancias: alcohol, heroína, cocaína o cannabis, que habiendo superado la fase de desintoxicación presentaban uno o varios de los síntomas siguientes: ideación paranoide, hostilidad, impulsividad o irritabilidad marcada, sensibilidad interpersonal, alucinaciones auditivas, o alucinaciones visuales. Los pacientes que habían sido diagnosticados de dependencia a la heroína ya se encontraban en tratamiento de mantenimiento con metadona antes de ser incluidos en el estudio. Se pautó una dosis inicial de Amisulpride, estandarizada en dos rangos (100-300 mg y \geq 400 mg) que fue aumentán-

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dose paulatinamente según la respuesta clínica. El seguimiento fue de 9 meses y se realizaron 4 controles a los 3, 6 y 9 meses.

Resultados. De un total de 97 pacientes seleccionados, 14 se excluyeron del análisis por violación del protocolo. Abandonaron el estudio 20 y finalizaron el seguimiento a los 9 meses un total de 63 casos. La dosis media de Amisulpride fue de $493,5 \pm 197,1$ mg/día. En los pacientes que cumplieron el tratamiento, hubo mejoría global del distress psicológico, disminución del craving y mejoría de la funcionalidad psíquica y social.

Conclusiones. El tratamiento con Amisulpride es efectivo en pacientes con dependencia a distintas sustancias y co-morbilidad asociada, tanto a corto como a medio plazo.

Palabras claves:
Amisulpride, distress psicológico, funcionamiento social, conductas adictivas

INTRODUCTION

According to the calculations of the United Nations Office on Drugs and Crime (2006), approximately 200 million persons, that is 5% of the world population between 15 and 64 years, have consumed some illicit substance at least once in the last year. The global calculation of drug dependent users is 0.6% of the 15 to 64 year old population. The growing tendency towards multiple consumption is clear.

The most prevalent abuse drugs in Spain¹ are those legally sold on the market, that is, alcohol and tobacco, and in regards to the so-called illicit ones, cannabis derivatives and cocaine, with prevalences of 11.2% for cannabis and 3.0% for cocaine in powder in the last 12 months. The indicator for treatment admissions for abuse or dependence demonstrates the problem of drugs in Spain. According to the report of the Spanish Observatory on Drugs¹ in the year 2005, 50,630 subjects were admitted to treatment, 46.9% of these due to cocaine, 36.8% due to heroine and 10.9% for cannabis.

Drug dependence (alcohol, heroine, cocaine, etc.) involves functional modifications in the neurotransmission of different brain circuits related with reinforcement induced by such substance, depending on the consumption time and pattern, tolerance to the drug and type of psychoactive substance consumed. The most recent advances in the theory of dependence have stressed the role of the central nervous system in the regulation of positive and negative reinforcement of the different abuse drugs,^{2,3} the common characteristic being stimulation of dopaminergic activity in the mesolimbic system.

One of the most important phenomena associated with the use of drugs is undoubtedly craving. All the models consider the implication and consumption of the affective states, attributing motivational characteristics to craving⁴. The existence of psychiatric comorbidity together with substance abuse disorder⁵, makes it necessary to design care protocols that contemplate both disorders. Given that there is no mental disorder for toxic consumption, on the one hand, and that the drugs cause severe psychopathological reactions with a very high frequency, studies dedicated to the evaluation of the effectiveness of the treatments initiated in patients with dual condition need to be done.

There is continuously greater information on the effectiveness of second-generation antipsychotics in patients with psychotic symptoms and substance abuse disorder^{6,7}. In this sense, the choice of Amisulpride and its inclusion in the therapeutic armamentarium may be a valid option, given its characteristics: action mechanism, limited side effects and lack of knowledge of this substance by the addicted population^{8,9}. The purpose of this study is to evaluate the utility of Amisulpride in patients with Substance Abuse Disorder, on several psychopathological dimensions and its possible incidents in the improvement of social functioning.

MATERIAL AND METHODS

Study design

An experimental, prospective study with evaluation of the outcome endpoints after the application of the treatment at 3, 6 and 9 months, using different evaluation instruments was performed. The study inclusion period began on December 1, 2002 and was completed on December 1, 2003.

Study subjects

Patients who initiated treatment and/or were under treatment at the time of this study in the Addictive Behavior Unit (ABU) of Paterna, Conselleria de Sanitat de la Generalitat Valenciana (SPAIN), in outpatient treatment for their addictive disorder were enrolled. Inclusion criteria were patients of both genders, age range 18 to 60 years, and diagnosed of dependence, according to the DSM-IV-TR, to one of the following substances: alcohol, heroine, cocaine or cannabis, who had overcome the detoxification phase (in those cases where necessary), who had one or several of the following symptoms: paranoid ideation, hostility, impulsiveness or marked irritability, interpersonal sensitivity, auditory hallucinations or visual hallucinations. Furthermore, patients with partial remission of the positive symptoms and/or presence of negative symptoms such as those with treatment resistant extrapyramidal symptoms or weight gain who required a change of the antipsy-

chotic were also included. All the patients had to voluntarily accept participation in the study and were diagnosed of heroine dependence since they were already under maintenance treatment with methadone (MTM) before being included in the study. Included among the exclusion criteria were diagnosis of prolactinoma or prolactin-dependent tumors as well as those who had hypersensitivity to Amisulpride.

Definition of the intervention

The patients were evaluated and diagnosed by the therapeutic team following the DSM-IV-TR coding. All of the patients in the sample were prescribed Amisulpride and all had been offered complementary psychological treatment, either individual and/or group therapy. Within the clinical interview context and after evaluating the characteristics and intensity of the symptoms manifested by the patient and/or evaluated by the clinician, an initial dose of Amisulpride, standardized into two ranges, was prescribed (100-300 mg. and \geq 400 mg). During the first 7 days, a dose lower than the therapeutic one was prescribed to evaluate the patient's response to the drug. The dose was then adjusted to reach the optimum dose according to the response expected.

Recruitment and follow-up strategy

A total of 97 patients, who came to the Addictive Behavior Unit of the outpatient clinic of Paterna, whether for follow-up or for the first visit, and in whom, based on their symptoms, who were candidates for treatment with an atypical neuroleptic, and those cases in which the prescription of Amisulpride was indicated were enrolled. Each patient recruited, who fulfilled the inclusion criteria, was incorporated into the study and followed-up for 9 months. In this 9-month period, 4 controls were made, independently of the medical visits that the patient required at each point-in-time.

Data collection and description of information tools

The information of the different study variables was obtained through clinical interviews, at different point-in-time of the evaluation, using the measurement tools indicated in the following.

- a) A structured interview was administered to all the patients incorporated into the study, using the General Evaluation Protocol elaborated by the methodology area of the School of Psychology of the University of the Balearic Islands¹⁰. This protocol includes different sociodemographic variables as

well as toxicological ones (years of consumption, previous treatment, maximum periods of abstinence, principal administration route, etc.), serological status against HIV and Hepatitis, beliefs on drug consumption, condition of readiness to change and consumption triggers.

- b) The Social Adaptation Self-Evaluation Scale (SAAS)^{11,12} was administered to evaluate behavior and/or adjustment or social motivation in a simple way. Change to the normality stage in those patients who were misadjusted was considered improvement.
- c) To evaluate craving intensity (consumption desire), a visual analogue scale (VAS) was used.
- d) The Symptom Checklist 90 Revised (SCL-90-R)¹³ was used to evaluate distress or psychological malaise. Intensity of suffering caused by each symptom should be graded by the subject from 0 (total absence of symptoms) to 4 (maximum discomfort). The time framework covered by the questions on the questionnaire is restricted to recent experience. The symptomatic dimensions measured are distributed into 10 groups, each one of which measures a different aspect of the psychopathology. These dimensions are: Somatization, Obsession-Compulsion, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, Psychoticism and miscellaneous symptoms. The global indexes provided by the questionnaire are: GSI Global Severity Index, known in Spanish as the "Índice Sintomático General"; the PST or 88 Positive Symptom Total, also called Total of Positive Responses; and the PSDI or Positive Symptom Distress Index. The GSI is a generalized measurement of the intensity of global psychic and psychosomatic suffering, which combines information on the number of symptoms and distress. The PST reveals the total number of symptoms that the surveyed person states he/she has experienced in any grade and that contribute to the interpretation of the global pattern, informing on the symptomatic extension of the individual's distress. The PSDI relates global distress with the number of symptoms and is therefore an indicator of the characteristic style of the individual to experience psychic suffering. It provides information on whether the subject maximizes or minimizes his/her responses.
- e) The RCQ (Readiness to Change Questionnaire)¹⁴ is a questionnaire elaborated to evaluate motivation for change, beginning with the theory of the stages of change of Prochaska and DiClemente.
- f) The GAF (Global Assessment of Functioning Scale of the subject) makes up Axis V of the DSM-IV-TR and informs on the opinion of the clinician on the general level of the patient's activity.

- g) Therapeutic compliance was evaluated through the clinical interview.
- h) Diagnostic approach to the personality disorders, performed during the treatment process in the clinical follow-up visits, has made it possible to rule out false positives and to make the differential diagnosis in periods of continued abstinence. The evaluation on axis II of the comorbid personality disorder was performed at least after 4 consecutive weeks of abstinence of the principal substance, with the diagnostic instrument International Personality Disorder Examination (IPDE) (WHO 1996) and its corresponding semistructured interview to confirm the absence or presence of the disorder.

Ethical and legal aspects

Each participating filled out the informed consent for enrollment in the study. Approval was requested from the Ethics Committee of the Hospital Arnau de Vilanova, which was the reference center, the being informed as favorable.

Analysis strategy

As a first step, a descriptive and exploratory study was performed of the clinical, sociodemographic and toxicological characteristics of the different subjects analyzed. The student's T test for continuous quantitative variables, with a normal distribution, was used for the bivariate analysis. The chi squared test was used for qualitative or categorical variables. The mixed-design analysis of the variance (ANOVA) was performed. In this analysis, the within-subjects factor was the time variable and the between subjects factor was therapeutic compliance. Because of the general improvement in the sample, although with different grade, it was decided to perform a within-subject unifactorial analysis. The parameters were compared with the ANOVA and when this was significant, they were compared with the Scheffé test. The SPSS 13.0 statistical program for windows on the Stata 8.1 were used.

RESULTS

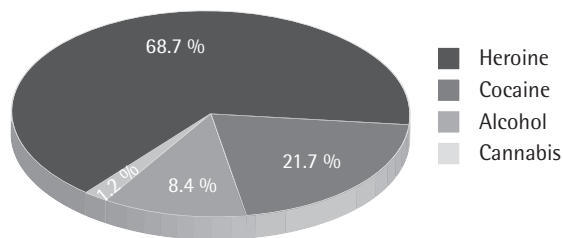
Our study was initiated with a sample made up of 97 patients, 14 of whom were excluded from the analysis due to protocol violation. Therefore, the initial sample was made up of 83 patients (65 men and 18 women). Twenty patients dropped out of the study, so that the follow-up at 6 months was conducted on 69 patients, there being a total of 68 patients remaining at 9 months. Among the reasons for dropout were entry into prison, into a residential detoxification unit (RDU) or voluntary withdrawal from treatment.

Mean age of the sample was 33.7 (SD=6.9) years. In the group of men, mean age was 33.1 ± 7.4 and in that of women, it was 33.0 ± 4.8 . Age range was predominantly from 21-44 years in both genders. Regarding civil status, 66.3% of the patients were single (72.3% for men and 44.4% for the women) compared to 21.6% who were married or had a significant other and 6% who were separated. The most frequent accommodation model was family of origin and type of accommodation in houses or apartments. A total of 42.2% of the subjects were high school graduates, 31.3% had only reached the Primary School certificate and 4.6% had university studies. A total of 49.4% of the patients had no criminal background. Analysis of the employment situation showed that more than one third of the patients were unemployed (37.3%), another third were employed (30.1%) and 14.5% were pensioners. Psychopathology was associated to the disorder due to substance abuse disorder (SAD) in 59 patients, that is, 71% of the sample had another clinical and/or personality disorder (table 1).

When the principal substance that led to the demand for treatment was analyzed, heroine was the psychoactive substance most represented in the cohort evaluated, it representing 68.7% of the demands (figure 1). In relationship to the diagnosis of Substance Abuse Disorder, it must be stressed that in every case, the dependence criteria according to the DSM-IV-TR were fulfilled. Most of the sample (74.7%) also fulfilled the criteria for polyconsumption, the combination of Cocaine Crack+Cannabis+Alcohol+Benzodiazepines being the most frequent.

The time spent in treatment in the addictive behavior unit (ABU) of the patients studied was a mean of 34.7 ± 19.9 months (figure 2). A total of 63% were treated in the unit for more than 2 years. In relationship to readiness to change when initiating the study, 61% of the patients were in an

Table 1	Psychiatric comorbidity on axis I and II according to the DSM-IV-TR	
Diagnosis	N	%
Paranoid schizophrenia	3	3.6
Non-specified psychiatric disorder	2	2.4
Schizoaffective disorder	1	1.2
Impulse Control disorder	1	1.2
Personality Disorder	52	62.6
Borderline Disorder	27	51.9
Antisocial Disorder	13	25.0
Avoidance Disorder	1	1.9
Antisocial + Borderline Disorder	7	13.4
Antisocial + Narcissistic Disorder	2	3.8
Borderline + Avoidance Disorder	1	1.9



	Alcohol	Cannabis	Heroin	Cocaine
Women	16.7	0	72.2	11.1
Men	6.2	1.5	67.7	24.6
Total	8.4	1.2	68.7	21.7

Figure 1 Principal diagnosis of substance dependence.

action stage, 29.5% in contemplation and finally 9.5% in the precontemplation stage, for the principal substance of their dependence. There were no variations based on gender.

From the pharmacological point of view, 69.8% of the patients (58 cases) were receiving monotherapy, that is, they received treatment only with Amisulpride, versus 30.2% who received concomitant treatment with other drugs (excluding data methadone). The mean dose of Amisulpride prescribed at the baseline visit was 246.5 ± 97.1 milligrams/day, this being 493.5 ± 197.1 mg/day at the end of the 9-month follow-up, with their range of 200-1000 milligrams, distributed into one or 2 doses daily. When the Amisulpride dose was related to whether there was dual pathology or not, it was observed that there were statistically significant

Table 2		Baseline values of the SCL-90 dimensions and indexes	
SCL-90 Dimensions	Mena	Standard deviation	
Somatization	1.44	0.85	
Obsessiveness-compulsivity	1.95	0.92	
Interpersonal Sensitivity	1.62	1.05	
Depression	1.94	0.91	
Anxiety	1.68	0.86	
Hostility	1.53	0.98	
Phobic Anxiety	1.03	0.83	
Paranoid Ideation	1.71	0.96	
Psychoticism	1.27	0.85	
GLOBAL SEVERITY INDEX (GSI)	1.63	0.74	
POSITIVE SYMPTOM DISTRESS INDEX (PSDI)	2.32	0.61	
POSITIVE SYMPTOM TOTAL (PST)	60.07	18.94	

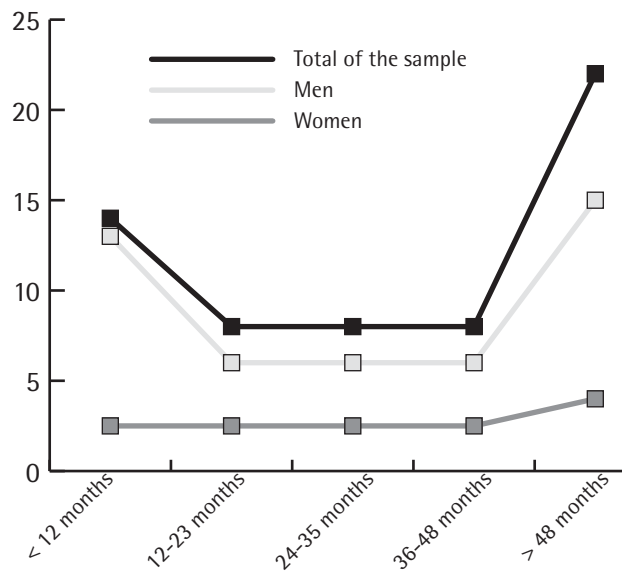


Figure 2 Continuance time in treatment in the ABU-Paterna.

differences between the type of personality disorder existing and the dose at which it stabilized ($\chi^2 = 34.59$; $p = 0.003$). Thus, the patients who had group B personality disorder (Antisocial Personality Disorder [APD], Borderline Personality Disorder [BPD], Histrionic, Narcissistic) required a mean dose of 400 milligrams daily and those who were diagnosed of schizophrenia or other psychotic disorders required a dose of 800 milligrams daily to stabilize their symptoms.

At the onset of the treatment (baseline value), elevated levels of psychological distress were found in most of the psychopathological dimensions evaluated, except for the phobic symptoms (table 2). When the principal substance that motivated demand for treatment and the level of distress in the baseline situation were considered, it was found that the mean scores of the cocaine addict patients were significantly higher in all of the dimensions versus those of the heroine addicts, the differences being statistically significant for all the symptoms except for obsessive-compulsive, interpersonal sensitivity and depression. The analysis of the evolution of psychological distress during the study observation period has made it possible to be able to conclude that there was global improvement of the malaise measured with the 9 symptomatic dimensions of the SCL-90 and the 3 global indexes. This improvement was statistically significant for all the levels measured, except for the time cutoff at 3 months of treatment, in which hostility and the total positive symptoms (TPS) did not significantly improve. At 6 months, phobic anxiety did not show any significant decrease, as can be observed in table 3.

Out of all of the patients who completed the follow-up at 9 months, 62% completed the drug treatment ver-

Table 3	T values of the differences for these related samples of the dimensions and global indexes of SCL-90					
	BASELINE - 3 MONTHS		BASELINE - 6 MONTHS		BASELINE - 9 MONTHS	
	T	gl	T	gl	T	gl
Somatization	2.770*	71	2.618*	68	3.859**	61
Obsessiveness/compulsivity	3.017*	71	3.128*	68	4.361**	61
Interpersonal sensitivity	2.568*	71	3.533**	68	4.999**	61
Depression	2.807*	71	3.348**	68	4.958**	61
Anxiety	3.201*	71	3.679**	68	4.799**	61
Hostility	1.410*	71	3.3440**	68	5.453**	61
Phobic anxiety	2.222*	71	1.556	68	2.984*	61
Paranoid ideation	2.752*	71	4.538**	68	4.911**	61
Psychoticism	2.014*	71	2.904*	68	4.258**	61
GSI	3.098*	71	3.653**	68	5.339**	61
PSDI	3.318**	71	3.773**	68	5.394**	61
PST	1.613*	71	2.604*	68	4.293**	61

*p<0.05; **p<0.001

Table 4	T values of the differences for related samples of the dimensions and global indexes of the SCL-90, according to compliance or noncompliance of treatment with Amisulpride					
	BASELINE - 3 MONTHS		BASELINE - 6 MONTHS		BASELINE - 9 MONTHS	
	Compliance	Non-compliance	Compliance	Non-compliance	Compliance	Non-compliance
Dimensions SCL-90	T	T	T	T	T	T
Somatization	2.85*	0.96	2.99*	0.52	3.24*	2.18*
Obsessiveness/compulsivity	3.99**	0.29	3.49**	0.94	3.66**	2.45*
Interpersonal sensitivity	2.59*	0.68	3.25*	1.45	4.21**	2.84*
Depression	2.98*	0.63	3.25*	1.22	4.49**	2.27*
Anxiety	3.86**	0.69	4.26**	0.79	4.79**	1.84
Hostility	1.55	0.00	3.15*	1.25	4.34**	3.03*
Phobic anxiety	2.28*	0.68	2.28*	-0.09	2.50*	1.70
Paranoid ideation	2.71*	0.97	4.42**	1.88	4.65**	2.13*
Psychoticism	1.33	1.59	2.71*	1.18	3.09*	2.95*
GSI	3.23*	0.93	3.71**	1.26	4.52**	2.87*
PSDI	3.35*	1.07	3.33*	1.79	4.75**	2.68*
PST	1.49	0.75	3.07*	0.55	3.89**	2.10*
Craving (VAS)	9.02**	9.81	18.41**	8.65*	19.73**	9.82*
Global Activity	-7.12*	-0.23	-8.84**	-5.54	-11.85**	-5.76
Social Functioning	-2.09*	-4.07*	-2.52*	-5.88*	-3.82**	-6.32*

*p<0.05; **p<0.001

sus 38% who did not complete the treatment prescribed. The patients who completed the treatment had a significant improvement in all of the time cutoff measured (table 4). On the contrary, the 9 non-compliers only had significant improvement at 9 months. When compliance

with Amisulpride and the change stage in which the patient was found were compared, statistically significant differences were found. Therefore, the majority of those who were in the action situation at the onset complied with treatment ($p=0.002$) versus those who began with a

previous motivational stage (precontemplation and contemplation, respectively).

A statistically significant relationship between discontinuation of cocaine-crack usage and treatment compliance with Amisulpride ($\chi^2 = 5.237$; $p < 0.05$) is observed in patients on maintenance treatment with methadone (figure 3). Treatment compliance is related to a lower usage, reducing it 50%, that is, it changed from 76.5% of the patients who were consumers to 35.7% in those who complied with the treatment. In the same way, it was observed how treatment compliance tripled the abstinence cases.

Measurement of craving at baseline obtained with the Visual Analogue Scale (VAS) was 47.8 ± 32.3 (scale from 1 to 100). This changed to 20.5 ± 28.3 at 9 months of follow-up in the patients who complied with treatment. For the evaluation of the Global Activity status when the subjects entered the study, there was a mean of 54.6 ± 11.9 , 50 being the most repeated value (*mode*). This indicates the presence of moderate symptoms or difficulties in the global activity of the patient. After treatment with Amisulpride, the evolution of the previously-described dependent variables shows changes in the patient's global activity as well as in social functioning. In relationship to capacity of development within the psychosocial, social-familial and occupational sphere measured with the GAF axis V (DSM-IV-TR), progress improvement was found. The mean values from 54.6 ± 11.4 at baseline to 64.3 ± 12.9 at 9 months. Median global activity level (GAF) was 55 when initiating the study, changing to 60 in the remaining time cutoffs.

In relationship to the social adjustment situation measured with the Social Adaptation Self-Evaluation Scale (SASS), it stands out that even though the scores obtained by the patients were not found at clear levels of maladaptation, the values were very close (26 ± 8) to the limits established (< 25). This situation improves globally at 3 (29 ± 7), 6 and 9 (30 ± 7) months of treatment with Amisulpride, the evolution being statistically significant (Table 4), as also occurs with the GAF. According to compliance or noncompliance to treatment and as occurs for psychological malaise, the global activity variable and desire for consumption or craving, significantly improve at the cost of the group of patients who comply with the drug treatment.

DISCUSSION

Treatment with Amisulpride seems to be effective in patients with dependence on different substances and associated comorbidity both in the short, middle and long term. Group B disorders are represented the most in the addicted population. Borderline Disorder is the most prevalent in the present research, on the contrary to that found by Rodríguez-Llera et al.,¹⁵ who stated that Antisocial Disor

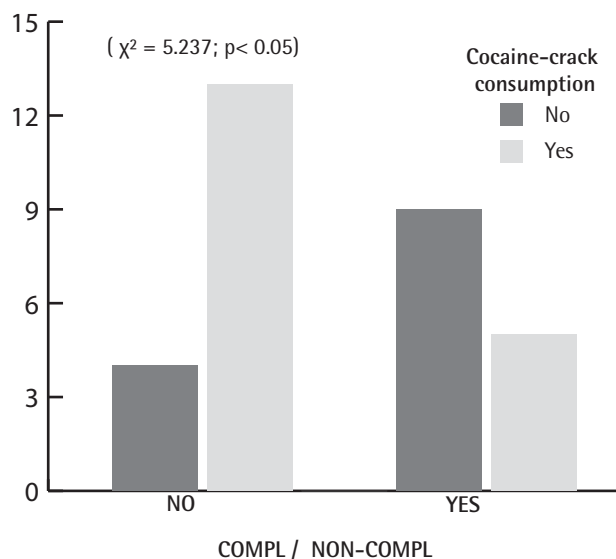


Figure 3 Cocaine-crack consumption and Amisulpride compliance

der was the most represented in his population (33%). This could be explained by the type of sample used because the Rodríguez-Llera et al. study¹⁵ was performed exclusively in young heroine users and the sample for our study was made up of long-evolution cocaine and heroine addicts. The results obtained would not support the thesis of Cervera et al.,¹⁶ who stated that gender is the differential characteristic that discriminates the type of disorder. In the same sense, Forcada et al.¹⁷ found a greater prevalence of Borderline Disorder versus that of Antisocial Disorder in Cocaine dependent subjects (BPD (52%) compared to 25% for ASPD), a circumstance which could be explained in the present work especially by the addictive shift to cocaine-crack that is produced in the heroine addict population.

Our study supports the use of Amisulpride in the drug dependent population with dual pathology, both in the short, middle and long term. As can be deduced from the values obtained in the SCL-90, a significant decrease is observed in the psychological malaise evaluated through the different dimensions and a reduction in the scores on the global indexes of GSI and PSDI. Evaluation of the results obtained based on the compliance or noncompliance of the treatment with Amisulpride revealed a statistically significant decrease after 3 months (first time cutoff) for all the dimensions, which was maintained at 9 months. The fact that the patients who complied with the treatment had significant improvements at 3 months while those who did not comply needed 9 months to present favorable changes offers us one more argument in favor of the possible effectiveness of Amisulpride in these patients. This positive evolu-

tion in the noncomplying group could be related with the Hawthorne effect.¹⁸ In relationship to social functioning, we have detected an improvement in all of the time cutoffs, although, there were no statistically significant differences based on treatment compliance or noncompliance.

On the contrary to other authors who have indicated higher levels of psychological malaise in heroine-addicted patients,¹⁹ our study found the higher levels of distress in the cocaine addicts (significantly higher than those found by Pedrero¹⁹). This could be explained by the fact that the sample in our research was receiving treatment at the time of the study. The results of Marines Higuera²⁰ would support those obtained in our work. One possible interpretation of these findings could be related with the greater deterioration, both emotionally and cognitively, caused by the continuing consumption of cocaine, that would reveal the existence of higher levels of psychopathology in the patients analyzed. A recent neuroimaging study in cocaine addict patients^{21,22} has demonstrated the existence of morphological and functional alterations of the different brain regions that would express the greater number of psychological deterioration presented by these patients.

On the other hand, and in regards to the influence of the atypical antipsychotics in the reduction of psychoactive substance usage, the analysis of the results would make it possible to conclude that the use of Amisulpride is effective in the therapeutic approach in the addictive shifting towards cocaine-crack, a situation that currently affects a large part of the users of the methadone maintenance programs. The observations on the homogeneity in the methadone dose prescribed to the resulting groups based on treatment compliance with Amisulpride supports this hypothesis, there being no statistically significant differences between them. Therefore, it could be deduced that the methadone dose does have a different effect regarding cocaine-crack consumption in the model of analysis performed.

Our study has strengths and limitations indicated by works with similar objectives²³. Among them, mention should be given to the pragmatic design of the work. Several authors have reported on the limited information that exists on the treatment in patients with dual pathology and the need to promote investigation in this field^{6,24}. In this sense, the designs that attempt to preserve the usual clinical practice provide useful information for the clinician, even more so in fields such as that of dual pathology where there continues to be more lack of knowledge than evidence. The initial hypothesis of the work, which is that treatment with Amisulpride improves psychological distress and social functioning of the addicts, seems to be ratified by the findings up to now detailed in relationship to psychological malaise. It would be interesting in the future to verify these results with a randomized and controlled, double-blind

experimental design that would provide us with the final evidence on the goodness of Amisulpride in these types of patients.

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