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Abuse or dependence on cannabis and other psychiatric disorders. Madrid study on dual pathology prevalence

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Objectives. Cannabis use has been associated to a wide variety of mental disorders, the possible causal role of this use in the etiology of severe mental disorders as schizophrenia or bipolar disorder standing out. Moreover, the cannabinoid system is involved in emotional regulation, so cannabis use could disturb this process and provoke anxiety and mood disorders. The main objective of this study was to analyze the cannabis addict subgroup from Madrid study of prevalence of dual disorders in community mental health and substance misuse services.

Material and methods. The sample consisted of 837 outpatients under treatment in the mental health network or drug network of the Community of Madrid (Spain). Of these, 353 subjects had a lifetime diagnosis of cannabis abuse or dependence and 357 subjects did not have cannabis substance use disorder. We used the Mini International Neuropsychiatric Interview (MINI) to evaluate axis I mental disorders, and Personality Disorder Questionnaire to evaluate personality disorders.

Results. It was considered that 76.5% of the cannabis addicts had a current dual disorder. The most prevalent ones were mood and anxiety disorders. Of those addicted to cannabis, 51% had a personality disorder. Most of them had several substance use disorders. Cannabis abuse or dependence subjects had an earlier onset in consumption of other drugs such as alcohol, cocaine, and tobacco than addicts without cannabis abuse or dependence. The cannabis addicts also differed from the other addicts because of an association to antisocial personality disorder, bipolar disorder, psychosis and agoraphobia. The presence of these mental disorders was significantly associated to a lower age at initiation of cannabis use.

Conclusions. Dual pathology is very high in cannabis addicts under treatment. Said consumption of cannabis, probably within a polysubstance use pattern, is associated to severe mental disorders as psychosis and bipolar disorder. An earlier age of onset in cannabis use is associated to a greater risk of said mental disorders.

Key words: Cannabis abuse, Cannabis dependence, Dual pathology, Psychosis, Bipolar disorder

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Abuso o dependencia al cannabis y otros trastornos psiquiátricos. Estudio Madrid sobre prevalencia de patología dual

Objetivos. El consumo de cannabis se ha asociado con una amplia variedad de trastornos mentales, destacando el posible papel causal de dicho consumo en la etiología de trastornos mentales graves como la esquizofrenia o el trastorno bipolar. Además el sistema cannabinoide está implicado en la regulación emocional, por lo que el consumo de cannabis también puede alterar dicha regulación y asociarse con trastornos de ansiedad y depresivos. El objetivo de este estudio es analizar el subgrupo de adictos a cannabis procedentes del estudio Madrid sobre prevalencia de patología dual en varios dispositivos asistenciales.

Material y métodos. La muestra está constituida por 837 sujetos en tratamiento en la red de salud mental o en la red de drogas de la Comunidad de Madrid, de los cuáles 353 tenían un diagnóstico de abuso o dependencia de cannabis a lo largo de la vida y 357 tenían otros trastornos por uso de sustancias pero no cannabis. Se usó la entrevista MINI (*Mini Internacional Neuropsychiatric Interview*) para el diagnóstico de los trastornos mentales del eje I y el cuestionario PDQ (*Personality Disorder Questionnaire*) para la valoración de los trastornos de personalidad.

Resultados. Se consideró que un 76,5% de los adictos al cannabis tenían un diagnóstico dual en el momento actual, destacando la prevalencia de los trastornos del humor

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y de ansiedad. El 51% de los adictos a cannabis tenían un diagnóstico de trastorno de la personalidad. La mayoría tenían varios diagnósticos de trastornos por uso de sustancias. Los sujetos con abuso o dependencia de cannabis tenían un inicio más precoz en el consumo de otras drogas como el alcohol, la cocaína y el tabaco que el resto de los adictos. Igualmente este subgrupo se diferenció del resto de los adictos por su asociación con el trastorno antisocial de la personalidad, el trastorno bipolar, la psicosis y la agorafobia. La presencia de estos trastornos mentales se asoció de forma significativa con una edad de inicio más precoz en el consumo de cannabis.

Conclusiones. La presencia de patología dual es muy elevada en adictos en tratamiento que tienen dependencia de cannabis y dicho consumo, posiblemente en el contexto de un patrón de policonsumo, se asocia con trastornos mentales graves como la psicosis y el trastorno bipolar. Una edad de inicio más precoz en el consumo de cannabis se asocia con más riesgo de presentar dichos trastornos mentales.

Palabras clave: Abuso de cannabis, Dependencia de cannabis, Patología dual, Psicosis, Trastorno bipolar

INTRODUCTION

Dual pathology is defined as the presence of an addictive disorder and a mental disorder in one individual, within a specific period. As indicated by important epidemiological studies in the general population,^{1,2} also in our clinical samples,³ said comorbidity is common. The comorbidity is associated to greater use of health care services, different phenotypes, greater severity of the picture, greater functional disability and worse evolution course.³

We have little data on the prevalence of dual pathology in the Spanish population and on the distribution of this among the two principal health care networks regarding its care, the drug network and that of the mental health. Knowledge on the distribution of dual pathology and the characteristics of these subjects may help optimize health care resources.

Cannabis consumption as well as that of cocaine and alcohol is associated to a wide variety of mental disorders. This is indicated in the different studies in the general and clinical populations.⁴⁻⁶ Specifically, several cohorts studies suggest that cannabis consumption may be a risk factor for schizophrenia.^{7,8} This possible role is also supported by the observation that early onset in cannabis consumption leads to an earlier age of onset of psychosis.⁹ Equally, data have been arising that indicate a possible causal role for bipolar disorders.^{10,11} On the other hand, cannabis consumption may alter adequate functioning of the endogenous cannabinoid system, whose role stands out in the emotional regulation and response to stress.¹²

Given the scarce care demand of these patients, it is difficult to evaluate the relation it has with mental disorders in cannabis addicts who request treatment. In the pilot study on the study of the prevalence of dual pathology carried out by the Spanish Society of Dual Pathology (SEPD), an association was observed between cocaine and alcohol dependence with the presence of mental disorders. However, these data were not analyzed for cannabis dependence due to the limited sample size.¹³ Said pilot studies served to design a study on the prevalence of dual pathology with a larger sample. The principal objective was to quantify the prevalence of the different types of pathologies included within the "dual pathology" complex (mental disorder and substance consumption disorder) in the two networks from the Madrid Community involved. The design and some global results of the study have been previously published.¹⁴ In the present work, we present the data regarding patients with cannabis dependence or abuse criteria.

METHODOLOGY

Sample

The patients were consecutively selected by their own therapists in the drug treatment centers (CAID and CAD: Center for Integral Attention to the Drug Dependent and Center for Attention to the Drug Dependent of the Community of Madrid and of the Local Government of Madrid, respectively) and the mental health centers (MSC) of the Community of Madrid. Therefore, both patients who came for the first time as well as those being followed up could be included. A total of 81 interviewers (psychiatrists, psychologists or general physicians with wide experience in addictions) from 64 drug centers in the Community of Madrid and from 17 mental health centers participated. All of the interviewers were trained in the administration of the structured interview. The participants signed an informed consent. The study was approved by the Ethics Committee of the Hospital Gregorio Marañón of Madrid. Participation was 87.2%.

The Mental Health Drug Dependence Service Network of the Community of Madrid provides specialized care to the population with criteria of accessibility and guarantee in continuity of health care and social health care during the entire disease process. The population accesses the Mental Health services, except in the case of urgent care need, through the Mental Health Outpatient Services (56 District Mental Health Centers) which they can access through referral, basically from Primary Health Care. A total of 159,881 cases were treated in the Mental Health Network in the year 2007, which means a rate of 2,169 cases per 100,000 inhabitants. On its part, the most frequent method of accessing the Drug Dependence Care Centers is by spontaneous demand of the subject going to them, followed by referral

from acquisition resources, basic health care and sensibilization for treatment. Said demand is directed, with territorial criteria, to the 38 existing outpatient centers in this Network. A total of 19,659 patients were treated in the Drug Dependence Network in 2007. This accounts for a rate of 222.70 cases per 100,000 inhabitants.

Methods

A Case Report Form was written based on the contributions collected in the pilot study mentioned on the most informative variables and on those having the greatest clinical interest at the time of the analysis. The structured interview *Mini International Neuropsychiatric Interview* (MINI) was used to establish the presence of mental disorders. It permits diagnosis according to DSM-IV and ICD-10 (Sheehan and Lecrubier, version 5.0, Fernando L, Bobes J, Gubert J, Soto M, Soto O, 2000) criteria. This interview makes it possible to study the principal psychiatric disorders on axis I at present and over the life time. The MINI has been compared with longer interviews such as the SCID-I and the CID-I with acceptably high validity and reliability scores. However, the MINI requires less time of application and a short training for the clinical interviewers.¹⁵⁻¹⁸ Those mental disorders that are not evaluated by said instrument over the life time were studied by clinical interview.

To establish the diagnosis of the personality disorders, the PDQ4+ (*Personality Disorder Questionnaire*) (Spanish Adaptation of Calvo et al.¹⁹) scale was used. This instrument combines fastness and comfort of use of a self-administered questionnaire with control of effect of the state symptoms of an interview. It is a good screening instrument on the clinical level. It behaves as a diagnostic tool, following the DSM-IV criteria when the clinical significance scale is administered.

Statistical analysis

The descriptive parameters were calculated in all the variables: mean and standard deviation in the quantitative variables that were adjusted to a normal distribution (Shapiro-Wilk test) and the median and interquartile range in those that were not adjusted. The qualitative variables were expressed by relative percentile frequencies. Comparison between two groups was performed using the Chi-square (χ^2) test or Fischer's exact test if appropriate for the categorical variables and using the Student's T test or the Mann-Whitney U Test for quantitative variables. The principal variable was calculated in the confidence interval for 95% security. The tests were considered significant if $p < 0.05$.

To evaluate the factors that may affect the differences in the presence of mental disorders among groups, a logistic multivariate regression model was used. This includes all

those factors that may affect the independent variable. The polycotomic qualitative variables are transformed into "dummy" variables, that having the least risk being established as reference. Furthermore, linearity of the quantitative variables was tested. As selection criteria of the model, the parameters that reached $p < 0.1$ were included and exit criterion was established at $p < 0.05$. However, all of those compounding factors whose χ^2 or that of the other parameters were modified by more than 20% were maintained. Furthermore, the corresponding interactions, including only the significant ones, were tested. In the case of the presence of linearity or co-linearity, the stratified data adjusted by the main possible compounding variables are shown. The statistical analysis was generated using the SPSS v.17 program.

RESULTS

A total of 837 patients were included: 208 (24.9%) from MHC and 629 (75.1%) from CAID and CAD. Accuracy reached for the total sample (drugs and mental health) was $\pm 3.38\%$ ($d = 0.0338$). Accuracy reached for the mental health subpopulation was $\pm 5.59\%$ ($d = 0.0559$). Accuracy reached for the drug dependent subpopulation was $\pm 3.74\%$ ($d = 0.0374$).

Of the 837 patients evaluated, 710 had some diagnosis of substance abuse disorder (SAD) during their life time (including alcohol and excluding tobacco). There were 127 (26.5%) subjects without SAD. Regarding cannabis use disorder, 353 patients had been diagnosed of it during their life (abuse or dependence), 133 having current cannabis abuse or dependence. Only 20 subjects had a diagnosis or cannabis abuse or dependence during their lifetime without other associated SADs (5.7% of all the subjects with SAD with cannabis consumption). Thus, in the analysis, all those diagnosed with cannabis abuse or dependence were included, even if they had other associated SADs. Table 1 shows the social demographic characteristics of the patients with cannabis use disorder over the lifetime.

Prevalence of dual disorders in cannabis use disorder addicts

Table 2 shows the distribution of the morbid mental disorders over a lifetime. Dual pathology was considered to exist when there was a diagnosis of current mental disorder established by the MINI and/or a diagnosis of personality disorder through the PDQ questionnaire. Table 3 indicates the distribution of personality disorders in patients with cannabis abuse or dependence during their life. Table 4 reflects the current diagnoses of disorders on axis I obtained through the MINI interview in subjects with current cannabis abuse or dependence.

Table 1	Characteristics of patients with cannabis abuse disorder over life time (n= 353)
Age (years)	35.2 (SD 8.6)
Male	306 (86.7%)
Single	229 (66.6 %)
Married	67 (19.5%)
Primary studies	162 (46.4%)
Secondary	140 (40.1%)
University	34 (9.7%)
Actively working	151 (43%)
Lives with origin family	166 (47.3%)
Lives with own family	88 (25.1%)
Origin:	
Mental Health	33 (9.3%)
Drug Dependence centers	320 (90.7%)
Medical Condition	130 (37%)
Hepatitis	101 (28.6%)
HIV	44 (12.5%)
SD= Standard deviation	

Table 3	Personality disorders in patients with cannabis abuse disorder over a lifetime
	N %
Presence of personality disorders	180 51.0
Paranoid D.	69 19.5
Schizoid D.	22 6.2
Schizotypic D.	36 10.2
Antisocial D.	69 19.5
Borderline D.	70 19.8
Histrionic D.	22 6.2
Narcissistic D.	24 6.8
Avoidant D.	65 18.4
Dependent D.	25 7.1
Obsessive D.	53 15.0
Passive -aggressive D.	41 11.6
Depressive D.	71 20.1
Number of PD diagnoses	1.6 (SD=2.3) [0-12]

Table 2	Mental disorders (Axis I) throughout the life in subjects with cannabis use throughout the life (N=353)
	N %
Presence of dual pathology*	270 76.5
Current presence a disorder on axis 1 (without Personality D.)	226 64.0
Diagnosis of past mental disorder	101 28.6
Psychiatric diagnosis during life	
Major Depressive Episode	92 26.1
Dysthymic Disorder	72 20.4
Risk of suicide (evaluated with the MINI)	116 32.9
Bipolar disorder	90 25.5
Anxiety Disorder	89 25.2
Agoraphobia	44 12.5
Social phobia	39 11.0
Obsessive-compulsive disorder	34 9.6
Post-traumatic stress disorder	20 5.7
Psychotic disorders	43 12.2
Bulimia	6 1.7
Generalized anxiety disorder	77 21.8
Number of diagnoses of mental disorders	1.5 (SD=1.7) [0-7]
*It was considered that there was a dual pathology if there was the presence of a current mental disorder established by the MINI and/or a diagnosis of personality disorder through the PDQ questionnaire.	

Table 4	Current mental disorders of axis I in subjects with current cannabis dependence or abuse (n=135)
	N %
Current mental D. (MINI)	88 66.2
Maj. Depressive Episode	26 19.5
Dysthymia	19 14.3
Suicide risk	40 30.1
Bipolar D.	39 29.3
Anxiety D.	31 23.3
Agoraphobia	21 15.8
Social phobia	14 10.5
Obsessive -Compulsive disorder	11 8.3
Posttraumatic Stress Disorder	6 4.5
Psychoses	16 12
Bulimia	2 1.5
Generalized Anxiety Disorder	32 24.1

Comparison between cannabis use disorder addicts and the rest of the addict subjects

Most of the subjects with cannabis use disorder had some other comorbid SAD. The most frequent were cocaine abuse or dependence (276; 78.2%), alcohol (269 subjects; 76.2%) and opiates (125; 35.4%). Mean diagnoses of SAD was 1.6 (SD=1.15, range 0-7). Only 20 subjects (5.7%) had an

Table 5

Age of onset in cannabis consumption and presence of mental disorders and age of onset of other consumptions in cannabis addicts

	Age of onset of cannabis (SD) (in years)		
	Presence of disorder	Absence of disorder	p
Agoraphobia	14.9 (3.3)	16.3 (4.4)	0.05
Bipolar disorder	15.5 (3.3)	16.4 (4.5)	0.05
Psychoses	14.6 (3.6)	16.4 (4.4)	0.02
Antisocial personality disorder	15.0 (4.25)	16.4 (4.3)	0.01
	Age of onset of other consumption in cannabis addicts (in years)		
	Cannabis addicts	Non-cannabis addicts	p
Alcohol	15.1 (4.1)	17.5 (6.9)	0.001
Cocaine	19.8 (5.5)	22.6 (7.4)	0.001
Tobacco	13.9 (2.9)	14.9 (3.6)	0.001

exclusive diagnosis of cannabis use disorder, 53 (15%) had another comorbid SAD and most of the subjects, 280 (79.3%) had more than two diagnoses of SAD. Mean age of onset of consumption of cannabis was 16.15 (SD=4.4).

There were no significant differences in mental disorder prevalence between cannabis addicts (n=353) and the other addicts (n=357). However, there was a tendency for greater presence of dual diagnoses (current mental disorder and/or personality disorder) in the cannabis group (64% vs 57.7%, p=0.09). There was a predominance of males in the cannabis group (86.7% vs 76.6%; p=0.001) and they were younger (35.2 vs 39.3 years, p=0.001). Antisocial personality disorder was more prevalent in the cannabis group (19.5% vs 9%, p=0.001) and less in the obsessive personality disorder (15% vs 21%, p=0.04). When the subgroup of current addicts to cannabis is considered (n=133), there is a greater prevalence of agoraphobia (16.5% vs 9.2%, p=0.01), of psychosis (16.5% vs 9.4%, p=0.02) and of bipolar disorder (29.3% vs 21.8%, p=0.05) regarding the rest of the addicts.

No information was collected regarding onset age of mental disorders. Onset age of initiation of cannabis consumption in patients was compared with the initiation of patients with the indicated mental disorders, there being a lower initiation age in the consumption of cannabis consumption in patients who suffered any of these disorders regarding the onset age of cannabis in subjects who were not diagnosed of said mental disorders. Equally, the age of onset of consumption of other drugs (alcohol, cocaine, tobacco) was lower in the subgroup of poly-consumers who were addicts to cannabis regarding the rest of the addicts (table 5).

Given that these three mental disorders (agoraphobia, psychoses, bipolar disorder) could be associated with drugs other than cannabis and that a logistic regression model was not adequate for the co-linearity and correlation between the different consumptions, a stratified analysis for each disorder was performed according to the presence of disorder by cocaine and alcohol use. Regarding agoraphobia, it remained associated to the diagnosis of current cannabis abuse or dependence in absence of alcohol abuse disorder (p=0.04), but in the presence of cocaine abuse disorder (p=0.02). The diagnosis of psychosis only remained associated to cannabis significantly in the presence of cocaine abuse disorder (p=0.004). The diagnosis of bipolar disorder remained associated to cannabis in absence of cocaine use (p=0.02), but not when stratified by alcohol. In the latter case, a tendency to the association in present of alcohol abuse was observed (p=0.1).

DISCUSSION

There is little information in our setting on psychiatric comorbidity in cannabis addicts. Most comes from epidemiological and clinical studies from other countries. The greatest difficulty existing to obtain information is that of obtaining an adequate sample size, because of the limited demand for treatment by these addicts. As far as we know, the data of the current study offer the most numerous information on the psychiatric comorbidity in the sample of addicts in our country. These data have the usual limitation of these studies in clinical samples. This limitation consists in the fact that the presence of poly-consumers is common, it being difficult to evaluate the specific effect of a certain drug.

Prevalence of dual pathology in cannabis addicts under treatment

While in the pilot study conducted by us,¹³ based on the information obtained from the clinical histories, we obtained a prevalence of dual pathology of 34% for the global sample, when the methodology is improved by means of a structured interview, it is observed that the cannabis addicts under treatment show some improvement in comorbid mental disorder. Some diagnosis on axis I based on the MINI interview and/or a diagnosis of personality disorder is found in 76.5% of the patients. The elevated comorbidity in cannabis addicts coincides with other studies.^{5,6}

The most prevalent disorders were the different mood and anxiety disorders. The high prevalence of manic or hypomanic pictures stands out. A high percentage of these may be due to induction by consumption, as has been previously described.¹⁰ Equally, the risk of suicide evaluated using the MINI interview was found in one third of cannabis addicts. Cannabis consumption is considered to increase said risk.²⁰ Said risk of suicide is greater in dual patients than non-dual patients.¹⁴ Half of the patients have a diagnosis of personality disorder, the most prevalent being antisocial, borderline, paranoid, depressive and avoidant disorder. This self-administered questionnaire may over-exaggerate the diagnosis of these disorders. However, this is verified subsequently by the interviewer using the clinical significance scale that can correct such overvaluation.

Comparison between cannabis use disorder addicts and nine consumers of cannabis

Approximately half of the sample of patients with some diagnoses of substance use disorder had cannabis abuse or dependence. Most had several diagnoses of substance abuse disorder (SAD). Possibly, in samples from the general population, there may be fewer concomitant diagnoses of SAD, however in addicts receiving treatment, this concomitance of consumption is common. There are few social demographic and clinical differences between both subgroups. This is possibly because of the high prevalence of alcohol and cocaine dependence in both subgroups. However, there was a greater predominance of males in the cannabis abuse or dependence addicts subgroup and the subjects were younger. Furthermore, there was an almost significant tendency to have greater presence of other psychiatric diagnoses.

The mental disorders associated most to the subgroup of cannabis addicts were bipolar disorder, agoraphobia and psychoses but they may all have possibly been related more to several substances (alcohol, cocaine) than specifically with cannabis. Given the limited number of patients with exclusively cannabis abuse or dependence, a stratified analysis was made by the principal drugs involved in said comorbidity.

For agoraphobia, it was observed that the association with cannabis was maintained when adjusting for alcohol, but not when adjusting for cocaine. Patients addicted to cannabis and cocaine were those who had the most diagnosis agoraphobia. In addition, the diagnosis of psychosis was also more prevalent in the subgroup of cannabis and cocaine addicts. However, bipolar disorder had a significant association with cannabis consumption when adjusted for cocaine. However, said association disappeared when adjusting for alcohol. Therefore, we cannot conclude that cocaine abuse or dependence is specifically associated to certain mental disorders with the current data. It can be stressed, however, that multiple consumption between the subject that includes cannabis consumption is associated with severe mental disorders such as psychosis and bipolar disorder. Given the nature of the study, we could not determine what type of relationship there are with these disorders. In any event, we have observed that onset age in the consumption of cannabis begins earlier in patients with these comorbid diagnoses. This suggests that cannabis consumption may play a causal or precipitating role of such disorders. Different current studies indicate that cannabis consumption is related with an earlier onset of psychoses^{21,22} and a recent meta-analysis has considered this.⁹ The earlier the initiation of cannabis consumption, the greater the risk that psychoses may appear.²³ Equally, a causal role of cannabis in induction of mania¹⁰ and earlier onset of age of bipolar disorder in cannabis consumers have been suggested.^{11,24} In a study in adolescence, 62% of comorbid mental disorders were observed in cannabis addicts, with an association with mood disorders (depression and bipolar disorder) and anxiety (especially in panic disorder).⁶ The induction of panic attack has also been described in cannabis consumption.²⁵ We have observed a high prevalence of panic attack in cannabis addicts, although the association was greater with agoraphobia when compared with the rest of the addicts. The close association of cannabis consumption with bipolar disorder and psychosis has been establishing multiple works.^{4,26}

Furthermore, given that they also initiate consumption prior to other drugs, such as alcohol and cocaine, approximately 2.5 years before the rest of the addicts who do not consume cannabis, it appears that this subgroup of cannabis consumers makes up a subgroup having greater severity. However, these data do not support cannabis as being the entry point into consumption of other drugs, since the onset age in tobacco and alcohol is younger than that of cannabis. In any event, the limitation in the method of collecting the onset age through clinical interview with the passable memory bias must be taken into consideration.

Limitations of the study

We consider that the principal limitation is the presence of multiple diagnoses of SAD that limits the differentiation

of the subgroup of cannabis addicts. Therefore, the data presented are more valid for addicts of multiple agents with cannabis consumption under treatment than for addicts to only cannabis or consumers of cannabis outside of the health care networks. SAD was diagnosed by clinical interview. It was not included in the protocol of toxicological analyses or use of other sources of information. However, most of the patients were known in the drug dependent attention centers, where they commonly underwent urine analyses and their consumption patterns were known. It is possible that the involvement of investigators who are more motivated in the dual pathology study may result in their over-diagnosing the problem. However, standardized instruments were used, the investigators underwent previous training, and a high number of investigators participated. In this way, we consider that the large number of investigators and participating sites is a strength of the study, given that the data may be extrapolated to subjects being treated in the mental health and drug network of the Community of Madrid. The use of a structured interview and the sample size obtained are other strengths of the current study.

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