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Psychoactive drug use in patients with panic disorder

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Introduction. The objectives of this study were to evaluate the prevalence of drug use in out-patients with panic disorder and their influence in evolution and therapeutic response of panic disorder.

Material and methods. The sample was made up of 79 out-patients diagnosed of panic disorder or agoraphobia with panic disorder according to the ICD-10 criteria and 83 controls from the same center with other psychiatric disorders. Subjects were followed-up for six months.

Results. Prevalence of regular lifetime drug use was: 13 % for alcohol, 52 % for nicotine, and 47 % for caffeine. No other drug use was observed. Patients with panic disorder used less caffeine than controls, there being no differences in other drug use. Caffeine use was associated with higher antidepressant dosages.

Conclusions. Thus, prevalence of regular drug use in panic disorder during the lifetime of out-patients with panic disorder was: 13 % for alcohol, 47 % for caffeine use, and 52 % for nicotine use. Those with panic disorder use less caffeine than other psychiatric patients, but there were no differences in other drug use. Presence of agoraphobia has no repercussion on consumption. There were no differences in clinical manifestations and treatment responses between users and non-users, but drug use may modify antidepressant dosages.

Key words:
Drugs use. Panic disorder. Agoraphobia. Alcohol. Caffeine. Nicotine.

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Consumo de sustancias psicoactivas en pacientes con trastorno de pánico

Introducción. Los objetivos de este estudio fueron evaluar la prevalencia del consumo de drogas en pacientes ambulatorios con trastorno de pánico, su repercusión sobre la evolución y la respuesta al tratamiento de dicho trastorno.

Material y métodos. La muestra está constituida por 79 casos con diagnóstico de trastorno de pánico o agorafobia con trastorno de pánico según la CIE-10 y 83 controles con otros trastornos psiquiátricos en tratamiento en el mismo centro. Se realizó un seguimiento durante 6 meses.

Resultados. Se obtuvo una prevalencia para el consumo habitual de drogas a lo largo de la vida del 13 % para el alcohol, el 52 % para el tabaco y el 47 % para el café; no hubo consumos de otras sustancias. El consumo actual de cafeína era inferior en los casos que en los controles, no existiendo diferencias respecto a los otros consumos, y el consumo de café se relacionó con requerimientos de mayores dosis de antidepresivos.

Conclusiones. Por tanto, la prevalencia de consumo habitual de sustancias a lo largo de la vida en pacientes con trastorno de pánico en tratamiento ambulatorio se sitúa alrededor de un 13 % para el alcohol, un 47 % para el café y un 52 % para el tabaco; hay un menor consumo de cafeína, aunque no existen diferencias en otros consumos respecto a un grupo de controles psiquiátricos. La presencia de agorafobia no repercute en el consumo. El consumo tiene escasas repercusiones sobre la clínica y la respuesta al tratamiento, aunque puede modificar las dosis requeridas de antidepresivos.

Palabras clave:
Consumo de drogas. Trastorno de pánico. Agorafobia. Alcohol. Cafeína. Tabaco.

INTRODUCTION

The first studies on the self-medication hypothesis stressed that phobic subjects drank alcohol to relieve their anxiety symptoms. Thus, cooccurrence between alcoholism and panic disorder with agoraphobia could be explained by this attempt to self-medicate their symptoms. In fact, many subjects suffering panic attacks report that they use alcohol as self-medication and believe that this procedure is effec-

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tive to prevent or reduce the attacks. Patients with agoraphobia attribute anxiety decreasing properties to alcohol and observe that alcohol helps them face fear situations, however their picture deteriorates when consumption increases and improves with abstinence[1].

On the other hand, caffeine, when administered at high doses, has the properties of a good panicogenic agent[2], given the similarity of the symptoms it causes with those of the panic attack, its specificity in inducing panic attacks in patients with panic disorder, replicability of the effects with repeated exposure to caffeine administration and blockage of caffeine induced attacks by some of the drugs useful in the panic disorder, such as imipramine or alprazolam. The mechanism by which caffeine produces these effects seems to be due to the adenosine receptor antagonism. In any event, the direct or indirect action of caffeine on noradrenergic, dopaminergic, gabaergic systems or through second messengers as it influences phosphodiesterase cannot be ruled out.

Clinical studies support the anxiogenic role of caffeine. Thus, patients with panic disorder stop drinking coffee more often than other medical or psychiatric patients. There is also a greater correlation between anxiety symptoms and caffeine consumption in patients with panic attack versus those having other psychiatric conditions or in healthy controls. This suggests that these patients are more sensitive to the effects of caffeine. Increased anxiety due to caffeine has been described in other psychiatric disorders such as obsessive-compulsive disorder or social phobia, however the degree of the intensity is intermediate between panic disorders and healthy controls[3-5]. Finally, it has been stated that smokers have a greater risk of developing a panic attack[6,7].

This study aimed to assess the use of substances in patients treated for panic disorder and their possible relationship with clinical manifestations, severity of the picture or treatment. The sample comes from a case-control study with 79 patients with panic attack and 83 controls enrolled from psychiatric out-patients.

MATERIAL AND METHODS

The sample is made up of 79 patients with panic attack criteria or agoraphobia with panic disorder according to the ICD-10 who were consecutively admitted to out-patient treatment and 83 controls with other psychiatric disorders treated in the same Unit, controlled by age and gender. They were assessed with the Hamilton Depression Rating Scale (HDRS) and the State-Trait Anxiety Inventory (STAI-State and STAI-Trait). All the patients were treated with paroxetine and behavioral exposure guidelines. The paroxetine dose was adjusted according to clinical criteria. A six month follow-up was performed for the patient group.

A bivariate analysis was performed with the chi-square or Fisher tests, as corresponded, and comparisons of means with the Student's *t* or McNemar tests. A multivariate analysis was conducted with a logistic regression model for predictive purposes. The SPSS v. 10 statistical program was used.

RESULTS

The sample characteristics are shown in table 1 and prevalence of regular, present and past use is expressed in table 2. Figures 1 and 2 show the number of cigarettes and coffee per day for cases and controls. Greater coffee intake and diagnosis of agoraphobia were associated with the need for larger doses of antidepressants (table 3).

The fact that 10 patients with panic attack stopped drinking coffee after their clinical picture began is important. There were no differences in onset age and psychoactive substance intake duration between cases and controls. No correlation was observed between the score on the STAI and the psychoactive substance doses. No relationship was found between intake of different substances and clinical characteristics of the picture with the presence of a secondary depressive syndrome or agoraphobia. Finally, there was no relationship between use of psychoactive substances and therapeutic response.

DISCUSSION

Based on the results obtained, the prevalence of regular lifetime use of substances in panic attack is approximately 13 % for alcohol, 47 % for coffee and 52 % for tobacco. Caffeine intake is less in patients with panic attack than in other psychiatric patients, there being no differences for

Table 1 Socio-demographic and baseline clinical characteristics

	Cases (n = 79)	Controls (n = 83)
Age (years)	37.1 (SD = 11.6)	37.8 (SD = 11.4)
Gender (% men)	20 (25.3 %)	19 (22.9 %)
Diagnosis of controls		Schizophrenia: 24 (14.8 %) Mood disorder: 30 (18.5%) OCD: 10 (6.2 %) Somatomorph D: 4 (2.5 %) Personality D: 8 (4.9 %) Others: 7 (4.3 %)
Presence of agoraphobia	53 (67 %)	
Secondary depressive syndrome	31 (39 %)	
STAI	Status: 7.3 (SD = 1.7) Trait: 6.4 (SD = 1.7)	
Hamilton depression rating scale	14.1 (SD = 6.0)	

Table 2 Regular consumption of psychoactive substances

	Cases	Controls
Present alcohol	7 (11 %)	6 (7 %)
Past alcohol	8 (13 %)	12 (14 %)
Sedatives*	50 (78 %)	45 (58 %)
Present tobacco	24 (38 %)	44 (53 %)
Past tobacco	33 (52 %)	47 (57 %)
Present coffee**	19 (30 %)	43 (53 %)
Past coffee	29 (47 %)	50 (62 %)

*Chi square: 8.1; df: 1; p = 0.005; OR: 2.9 (95% IC: 1.4-6). **Chi square: 7.60; df: 1; p = 0.006; OR: 0.38 (95% CI: 0.19-0.76)

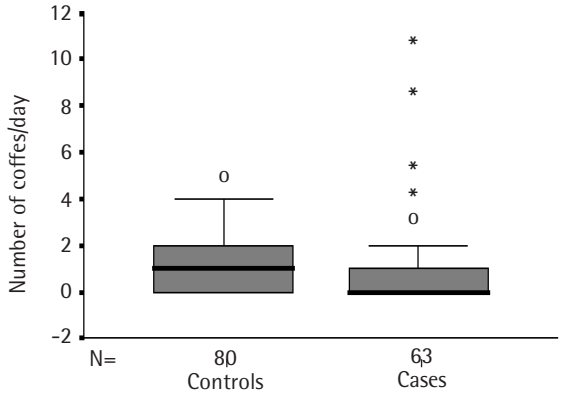

Figura 2 *Coffee intake in cases and control.*

alcohol or tobacco consumption. Substance use may modify the maintenance dose of antidepressant used, although there are no differences in the clinical characteristics of the panic disorder or in the response to treatment or between agoraphobics and non-agoraphobics between those taking substances and non-consumers.

In a different sample of out-patients with panic disorder or agoraphobia, made up of 55 subjects, the prevalence values for regular drug consumption obtained were higher for alcohol and lower for tobacco and caffeine than those obtained in the sample we present. We also evaluated the prevalence of patients with criteria for drug dependence, the values corresponding for alcohol being 5.5 % for present dependence and 9.1 % for past and 32.7 % for tobacco at present and 43.6 % in the past. As in the present study, we did not observe differences between consumers and non-consumers in response to treatment, in prevalence of consumption between agoraphobics and non-agoraphobics or in relationship with other relevant clinical characteristics. However, patients who drank alcohol required a lower dose of antidepressants (unpublished data).

However, a major prevalence of tobacco consumption associated to panic attacks is observed in samples from the general population. In one study, prevalence for regular lifetime tobacco consumption was 81 % in patients with panic attacks, superior to the subjects without attacks (69 %) and the panic attacks were associated to a greater risk of tobacco consumption[8]. An association between tobacco consumption and panic attacks was also seen in another sample of young individuals from the general population. Previous tobacco dependence increased the risk of developing panic attacks, while the existence of previous panic attack was not associated with an increase in tobacco consumption. Thus, the association was fundamentally between previous tobacco dependence and the production of panic attacks, but not with a panic attack as such[7]. Other authors also state that tobacco consumption is a risk factor for panic attacks in addition to the existence of a greater prevalence of consumers among patients than in the general population, with 56 % smokers out of 102 patients with panic disorder and 28 % ex-smokers. Although a large number of patients stopped smoking due to their panic disorder, they did not show a clear benefit in their symptoms[6]. We did not find this greater prevalence, possibly due to the fact that

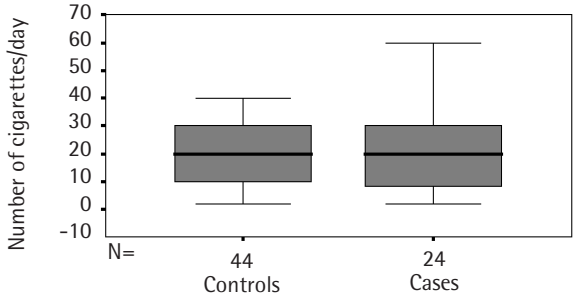

Figure 1 *Consumption of cigarettes (subjects with daily consumption).*

Tabla 3 Múltiple regression model-predictor of paroxetine dose

Variable	B	EE (B)	IC of B (95%)	t	p
CDCC	2.78	0.81	1.15-4.41	3.45	0.0013
DX	7.00	2.77	1.40-12.60	2.52	0.0155
Constant	12.22	5.07	1.98-22.45	2.41	0.0205

CDCC: caffeine doses in coffee cups (1 cup: 75-100 mg of caffeine base); DX: type of panic disorder (0: without agoraphobia; 1: with agoraphobia); multiple correlation coefficient: 0.55; F. of model: 8.88; significance of F: p = 0.0006.

our control group is made up of psychiatric patients who have already had a high prevalence of tobacco consumption. In addition, these studies frequently observe an association between consumption and anxiety attacks that do not necessarily constitute a panic disorder as such. In any event, our consumption values are lower than those obtained by the studies mentioned, and do not support the use of tobacco as self-medication of panic disorder or a causal relationship of tobacco as an inductor of such disorder. This does not rule out that there may be a more intense association between tobacco consumption and anxiety symptoms than with a specific psychiatric disorder such as panic disorder. Equally, we did not observe a negative impact of tobacco consumption on anxiety attacks, the same as suggested by other authors[8].

The fact that caffeine consumption is high in schizophrenia but low in patients with anxiety stands out in hospitalized psychiatric patients[5]. This low caffeine consumption has been observed in out-patients with panic disorder[3]. Different electrophysiological measures have shown that patients with panic disorder are more sensitive to the effects of caffeine than the controls[4]. Thus, many patients with panic disorder possibly avoid coffee due to the elevated sensitivity to its anxiogenic effects. This is supported by the fact that a high percentage of our patients stop drinking coffee after the onset of the panic picture. Furthermore, this anxiogenic effect may have a repercussion in a worse course of the picture or a need for higher antidepressant doses.

Contrary to that which would be expected by the self-medication hypothesis, according to which there should be high alcohol consumption in patients with anxiety, we have not observed this increase. Other studies also find no differences in alcohol consumption in patients with anxiety versus the general population. They even observe that patients with agoraphobia drink slightly less, which does not support its use to relieve anticipatory anxiety[9]. Other authors have also estimated prevalence of alcoholism in patients diagnosed of agoraphobia with panic attacks to be from 10 % to 20 %[10], or even up to 24 % of alcohol dependence in the past in these patients[11]. As some authors have not observed a greater risk of alcohol consumption in patients with anxiety, they have concluded that there is no support for the self-medication hypothesis in patients with anxiety and that there are data that support avoidance of psychostimulants[12].

One review[1] reports a 10 % to 20 % prevalence of alcoholism among patients with panic disorder, but they suggest that the presence of agoraphobia may be a better predictor of consumption than the attacks per se, something that our data does not support. It has also been suggested that consumption is useful to relieve anticipatory anxiety and would have little effect on panic attack. Furthermore, many patients report alcohol consumption as self-medication of their anxiety symptoms and perceive it as an effective method, even though it may exacerbate their picture and that its efficacy is not clear[1]. Agreement on the presence of a high percentage of panic attacks in alcoholic patients does not seem to exist[13,14].

In any event, the anxiolytic effects of alcohol were demonstrated in an experiment with patients with panic assigned to alcohol or placebo consumption, the effects of alcohol being superior to that of placebo in decreasing the number of panic attacks and anxiety[15]. That is, in those alcohol consuming patients with panic disorder, this consumption may be highly reinforcing and persistent due to its immediate positive effects, although most of the patients with this disorder are not going to use alcohol as self-medication. Equally, alcohol consumption may be used more to relieve anxiety symptoms of different origin than for self-medication of a defined psychiatric disorder.

Finally, in patients with panic disorder who use drugs, possible drug interactions that may change the dose of antidepressants required must be considered. We have observed possible changes in the drug dose with caffeine and alcohol, although not with tobacco. Caffeine is metabolized by the P-450 system, so that it may have interactions with some antidepressants[16]. Equally, alcohol may interact with antidepressants[17] or may have an anxiolytic effect that decreases the required dose of the antidepressant. In any event, this is an issue that needs larger studies.

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