Cannabis dependence: clinical implications. Based and one case

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Implicaciones clínicas de la dependencia de cannabis. A propósito de un caso

Summary

Cannabis has been commonly regarded as an innocuous drug, and has been used for centuries due to its multiple therapeutic effects (analgesic, anticonvulsant, sedative, antidepressant, etc.). However, growing evidence in recent years highlights the risk of adverse effects secondary to dependence and withdrawal syndrome. We report a case of severe cannabis dependence, that led to a variety of psychopathological, cognitive and somatic symptoms. This is compared with the bibliography and we analyze the influence of a possible underlying psychiatric disease. The adverse effects include affective and eating disorders, and the possibility of seizure induction. A novel therapeutic strategy in cannabis dependence is reported.

Key words: *Cannabis. Mania. Bulimic behaviors. Epileptic seizure. Lithium.*

Resumen

El cannabis ha sido considerado históricamente una droga inocua y utilizado durante siglos por sus múltiples efectos terapéuticos (analgésico, anticonvulsivante, sedante, antidepresivo, etc.). Sin embargo, en los últimos años existe una creciente evidencia de la existencia de efectos adversos, derivados de la dependencia y abstinencia. Describimos un caso clínico de dependencia grave a cannabis que presenta una sintomatología polimorfa, a nivel psicopatológico, cognitivo y somático; la contrastamos con la bibliografía y analizamos la influencia de un posible trastorno psiquiátrico subyacente. Del síndrome clínico destacan las alteraciones afectivas y de la conducta alimentaria, así como la posible relación con una crisis comicial. Comentamos por último una nueva estrategia terapéutica en la dependencia de cannabis.

Palabras clave: *Cannabis. Manía. Conducta bulímica. Crisis convulsiva. Litio.*

CLINICAL CASE

A 20 year old woman who was admitted in our center due to a maniform syndrome in the context of serious cannabis dependence is presented. She presented a genetic load of affective disorder: a twin brother of the father diagnosed of bipolar disorder and maternal grandmother of recurrent major depressive disorder, with melancholic symptoms. Her premorbid personality is described as responsible, extrovert, perfectionist, active, well adapted and with good academic performance. No somatic background of interest is reported.

Her clinical history began at 17 years of age, coinciding with the onset of cannabis use in progressively increasing amounts until 10-20 cigarettes/day, although this included periods of less consumption and abstinence. She presented a depressive syndrome in form of asthenia, anhedonia, feelings of lack of ability and anorexia with significant weight loss. She didn't refer megalomaniac cognitions she went to a psychiatrist who prescribed paroxetine 20 mg/day, initially observing a good clinical response.

In the next two years, the symptoms were marked by emotional instability, with periods characterized by irritability, concentration difficulties, psychomotor restlessness and progressive abandonment of usual tasks. During the last year, eating behavior disorders, with bingeing secondary to increased appetite and frequent vomiting due to intolerance to the intake, stood out. The symptoms became worse in the months prior to admission, and she presented a restrictive diet due to intolerance to fats, with significant weight loss. The patient denies distortion of the body image and self-induced vomiting at all times, a fact corroborated by the family.

On admission, the patient showed correct temporal-spatial orientation; significant distractibility, and concentration difficulties. There were also logorrheic speech and thought with tachypsychic and flight of ideas tendency; hyperthymic mood, at times dysphoric with irritability and emotional lability; psychomotor restlessness and moderate hyperactivity, with progressive abandonment of usual activities. In addition, there was also important psychic and somatic anxiety. She was aware of her disease, recognizing difficulties in cognitive performance secondary

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to the addiction. She presented first and third phase insomnia in the weeks prior to hospitalization.

In the beginning of her hospitalization, treatment was prescribed with olanzapine 10 mg/day and clorazepate 30 mg/day. On the third day, coinciding with the decrease in treatment mentioned due to clinical improvement, the patient presented a generalized tonicoclonic epileptic seizure with tongue biting, sphincter relaxation, post-critical period and posterior amnesia. The complementary examinations (complete blood test, biochemistry, coagulation tests, protein analysis, HIV, HBV, HCV and syphilis serologies, thyroid hormones, folates, cobalamines and cranial CT scan) were within normality, except for a mild anemic syndrome and decrease of folates, with later normalization in the control analysis. The neurological assessment advised against treatment with antiepileptics and 1 mg/day of clonazepam was prescribed, without observing seizure pathology during the rest of the admission.

Due to the familial genetic load of bipolar disorder, to the presence of differentiated periods of hypothymia and hyperthymia during recent years, the maniform symptoms of the present episode as well as the persistence of some dysphoria, anxiety and psychomotor restlessness in spite of the treatment prescribed, a decision was made to prescribe increasing doses of lithium until 800 mg/day, observing good tolerability and progressive clinical improvement until the premorbid level. On discharge, the patient was euthymic, without significant anxiety, with restoration of cognitive performance, as well as normalization of the eating behavior and good tolerance to intake.

DISCUSSION

Cannabis has been historically considered as an innocuous drug, however in recent decades and in relationship to a greater amount and frequency of the pattern of use, there has been growing evidence of the existence of symptoms from dependence and abstinence of this toxic agent. Adverse effects after acute intoxication as well as continued use has given rise to many experimental and observational studies, that have described psychopathological, cognitive, somatic and neurophysiological disorders. Most of the effects derived are dose dependent and strengthened by constitutional factors including low age at onset of consumption, personality features and vulnerability to serious psychiatric diseases[1].

The responses derived from acute intoxication include euphoria and sedation, but adverse effects, such as panic attack[2], hypothymia[3], and psychotic symptoms[2,4] are frequent. Previous history of schizophrenia or personality disorder has been associated to greater seriousness and duration of the symptoms. The psychotic episodes are characterized by a greater confusional component, more disorganized and violent behavior, grandiosity and hyperthymia, greater insight, less evidence of thought disorders and rapid response to neuroleptics[5-7]. It has been suggested that toxic psychosis can be produced in individuals without a previous history of serious mental disease in some studies[5].

The validation of the cannabis dependence concept, according to the DSM-IV, has been verified in different empiric investigations based on the cognitive, psychopathological and behavioral disorders that it causes, and to the continuation of its use in spite of them[8]. Irritability, dysphoria and insomnia are produced in the continued use from the psychopathological point of view. The abstinence syndrome causes anxiety, lack of motivation, dysphoria, irritability, anorexia, insomnia and autonomic effects[9-11].

Cognitive dysfunction in cannabis dependence is related with the years of use, observing impairment in the selective attention, manifested by inability of frontal processing to filter irrelevant stimuli[12]. Impairment has also been observed in work memory, evocation and learning[13]. In addition, it has been possible to relate delay in data processing with increase in P300 wave latency of the evoked potentials in patients who are cannabis users in regards to the controls[12].

Among the somatic effects derived from cannabis use, we can find conjunctival reddening, photophobia, tearing, tremor, ataxia, tachycardia, blood pressure changes, increased appetite, as well as hormonal and immunological abnormalities. The therapeutic effects such as analgesic, antiemetic, muscle relaxant, bronchodilator and the decrease of intraocular pressure ones are also known[14,15]. In studies on isolated cases, the possibility that cannabis causes electroencephalographic alterations, such as neuronal deregulation or decrease of the REM phase, are described[16,17]. It has been hypothesized that the cannabinoids would act by altering the synaptic morphology in several receptors (opioids, benzodiazepinics, anandamides) as well as by interacting with multiple neurotransmitters, modifying the cholinergic, catecholaminergic, serotoninergic and GABAergic activity[15,17].

In the clinical case presented, the clinical symptoms began with a depressive syndrome coinciding with the onset in cannabis use; these symptoms present with considerable frequency in individuals who consume this substance and with greater prevalence in women (16% adaptive disorder with depressive symptoms, 10.5% dysthymia)[3]. During the following years, there was a predominance of emotional instability, irritability, dysphoria, concentration difficulties, with decrease in productivity in usual tasks as well as in social interaction, a psychopathology that could be explained by overlapping periods of continued use and abstinence.

It is likely that the alterations of the eating behavior would be a consequence, on the one hand, of voracious appetite that the patient described in the times of intoxication, provoking binges[14]; and in the second place, a progressive gastrointestinal deterioration that lead to intolerance to intake (dyspepsia, slow digestion, abdominal pain, constipation, etc.), vomiting, anorexia in periods of abstinence and important weight loss.

The psychopathological examination of the patient on admission, resembling a maniform syndrome, has al-

ready been described in the bibliography, as a consequence of cannabis abuse, in regards to circumstantial, logorrheic, fragmented speech, flight of ideas, with interruption in thought flow and cognitive alterations in attention, concentration, memory, and distortion of experience of time[15].

Within the clinical signs and symptoms derived, we describe a generalized epileptic episode that coincided with the decrease of the benzodiazepines. The abstinence itself of cannabis could have contributed to this fact, given the potential of this drug to produce electroencephalographic alterations in the intoxication and in the abstinence, its close relationship with the GABAergic system and its use as antiepileptic[16-19].

The treatment scheduled with lithium carbonate and olanzapine satisfactorily improved the signs and symptoms until the premorbid level. The possibility that some patients with affective symptomatology and substance abuse could really be attenuated bipolar or cyclothymic disorders has been described; in our case, this would not be unlikely if we also consider the family background[20]. On the other hand, treatment with lithium has been proposed to avoid the cannabis withdrawal syndrome mediated by the neuronal oxytocinergic activation in the hypothalamus and supraoptic nucleur, observed in experimental animals.

We believe that the signs and symptoms derived from cannabis dependence associated to an underlying psychiatric disorder can cause a polymorphus syndrome with clinical alterations in different areas. In this case, we have observed psychopathological, cognitive and vegetative disorders already described in the bibliography. Furthermore, the hypothesis is made on the relationship of this drug with some other manifestations, such as eating behavior disorders and its potentiality to influence the convulsive threshold. In addition, we have observed good results with lithium therapy, perhaps even with a preventive value. New and more extensive investigations would be necessary to define the direct effects of cannabis dependence and the potentiated or precipitated ones, in patients with constitutional predisposition to psychiatric disease.

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