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Beta blocker induced depression. A case report

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Introduction. Although association between beta blockers and depression has been reported since decades ago, the subject is still controversial. Most evidence supporting an association has been based on case reports or case series. Epidemiologic studies and randomized clinical trials have not generally supported this association. If this association exists, possible causes of disparity of findings may include methodological difficulties, and/or weak association.

Clinical case. We present a case of a 67 year old woman, without personal history of psychiatric illness or stress factors, who develops a depressive episode after initiating treatment with atenolol. The symptoms remitted rapidly when atenolol was discontinued, and an antidepressant was prescribed during a short period.

Conclusions. This case report suggests the existence of an association between a beta blocker, atenolol, and depression.

Key words:
Depression. Atenolol. Beta blockers. Drug-induced depression.

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Depresión inducida por betabloqueantes. A propósito de un caso

Introducción. Aunque desde hace décadas se ha señalado la asociación entre betabloqueantes y depresión, este tema permanece en controversia. La asociación ha sido señalada fundamentalmente en estudios de casos únicos o series de casos, mientras que los estudios epidemiológicos y ensayos clínicos aleatorizados han ofrecido escaso sustento a esta hipótesis. De existir tal asociación, las posibles causas de la disparidad de hallazgos serían las dificultades metodológicas, y/o que se trate de una asociación débil.

Caso clínico. Se presenta un caso clínico de una paciente de 67 años, sin antecedentes psiquiátricos ni factores estresantes, que desarrolla un episodio depresivo tras iniciar tratamiento con atenolol, el cual remite rápidamente tras la supresión del mismo y de iniciar tratamiento antidepresivo durante un corto período de tiempo.

Conclusiones. Este caso sugiere la existencia de asociación entre un betabloqueante, el atenolol, y la depresión.

Palabras clave:
Depresión. Atenolol. Betabloqueante. Depresión inducida por fármacos.

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INTRODUCTION

Although the probable association between propanol and depression has been mentioned since the 1960's, the association between taking beta blockers and depression is presently controversial[1-3].

Beta blockers produce a chronic blockage in beta adrenergic receptors, which leads to an increase in their density. It has been suggested that this could be the mechanism causing the probable association in the brain[4,1].

Most of the studies that have found an association are single cases or case series. Cross-sectional, observational and cases and controls studies have offered heterogeneous results. Randomized clinical trials with control group and double blind ones have offered scarce support to the hypothesis of the association[2].

The many methodological difficulties described in the following have probably been the main determining factor of the disparity of findings.

In regards to the design, the existing studies and the epidemiological ones in general lack statistical power to detect rare effects[8]. Retrospective studies on clinical histories have the disadvantage that they use indirect indicators of depression[2].

Another one of the fundamental aspects is the criterion used to define depression. No study that has used a clinical

diagnostic has found an association[2]. In general, the episodes described are mild-moderate, with atypical clinical characteristics[3].

On the other hand, beta blockers cause adverse effects that affect the CNS and somatic ones, such as decreased attention, apathy, muscle weakness, decreased energy, sleep disorders or sexual disorders. This has caused incorrect diagnoses[6] and thus less consistency in the associations found in some studies[2]. Due to these somatic adverse effects and the probable behavioral repercussion, it is recommended to focus on affective and cognitive symptoms[2].

Furthermore, there are confounding variables, such as the disease leading to the use of beta blocker, that may increase the risk of suffering depression (due to psychological, biological or social mechanisms)[3], or the concomitant use of other drugs[2,5].

On the other hand, it has been indicated that lipophilic beta blockers (for example, propanolol) may have a greater likelihood of causing depression than hydrophilics (for example, atenolol)[6]. In addition, cases of remission of major depression have been described after the substitution of propanolol with atenolol[7], although the global findings in this regards have been inconsistent[2]. The different doses have not been studied. Furthermore, there could be subgroups of patients that are more vulnerable to the effects of the beta blockers[2].

It is possible that the beta blockers are not a sufficient factor for the development of depression, but are a contributing factor in the multifactorial model of depression[3].

In regards to the time relationship between indication of beta blocker and onset of depression, one month or less has been given as the period having the greatest relevance for the maintenance of an association[2].

There are no clear recommendations based on scientific evidence on the clinical action when there is suspicion of drug induced depression[3]. Although there is no consistent evidence on an association, the studies also have not been able to demonstrate evidence against it. This, together with the fact that the possibility is plausible from the biological point of view orients to the fact that such association could exist[4].

CLINICAL CASE

A 67 year old married woman with 2 children. She lives with her husband who is retired.

She has no personal psychiatric background. As family background, a daughter under treatment for work conflictivity reactive depression. As somatic background, arterial hypertension treated with captopril 150 mg/day and atenolol 150 mg/day. Treatment with atenolol was added 3 months prior to the initial consultation. She is also being treated with pravastatin 20 mg/day due to hypercholesterolemia and acetylsalicylic acid 100 mg/day for prevention of cardiovascular accidents. Beginning 15 days ago, she initiated antidepressive treatment with sertraline 50 mg/day, indicated by her primary health care physician.

About two months prior to the initial consultation, and without apparent precipitating cause («I have no personal problems, nor with my family; I have a normal life»), the patient began to feel sad, labile, with daily outbreaks of crying, apathic, with partial anhedonia and decrease in usual activity, avoiding going out as she had usually done. During the day, she was generally in bed. She had mild anxiety and desires of death, although she had not had suicidal ideas. She ate more than usual. She had no sleep alterations, nor attention and concentration failures.

She also complained of muscle tension in shoulders and neck («It is difficult to hold up my head»). She relates its intensity chronologically with taking beta blocker. She also is pessimistic, thinking that she will never regain her previous state.

The psychopathological examination showed sad affect, with spontaneous crying, although she conserves affective resonance. Her speech is spontaneous, fluid and coherent and she has no psychotic symptoms. Her normal baseline personality is impressing.

Diagnostic impression was drug depression (ICD-10: F 06.32 Organic depressive disorder). Due to the absence of improvement and low dose of antidepressant, it was indicated to increase sertraline to 100 mg/day, and to recommend to her physician that he should substitute atenolol with another antihypertensive drug of another drug group. On the next day, her physician discontinued atenolol, initiating valsartan 160 mg/day in its place. Beginning in the following week, she began to experience improvement, being asymptomatic at two weeks. Given the clinical remission and diagnostic impression, in the one-month check-up it was indicated to withdraw antidepressive treatment progressively over one month. In the two check-up consultations, at 6 months and one year, the patient had no depressive symptoms and developed her previous activity and usual way of life.

In the initial consultation and in the check-ups at six months and one year, a complementary evaluation was conducted with the Spanish version of the Montgomery-Asbert depression scale[9]. The scores were 20, 0 and 0, respectively. Score of 20 according to the recommended cut-offs corresponds with the lower limit for «moderate depression». This scale was used since it affects emotional symptoms more and does not profoundly evaluate vegetative aspects, so that it is useful to evaluate patients with physical diseases who have somatic symptoms[10].

DISCUSSION

Although this is a single case, this clinical case has important aspects that suggest an association between a beta blocker, atenolol, and depression.

In the first place, the clinical picture is classified as «moderate depression» according to the scale used and fulfills ICD-10 criteria of «mild depressive episode.»

In the second place, the relationship between drug and depression seems clear, both by a very close time relationship between both in the period of greater relevance[2], as well as due to the absence of stress factors, pathological personality traits or personal psychiatric background. Furthermore, the grade in which the hypertensive disease may be a psychological risk factor for depression is clearly less than that of other diseases, such as previous Myocardial Infarction[2].

In the third place, the evolutive course of the episode, with remission of the symptoms two weeks after changing the drug and absence of relapses in the evaluation during one year, in spite of having withdrawn the antidepressive treatment early.

On the other hand, it is of interest that the depression began after the initiation of atenolol, a hydrophilic beta blocker. This suggests that this group of beta blocker is also a factor associated to depression.

As limitations, coinciding with the withdrawal of the beta blocker, the patient received antidepressive treatment. However, its early withdrawal, the other data and her subsequent course orient towards a causal relationship with atenolol.

On the other hand, it is possible that the muscle tension was compensatory due to the muscle weakness and that this appeared as an adverse effect of the high doses of beta blocker she received. This possible adverse effect seems to have had a behavioral and emotional repercussion in the patient. In any event, it alone does not seem to justify the combination of symptoms that patient had.

As a cause of the disparity of the findings, in addition to the methodological difficulties described, it is possible that the beta blockers are a risk factor for depression, but that its association is weak[1], or even that it only occurs in subgroups of patients[2], as for example in genetically more vulnerable persons[7], Thus, larger samples that allow for greater statistical power would be necessary.

It would be recommended that future studies have larger samples, control groups, that require a clinical diagnosis of depression according to ICD or DSM criteria, or standardized scales, with designs as randomized, double blind studies that make it possible to clarify this possible association, since it is a clinical question of great importance.

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