Enhanced suppression of cortisol after dexamethasone in borderline personality disorder. A pilot study

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Hipersupresión de cortisol con dexametasona en el trastorno límite de la personalidad. Un estudio piloto

Summary

Introduction. *Some studies have suggested the etiological role of childhood traumatic events in borderline personality disorder (BPD), involving the stress response mechanisms and the activity of hypothalamic-pituitary adrenal (HPA) axis. Recent preliminary results show that BPD, similar to that found in post-traumatic stress disorder (PSD), might have a hypersensitive response to the dexamethasone test.*

Methods. *Fourteen BPD patients, diagnosed according to DSM-IV criteria, without a major depressive episode or history of bipolar or psychotic disorder, were compared with 10 patients with other personality disorders (OPD). Plasma cortisol was measured at baseline and following an oral test with 0.25 mg of dexamethasone.*

Results. *Nine out of 14 (64%) BPD patients were cortisol suppressors in the test versus only 2 out of 10 (20%) patients with other personality disorders (chi square 4.6, degree factors [df] 18,* $p < 0.05$*). The degree of cortisol suppression was significantly greater for BPD patients (73%) than for patients with other personality disorder (34%). Baseline cortisol concentrations, although lower in BPD patients, were not significantly different among groups.*

Conclusions. *BPD could be associated with hypersensitivity of feedback mechanisms of the HPA axis similar to PSD, which suggests a possible role for traumatic experiences in the pathogenesis of the disorder.*

Key words: *Borderline personality disorder. Trauma. Cortisol. Hypothalamic-pituitary adrenal axis. Dexamethasone. Childhood abuse.*

Resumen

Introducción. *Algunos estudios han destacado la importancia de los acontecimientos traumáticos infantiles en la etiología del trastorno límite de la personalidad (TLP), sugiriendo que las alteraciones en los mecanismos de respuesta al estrés y en el funcionamiento del eje hipotálamo-hipofisario-adrenal (HHA) pudieran ser de importancia en la fisiopatología del trastorno límite de la personalidad. Algunos hallazgos preliminares sugieren que el TLP, al igual que el trastorno por estrés postraumático, presenta un estado de hiperreactividad del eje HHA con un aumento de la sensibilidad para la dexametasona.*

Métodos. *Catorce pacientes diagnosticados de TLP según criterios DSM-IV, sin episodio depresivo mayor actual ni historia de trastorno bipolar o psicótico, fueron comparados con 10 pacientes diagnosticados de otros trastornos de la personalidad. Se estudió el cortisol plasmático basal y tras un test oral con 0,25 mg de dexametasona.*

Resultados. *Nueve de 14 (64%) pacientes con TLP fueron supresores en la prueba frente a sólo dos de 10 (20%) pacientes con otros trastornos de la personalidad (chi cuadrado 4,6, df 18,* $p < 0,05$*). La reducción de las cifras de cortisol tras la prueba fue significativamente mayor (73%) en el grupo de TLP que en el grupo de otros trastornos de la personalidad (34%). Las concentraciones de cortisol basal, aunque menores en el grupo de TLP, no presentaron diferencias significativas.*

Conclusiones. *El TLP pudiera estar asociado a una hipersensibilidad de los mecanismos de retroinhibición del eje HHA al igual que el trastorno por estrés postraumático, lo que sugiere un posible papel de los acontecimientos traumáticos vitales en la patogénesis del trastorno.*

Palabras clave: *Trastorno límite de la personalidad. Trauma. Cortisol. Eje hipotalámo-hipofisario-adrenal. Dexametasona. Abuso infantil.*

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INTRODUCTION

A syndrome characterized by the presence of chronic symptoms of affective instability, impulsive behaviors, self-aggressions and feelings of emptiness that include high morbidity and mortality defines the term borderline personality disorder (BPD). These syndromes are con-

sidered as personality disorder in the DSM-IV, which implies that it is an abnormal personality pattern that becomes clear before 18 years and persists inflexibly until the adult age[1].

Although the term of borderline disorder has a psychoanalytic root in its origin, investigations in these last two decades have shown a series of biological findings that suggest the existence of physiopathological alterations in the disorder. The most consistent results verify the presence of abnormalities in the cerebral serotonergic activity, including a flattened response of prolactin after the administration of serotonin agonists[2], a decrease in platelet MAO activity[3] and a favorable response to treatment with SSRI[4]. Together with this, abnormalities have been described in the function of other neurotransmitters such as noradrenaline[5] and acethylcholine[6] that could be involved in some of the symptoms of the disorder.

As a result of the discovery that a high proportion of patients with borderline disorder have suffered intense or continuous childhood traumas, some studies have tried to relate this disorder with the post-traumatic stress disorders and with the alterations of the stress response mechanisms. Preliminary studies[7] have found that the response of the hypothalamic-pituitary adrenal axis (HPAA) in the borderline personality disorder is similar to the post-traumatic stress disorder (PST) in which, in both cases, there is excessive suppression of the cortisol suppression test with dexamethasone[8]. This would suggest a hypersensitivity of the feedback systems of the axis in the hypophyseal glucocorticoid receptors.

In order to verify the inhibitory hypersensitization of the response mechanism to stress in patients with borderline personality disorder, the present study investigates the suppressor response of cortisol, using a minimum stimulus of 0.25 mg of dexamethasone.

METHODS

Those patients who fulfilled diagnostic criteria of BPD were selected by structured interview from a sample of 32 patients referred by specialists to the Personality Disorders Unit of the hospital. A sample of 16 BPD was obtained from the diagnostic interview. The rest were diagnosed of other personality disorders (n = 10) and axis I disorders (n = 4). Of the personality disorders, three were diagnosed of histrionic personality disorder and seven were diagnosed of NOS or atypical personality disorders, since they fulfilled criteria of several disorders without completely fulfilling the criteria of any of them. Of the four patients diagnosed of axis I disorders, two were short recurrent depressive disorders and two other were eating behavior disorders. The patients selected as BPD had no associated diagnosis of bipolar disorder or psychotic disorder in their life history and did not present a major depressive episode or active disorder due to toxic dependence at the time of the study. The patients had not received drug psychiatric treatment in the last month and no occasional consumption of any drug was permitted the week prior to the time of the study. Two patients with BPD could not enter into the study as they did not achieve total abstinence from drugs. All the subjects of the sample were interviewed by a psychiatrist by the diagnostic interview of the DSM-IV for axes I and II (SCID I and II)[9].

The first day of the study, blood was drawn at 9 am to measure plasma cortisol. That same night, the patient took 0.25 mg of dexamethasone orally, and blood was drawn again the next day at 9 am to measure cortisol. Suppression criteria were considered to be the normal ones in the disease, that is, post-dexamethasone cortisol less than or equal to 5 µg/dl.

The statistical analysis included comparison of frequencies (Chi squared and Fisher's exact test) for the comparison of suppressor rates between the groups and the Student's «t» test for comparison of the cortisol values and of the intensity of its suppression between the groups. The statistical procedures were performed with the statistical package SPSS, version 10.0.0.

RESULTS

All the patients chosen gave their consent to undergo the suppression test with 0.25 mg of dexamethasone. No adverse effects occurred during the test or in the posterior days.

The baseline values of cortisol did not present significant differences between the BPD and the non-borderline PD (14.5 SD 8.8 vs 17.4 SD 4.2). The results of the dexamethasone test with 0.25 mgs indicate that 9 of the 14 patients diagnosed of borderline personality disorder were considered suppressors, that is, they presented a post-dexamethasone cortisol less than or equal to 5 µg/dl. Compared to them, in the group of non-borderline personality disorders, only two of the 10 patients (20%) were suppressors, there being a statistically significant difference between both groups (chi squared 4.608, df 1, $p = 0.032$). The magnitude of the cortisol suppression was significantly greater in the BPD group

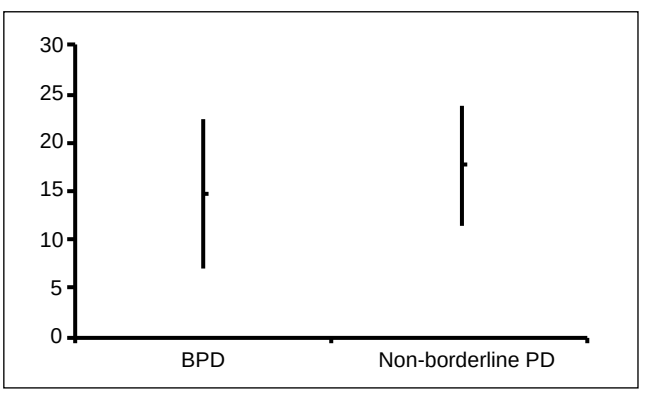

Figure 1. Plasma cortisol in borderline personality disorder (BPD) and in non-borderline personality disorder (non-borderline PD).

TABLE 1. Percentage os suppressors and non-suppressors

	Borderline personality disorder	*Non-borderline personality disorders*
Suppression of cortisol with 0.25 mg dexamethasone	9 (64 %)	2 (20 %)
No suppression of cortisol with 0.25 mg dexamethasone	5 (36 %)	8 (80 %)

(73.1 %) than in the non-borderline PD (40.3 %) ($t = 2.608$, df 18, $p = 0.018$). Cortisol suppression significantly correlated with the amount of borderline personality disorder criteria present in the patients ($r = 0.45$, $p > 0.05$).

DISCUSSION

The preliminary results of this study indicate, at first, a strong association between the BDP diagnosis and the enhanced suppression in the dexamethasone test. In this sense, it coincides with the scarce previous literature related with this subject. Grossman et al.[7] found an excessive suppression of cortisol in a group of BPD patients using a 0.5 mg dose of dexamethasone. The authors also found a significant hypocortisolism in their sample, as in the previous studies performed in patients with post-traumatic stress disorder (PSD)[8].

The idea of investigating the functioning of the hypothalamic-pituitary-adrenal axis (HPA axis) with low doses of dexamethasone in BDP comes from the finding of an enhanced suppression response in patients with PSD. In these patients, a suppression of cortisol response as well as a hypocortisolism has been described with 0.5 mg of dexamethasone[8]. The relationship between BPD and PSD is a consequence of the relationship between BPD and childhood trauma. Some studies have found a high prevalence of serious childhood abuse, both physical as well as sexual, in the background of the patients with BPD[10,11] and the seriousness of BPD could be related with the frequency of such abuses[12]. Some authors have dared to conceptualize the BPD as a form of complex PSD given the presence of dissociative symptoms, diffusion of identity, impulsiveness, somatization and affective instability[13]. This does not mean that all the patients with BPD who have experienced abuses in childhood present the classic PSD symptoms. However, the biological investigation of the same phenomena can give an idea of the relationship between both disorders as well as the role played by trauma in the neurobiology of BPD.

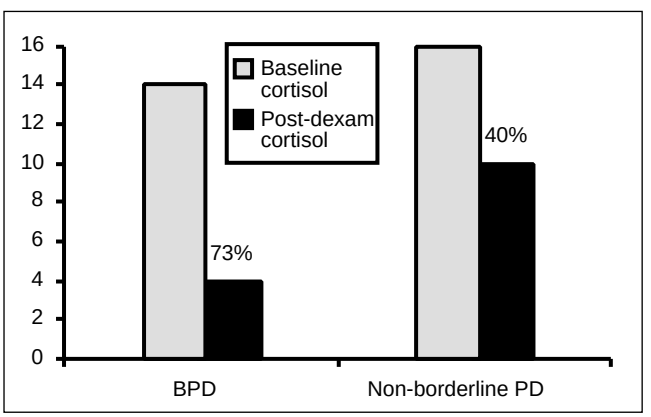

Figure 2. Percentage of plasma cortisol suppression in borderline personality disorder (BPD) and in non-borderline personality disorders (non-borderline PD).

The results of this pilot study suggest that there is some biological feature in the functioning of the HPA axis of the borderline disorders that causes an enhanced suppression response to dexamethasone. This hypothalamus-hypophyseal dysfunction has been supported by recent studies with a more complex study methodology of the HPA axis. Along this line, the ACTH response to the corticotropin-releasing hormone (CRH) and combined dexamethasone tests was found to be worse in a group of women with borderline personality disorder[14], also suggesting an excessive reactivity of the stress response.

This response indicates increased sensitivity for feedback and is probably related with an increase in the glucocorticoid receptor (GR) density, as the studies performed with PSD suggest. The use of analysis of cytosolic radioligands has made it possible to describe an increase in glucocorticoid receptor density in the plasma lymphocytes of patients with PSD[8], which is considered an indicator of the density of the GR in the CNS[15]. This increase in density of the lymphocytic GR has been suggested in pilot studies with BPD[7], but it has not been studied in the present study.

Significantly low values of cortisol have not been found in the BPD group in this study, on the contrary to previous studies with BPD and PSD. This could be due to the reduced sample of this pilot study, although it may also be due to the elevated standard deviation of the cortisol values in the BPD group. This elevated intragroup variation probably suggests a heterogeneity in the BPD that affects the mean concentrations of cortisol.

The alterations in the response mechanisms to stress and in the functioning of the HPA axis are consistent with the dysfunctions of the serotonin activity continuously described in the borderline personality disorders[2,3]. The serotonergic pathways constitute one of the principal modulators of the HPA axis. Thus, the alteration of the serotonergic activity associated with the impulsive behaviors of individuals with BPD could alter the modulation and reactivity of their HPA axis[15,16].

The study is limited by the reduced sample, from which it is not possible to draw very many conclusions. Furthermore, due to the lack of a healthy control group, the comparative group of other personality disorders is

a group that is not defined nosologically and that may be heterogeneous. In spite of this, it is deduced from the results that the hypersensitivity to the feedback of the HPA axis could be an element of the BPD physiopathology that should be investigated more extensively. Larger samples of patients and healthy controls are needed and it is necessary to define more homogeneous sub-samples of such a heterogeneous disorder as this. Thus, it should be studied if the enhanced suppression is associated to the BPD itself or to different subtypes or clinical dimensions of it and its relationship with the childhood trauma backgrounds and with the therapeutic evolution and response should also be studied. Finally, it is necessary to know if these alterations reflect a factor of disorder state or a factor of personality trait. Since the dexamethasone test is a simple test to perform, it could become, if the results are confirmed, a valuable indicator of aspects of the borderline personality disorder.

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