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The efficacy of lamotrigine in a resistant case of depersonalization disorder

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The individuals with depersonalization disorder suffer from a painful feeling that their body and mental experiences or the experiences of the environment seem become unreal, distant or mechanical. This phenomenon is often associated with other mental disorders, as in the case presented. Among the many psychoactive drugs studied, none of them has been shown to be the treatment of choice. Among those with which the best results are obtained are opioid receptor antagonists, the combination of selective serotonin reuptake inhibitors with lamotrigine and clorimipramine. We are presenting a resistant case that responded to lamotrigine.

Key words:

Lamotrigine, Treatment, Depersonalization syndrome, Depersonalization disorder.

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Eficacia de lamotrigina en un caso de trastorno de despersonalización resistente

Cuando sufre despersonalización, el individuo se queja espontáneamente de la vivencia de que su propia actividad mental, su cuerpo, su entorno o todos ellos, están cualitativamente transformados, de manera que se han vuelto irreales, lejanos o mecánicos. Este fenómeno está asociado frecuentemente con otros trastornos mentales, como en el caso que presentamos. Entre los muchos fármacos estudiados, ninguno ha mostrado ser el tratamiento de elección. Entre aquellos que han obtenido mejores resultados están los antagonistas de los receptores de los opioides, la combinación de inhibidores selectivos de la recaptación de la serotonina con lamotrigina, y la

clorimipramina. Presentamos un caso resistente que respondió a lamotrigina.

Palabras clave:

Lamotrigina, Tratamiento, Síndrome de despersonalización, Trastorno por despersonalización.

INTRODUCTION

Depersonalization disorder is classified within the **dissociative disorders** of the DSM-IV TR (300.6),¹ whereas the ICD-10 includes the **depersonalization - derealization disorder** (F48.1)² within the section of "other neurotic disorders," the criteria being similar to those of the DSM-IV TR.

It is indicated that the individual spontaneously complains that his or her mental activity, body, and surroundings are qualitatively transformed in such a way that they have become unreal, remote, or automatized (lacks of spontaneity). The subjects may feel that they no longer govern their own activity of thinking, imaging or remembers, that their movements and behavior are somehow foreign, that their body seems devitalized, dissociated from oneself or strange, that their surroundings seem to lack color and life, as if it were artificial or like being in a setting in which the persons act with predetermined roles. In some cases, they can feel that they are observing themselves from a distance or as if they were dead. The complaint of loss of feelings is the most frequent among the different phenomena. Generally, the disorder appears within the context of depressive diseases, phobic disorders and **obsessive-compulsive disorders**.²

The depersonalization syndrome is not uncommon in the general population, it having an estimated prevalence of 0.8 to 2%.^{3,4} Dissociative disorders are associated to worse functioning, with elevated comorbidity with other mental disorders, especially with **Personality Disorders** (58% cluster A, 68% cluster B, 37% cluster C).⁵ In a few cases, it may be the main symptom of the disorder, so that it would thus be a primary depersonalization disorder.⁶

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Regarding **treatment**, in a review of the existing literature, it can be seen that this syndrome is a condition with no definitive treatment and in which the conventional treatments, such as antidepressants or antipsychotics, have low efficacy. Among the multiple psychopharmaceuticals studied, none of them have been demonstrated to be the treatment of choice.⁴

Different studies have been underway in recent years with promising results as drugs are being found that could be useful in said syndrome. However, more rigorous studies are needed in this regards. For example, some studies have suggested that the **opiate receptor antagonists**, such as naltrexone and naloxone, are useful in at least one subgroup of patients.^{4,7,8} The **selective serotonin reuptake inhibitors** (SSRI), and above all, fluoxetine, were the drugs prescribed the most for the disorder until Simeón et al. (2004)⁹ conducted a clinical trial that showed that fluoxetine was not superior to the placebo. Similarly, the use of **clonazepam**, especially in combination with the SSRI antidepressants, seems to be beneficial in patients with elevated levels of baseline anxiety.⁴ One study with **chlomipramine** with a limited number of cases (8 in all), found a significant improvement in seven of them, however three had to leave the study due to adverse effects.¹⁰ Finally, although with practically no evidence, one case with good response to **methylphenidate**, was presented.⁶

We present this case due to the effective response to the introduction of **lamotrigine** on the key symptoms of depersonalization.

CLINICAL CASE

A 22-year old female patient without any personal background of interest, except alcohol consumption in the past. She was adopted at one month of life. She found out when she was 6 years old: *"it is something I don't understand; I would like to know them; to see if I look like them, nothing is mine, nothing is real, everyone has their parents, it is as if I do not belong to this life."* Her adoptive mother was under psychological treatment due to adaptive picture. Normal evolutive milestones. Intense separation anxiety during childhood, with school performance problems and she dropped out of school very early. No work activity in the last three years.

Her first contact with a psychiatrist was at 10 years due to **learning disabilities** and at 12 years due to **anxiety attack with phobic symptoms**, without beginning any treatment. At 15 years, she was referred to the Mental Health Service due to **anxious-depressive symptoms**. She began psychotherapy and psychopharmaceuticals treatment that she followed irregularly. During this, symptoms, with

fluctuations, characterized by **obsessions and rituals with predominant content of harm/disease and impulsion phobias**, isolated anxiety episodes and **episodes of derealization-depersonalization** stood out. Instability of identity, emotional vulnerability, emotional vulnerability. Lack of tolerance to frustration, marked impulsiveness and violent reactions. Self-harm gestures arising in relationship to feelings of emptiness. Intense dependence- independence conflict related with fears of overprotection- abandonment, which generates instability in her relationship with partners. Transient paranoid ideation. Elevated introspective capacity.

She was diagnosed of **Obsessive-Compulsive Disorder and borderline personality traits**. She has received group, individual and family therapy, training in relaxation techniques and psychopharmaceutical treatment with sertraline 100 mg day that she abandoned and then with citalopram 30 mg a day. Poor response to all of them.

The patient reported having the first symptoms at 11 years of age. She stated that during Religion class, the idea came to her that if she did not do something, her parents would die. *"I thought that my mother was going to die or that I was going to kill her, Now I am afraid that I am going to die."* *"I had to move an eraser so that nothing would happen, I don't know what."* At 11 years of age, while swimming in the pool with her cousins, she reports having a **sensation of unreality** *"it was as if I did not know them, after I began to think in what had happened "* *"playing football, the view changed ..."* She described having had transitory obsessions that changed over time. She currently is **concerned about contamination and diseases** *"I cannot drink from an open bottle"* *"I always order the same as my mother does in restaurants in case something happens, sometimes I think I have eaten a soul ..."* *"When I listen to someone speaking about a disease, I think that I have it, then I make sure asking my mother and I become calm."* She describes rituals *"when I brush my teeth, I have to provoke 3 retches"* *"I count the number of times I smell something, I always take a shower before going to sleep,"* while showing some indifference when talking about them. Her greatest concern is **not knowing what is happening to her** very often I feel like **I am in a parallel world, that the environment is rare I have been told that this is derealization** *"everything seems unreal, there are things I don't understand."* She expresses elevated anxiety when faced with uncertainty. She reports having inflicted **cuts on her arms** in order to *"feel something, although not pain," and to assure herself of the limits of her body."* She describes herself as changeable, impulsive, she speaks feeling sadness and unsatisfied with life.

During the evaluation, **fundamentally marked depersonalization and derealization symptoms** were observed. These had already appeared continuously in the

patient's biography, causing her intense anxiety and malaise and interfering in her daily life. She expressed her ideas in the following way: *"Everything is arranged for me ..for me to look for signs and answers"* **"everything is a pose and I cannot find the meaning."** She stated that she has always had these pseudophilosophical-magical concerns *"I feel unprotected from the world, everything seems too big, everything is too big for me, I feel alone and as if everything was a story, that I alone exist, that all the world sees me, I think that everything is made for me and this frightens me besides making me feel observed..."* *"I don't know what to believe or think, Everything seems so strange to me ..."* existence... how can it be? I don't understand, I don't understand anything" *"it is as if all the world was hiding something ..."* *"I am afraid of life, it is like unknown to me, like someone who does not want to get along with me and does not make an effort to get along with me. ...nothing makes me feel sure of myself because everything seems like a lie..."* *everyone is observing me, and who are all of them and where are they from ... well, I don't know ..."* "sometimes I feel afraid and I don't know about what, sometimes I feel very disturbed about everything ..." "I see everything different, this is close but I see it as far away...."

She was diagnosed of **Depersonalization Disorder**, as she met the diagnostic criteria for this disorder.^{1,2} Standing out among the psychometric instruments used most in depersonalization are the **Dissociative Experiences Scale**¹¹ (DES-II) and the Spanish version of the **Cambridge Depersonalization Scale** (CDS).^{12,13} The former measures the percentage of time the symptoms occur (from 0% to 100%) while the latter measures the frequency and duration of the depersonalization symptoms in the last 6 months. The patient obtained a direct score of **24.64** on the DES-II (scores >30% are associated to the diagnosis of dissociative disorder, and healthy patients and other psychiatric patients obtained scores of <20%.) and of **146** on the CDS, the proposed cutoff being 70. Both scores support the diagnosis. The diagnoses of Obsessive-Compulsive Disorder and Borderline Personality Disorder are maintained.

Her treatment was modified, replacing citalopram with sertraline (progressively increasing the dose to 200 mg per day) together with chlomipramine in doses of 125 mg per day. As no improvement was observed with said treatment, **lamotrigine** was also prescribed in combination until reaching a dose of 100 mg per day.

DISCUSSION AND CONCLUSIONS

This is the patient whose depersonalization symptoms have been maintained over time, negatively influencing treatment adherence since the patient comes inconsistently to the therapies, basing this on the intense anxiety causing

the symptoms, which, simultaneously, makes it impossible to use a psychological approach because of the incapacitating aspect of her picture.

After the establishment of lamotrigine, the patient began to verbalize a **significant improvement of the depersonalization picture**, the impulsiveness symptoms persisting. Improvement of the depersonalization symptoms contributed to better therapeutic compliance by the patient. She came to the Unit more consistently. This improvement made it possible to carry out focalized treatment of her Personality Disorder.

All the previous studies coincided showing that **lamotrigine** as a single agent is not effective in the treatment of depersonalization syndrome. However, these studies suggest that it could be effective in combination with antidepressants. The studies define response to the drug as being present when there is a 50% reduction in the CDS.^{3,4,14,15} Clinical trials suggest that the use of lamotrigine as combined treatment with SSRI is beneficial in a substantial number of patients with depersonalization syndrome.^{4,14} Thus, lamotrigine in monotherapy has not been shown to be effective in a study performed at 9 patients.¹⁵ On the other hand, the combination of lamotrigine plus SSRI was studied in a sample of 32 patients. Of these, 18 improved since they showed a reduction of $\geq 30\%$ on the depersonalization scales during follow-up.¹⁴ The most frequent and problematic adverse effect found was skin rash. There is evidence that the glutamatergic hyperactivity could be relevant in the neurobiology of depersonalization and that lamotrigine could be effective as it decreases the release of glutamate.¹⁵

Based on the results obtained in this case, we could consider that **lamotrigine may be a good anti-depersonalization drug**. We stress the need for a larger number of studies since the results obtained in the present case, together with those existing in the literature, are sufficiently positive to propose treatment with lamotrigine as a complementary treatment in depersonalization syndrome.

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