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Case Report

Depersonalization-Derealization Syndrome Induced By Duloxetine Discontinuation

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Abstract

Depersonalization (DP) and Derealization (DR) symptoms are experiences in which the individual feels a sense of unreality and detachment from him/herself and/or a sense of reality of the external world is lost. DP/DR symptoms may be related to the abruption of antidepressant Serotonin Selective Reuptake Inhibitors (SSRIs) like paroxetine. Serotonin and norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine and duloxetine have been reported to be associated with withdrawal syndromes. We describe a case report of Depersonalization Derealization Syndrome induced by duloxetine discontinuation.

Keywords: *Duloxetine; Depersonalization-Derealization Syndrome; SNRIs; ADS; SCI-DER*

Introduction

Depersonalization (DP) and Derealization (DR) symptoms are experiences in which the individual feels a sense of unreality and detachment from him/herself and/or a sense of reality of the external world is lost [1,2]. DP has been associated with different neurological (migraine, temporal epilepsy) and psychiatric condition (panic disorder, major depression, bipolar disorder, schizophrenia), substance use/abuse (tetrahydrocannabinol, ketamine, salvia divinorum, etc.) as well as may occur in healthy individuals, under condition of stress, fatigue, or sleep deprivation. DP/DR symptoms are part of oveall symtomatology of panic disorder. Moreover, DP/DR symptoms may be related to the abruption of antidepressant SSRIs like paroxetine [3] or SNRIs liker venlafaxine and duloxetine [4-6]. The aim of our case report is to describe Depersonalization Derealization Syndrome induced by duloxetine discontinuation.

Case Report

We hereby describe the case of G.D., a 33-year-old Caucasian Lady affected by depressive episode, panic disorder comorbid with somatopsychic and autopsychic depersonalization (DP), referred to our clinic for re-occurrence of severe DP and derealization (DR) symptoms after duloxetine abruption. She had a negative family history for mental disorder. There is no past history of substance use/abuse. A fist-level brain imagin (MRI), a neurological and somatic evaluation as well as Electroencephalogram EEG) were negative. At the age of 30-year-old the patient presented first depressive episode with sadness, asthenia, anergia, insomnia, and she experienced her first panic attack characterized by DR and DP symptoms, She was treated with duloxetine 60 mg/day for 6 months with good response and resolution of depressive episode, panic attack and DP/DR symptoms, as well as without particular side effects or adverse events. After this period of time the patients, without medical recommend, had suddenly abrupted the treatment with duloxetine, with emergence of dissociative symptoms. At the first outpatient visit the patient primarly presented with derealization "feels that the ouside world was strange and unreal", somatopsychic DP "feels that a part of body was disconnetted from the rest of the body" and autopsychic DP "feels that she was a stranger observer of herself", "feels that behaviour was out of control" without a presence of panic attack. She experienced muscle and head aches without other psychosomatic symptoms. Moreover, we assessed the DP and DR symptoms severity with: Depersonaliza-

tion Severity Scale (DSS) and the score was 12; Cambridge Depersonalization Scale (CDS) and the score was 83; Structured Clinical Interview for Depersonalization Deralization Spectrum (SCI-DER) and the score was 35. We initially reintroduced duloxetine 60 mg/day and alprazolam 1,5 mg/day, with a resolution of DP/DR symptoms (CDS total score was 10; DSS total score was 4; SCI-DER total score was 10) in six months without side effects. Therefore, after other six months, we decided to reduce slowly alprazolam and then duloxetine. After slowly abruption of duloxetine the patient present rapid new-onset of DP/DR symptoms.

Discussion

In our opinion this is the first report of Depersonalization Derealization Syndrome induced by duloxetine discontinuation. Serotonin and norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine [4] and duloxetine [5] have been reported to be associated with withdrawal syndromes [6]. In literature risk factors for antidepressant discontinuation syndrome (ADS) are duration of the treatment, and discontinuing agents with relatively short half-lives (paroxetine, escitalopram), but there aren't significant added risks with age, gender, or diagnosis [7]. Our case report underlie the possible appearance of DP/DR symptoms at the abruption of duloxetine, independently of the time of abruption. SNRIs like venlafaxine may be of some value in patient presentig DP/DR symptoms [8]. SNRIs have "two-and-a-half" mechanism: boosting serotonin and norepinephrine throughout the brain, and boosting dopamine in prefrontal cortex (but not in other DA projection areas) [9]. Although several hypotheses exist for antidepressant discontinuation syndrome (ADS) but remains unknow the definitive pathophysiologic explanation. Long-term use of SSRIs increases synaptic levels of serotonin through blockade of the serotonin reuptake pump, resulting in down-regulation of postsynaptic receptors [10]. This is believed to result in ADS directly or indirectly via downstream effects on other neurotransmitter systems (e.g., norepinephrine, dopamine, and g-aminobutyric acid) implicated in depressive and anxiety disorders [11]. In particular not only the modulation of cortico-limbic circuit (superior and medial frontal cortex) that have been found in the treatment response due to the activity on the serotonin and noradrenergic pathways but also duloxetine therapy that effectively increased frontal regional homogeneity and decreased temporal regional homogeneity [12-14], play a role in the appearance of DP/DR symptoms. So a possible underline mechanism of this particular withdrawal condition may probably connected to the synchronizing abilities of neuronal activation in a specific region (superior and medial frontal cortex) due to duloxetine and, the disapperarance of neural activation after duloxetine abruption [11] with the appearance of DP/DR symptoms. In literature right-sided and bilateral disease but more left-sided temporal lobe dysfunction, are suggested factors in the development of depersonalization [13,15], may be a risk factor for the development of depersonalization and may facilitate the development of a secondary psychiatric illness [15]. In the majority of cases in literature there is neurophysiological or radiological evidence of temporal lobe involvement [13,15,16], but there are some cases without this involvement [15,17].

Conclusion

Obviously, further research is warranted to replicate our clinical observation but, in general terms, controlled studies are needed to confirm this particular DP condition.

Bibliography

1. American Psychiatric Association. Diagnostic and statistical nmanual of mental disorders (4th ed-text revision). Washington DC: American Psychiatric Association: (2000).

2. American Psychiatric Association. Diagnostic and statistical nmanual of mental disorders (5th edition). Washington DC: American Psychiatric Association. (2013).

3. Bhanji NH., *et al*. "Persistent tardive rebound panic disorder, rebound anxiety and insomnia following paroxetine withdrawal: a review of rebound-withdrawal phenomena". *Canadian Journal of Clinical Pharmacology* 13.1 (2006):e69-e74.

4. Agelink MW., *et al.* "Withdrawal syndrome after discontinuation of venlafaxine". *Journal of Psychiatry* 154 (1997): 1473-1474.

5. Hou YC and Lai CH. "Long-term duloxetine withdrawal syndrome and management in a depressed patient". *The Journal of Neuropsychiatry & Clinical Neurosciences* 26.1 (2014): E4 *Erratum: The Journal of Neuropsychiatry and Clinical Neurosciences* 26.2 (2014):: 133.

6. Perahia DJ., *et al*. "Symptoms following abrupt discontinuation of duloxetine treatment in patients with major depressive disorder". *Journal of Affective Disorders* 89.1.3 (2014): 207-212.

7. Coupland NJ., *et al.* "Serotonin reuptake inhibitor withdrawal". *Journal of Clinical Psychopharmacology* 16 (1996): 356-362.

8. Preve M., *et al.* "Venlafaxine in somatopsychic and autopsychic depersonalization". *Progress in Neuro-Psychopharmacology & Biological Psychiatry* 35.8 (2011): 1808-1809.

9. Stahl SM. *Stahl's Essential Neuropsychopharmacology*. Cmbridge: Cambridge University Press (2013).

10. Warner CH., *et al.* "Antidepressant discontinuation syndrome". *American Family Physician* 74.3 (2006): 449-456.

11. Lane RM. "Withdrawal symptoms after discontinuation of selective serotonin reuptake inhibitors (SSRIs)". *Selective serotonin reuptake inhibitors and the risk of osseointegrated implant failure* 3.2 (1996): 75-83.

12. Lai CH and Wu YT. "Frontal regional homogeneity increased and temporal regional homogeneity decreased after remission of first-episode drug-naïve major depressive disorder with panic disorder patients under duloxetine therapy for 6 weeks". *Journal of Affective Disorders* 136.3 (2012): 453-458.

13. Mula M., *et al.* "The neurobiology and clinical significance of depersonalization in mood and anxiety disorders. A critical reappraisal". *Journal of Affective Disorders* 99 (2007): 91-99.

14. Qadir A and Haider N. "Duloxetine withdrawal seizure". *Psychiatry (Edgmont)* 3.9 (2006): 10.

15. Lambert MV., *et al.* "The spectrum of organic depersonalization: a review plus four new cases". *The Journal of Neuropsychiatry and Clinical Neurosciences* 14.2 (2002): 141-154.

16. Sierra M and Berrios GE. "Depersonalization: neurobiological perspectives". *Biological Psychiatry* 44.9 (1998): 898-908.

17. Deutsch SI., *et al.* "Temporal lobe epilepsy confused with panic disorder: implications for treatment". *Clinical Neuropharmacology* 32.3 (2009): 160-162.

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