# An interesting discontinuation syndrome with citalopram: A case report

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**BACKGROUND:** A group of psychological and psychical symptoms that exist after regular use of selective serotonin re-uptake inhibitor (SSRI) antidepressants are called "SSRI discontinuation syndrome". In this syndrome, medication is reduced or completely terminated in cases where some unwanted and distressing situations exist for the patient.
**CASE PRESENTATIONS:** We report a case in which a 33-year-old woman tries to end citalopram 20 mg after one year of regular use. This patient was faced with discontinuation problems after the first 1-3 days, and after 8-10 days.
**CONCLUSIONS:** In this report, due to the emergence of problems such as headache, dizziness, anxiety, sleep disturbances, nightmare, confusion, emotional instability, irritability, we present a case report of a patient who had to use to 20 mg tablet every 8-10 days for one year.
**Key Words:** Citalopram; Discontinuation syndrome; Antidepressants
**Abbreviations:** SSRIs: Selective Serotonin Re-uptake Inhibitors; DS: Discontinuation; MAOIs: Monoamine Oxidase Inhibitors; GABA: Gamma Amino Butyric Acid.

## INTRODUCTION

Because of the advantages such as efficacy, reliability, side effects, tolerability and easy use, selective serotonin re-uptake inhibitors (SSRIs) are the most prescribed antidepressants.It is used widely in the treatment of many psychiatric disorders, especially in depression and anxiety disorders [1].A group of symptoms after the cut-off of SSRIs is named "SSRI Discontinuation (DS)" or "Withdrawal Syndrome".These symptoms are generally dizziness, sensory disturbances (including paresthesia), sleep disturbances (including insomnia and intense dreams), agitation or anxiety, nausea and/or vomiting, tremor, confusion, sweating, headache, diarrhea, palpitations, emotional instability, irritability, and visual disturbances [1].This syndrome has been included in the literature for nearly 20 years [2].Various case reports and the placebo-controlled studies have been conducted on this issue [3,4].Also, DS has been reported to be related to citalopram [5]. Except SSRIs, this syndrome can be seen with monoamine oxidase inhibitors (MAOIs), tricyclics and SNRIs [6].

Generally, these symptoms are mild to moderate; however, in some patients, they may be severe in intensity. Even a delirium case has been reported due to cessation venlafaxine [7].They usually occur within the first few days of discontinuing treatment, but there have been very rare reports of such symptoms in patients who inadvertently missed a dose. Generally, these symptoms usually resolve within 2 weeks, though in some sub-jects they may be prolonged 2-3 months or more [1].

Here we explain an interesting DS associated with the citalopram.

## CASE PRESENTATION

Mrs. DA, 33-year-old woman applied to our outpatient clinic 2 years ago with the problem of depressive mood, anhedonia, anxiety, fatigue, sleep disturbances and attention deficit that continued for 6 months. The diagnosis was depression, and 20 mg/day citalopram was started. With this treatment, her symptoms remitted and the drug was used for one year. After this period, she stopped using it. Stopping the citalopram, she faced symptoms such as headache, dizziness, anxiety, sleep disturbances, nightmare, confusion, emotional instability, irritability, sense of shaking and insufficiency after 1-3 days, and then this period increased to 8-10 days. These symptoms disappeared in hours after taking one 20 mg citalopram tablet. So, she was unable to stop the usage, taking nearly every 8-10 days, for one year. She did not want to take this drug because of her pregnancy planning, but she could not deal with the symptoms, and she went on taking. She said, "as if the drug completes something in my brain", "it is a malady for me".

Previously, she had used sertraline 50 mg/day and fluoxetine 20 mg/day for 6 months separately because of depression and anxiety. She reported that these tablets were not as good as citalopram for her, but she added that she did not experience these symptoms after stopping them.

She did not use any medication regularly that could interact with citalopram. She had smoked 10 cigarettes a day for 10 years.

## DISCUSSION

Pathophysiology of SSRI DS is not clear exactly [8]. In fact, clinical investigation only focuses on the possible chemical and molecular mechanisms [9]. It is especially associated with SSRI half-life, with more reports of symptoms occurring in patients treated with paroxetine compared to other SSRIs [3,10-12]. However, paroxetine has a similar half-life with fluvoxamine, but the rate of DS for the fluvoxamine is 10 times lower [13]. Generally, the cause of this syndrome is stated as sudden lack of normal action of the drug in brain especially those related to serotonin. As the drug clearance from the body is fast, the discontinuation symptoms are seen intensely [4]. Some genetic factors can take a role on pathophysiology [8,14]. For instance, a recent clinical study indicated a possible involvement of the C (-1019) G polymorphism of the serotonin 5-HT1A receptor gene in the occurrence of par-oxetine DS [14]. Some authors reported that this syndrome was more common in patients with earlier onset of dysthymic disorder and was also more common in females. 10 However, some reports show that there is no difference between depression and anxiety disorders [12]. Citalopram's pharmacologic characteristics and *in vitro* and *in vivo* studies in animals suggest that it is a highly selective serotonin reuptake inhibitor that has no or very low affinity for 5-HT1A, 5-HT2A, dopamine D1 and D2, α1-, α2-, and β-adrenergic, histamine H1, gamma aminobutyric acid (GABA), muscarinic cholinergic and benzodiazepine receptors.

Citalopram is metabolized in the liver mostly by CYP2C19, but also by CYP3A4 and CYP2D6. Metabolites desmethylcitalopram and didesmethylcitalopram are significantly less active and their contribution to the overall action of citalopram is negligible. The half-life of citalopram is about 35 hours [15]. In our case, withdrawal symptoms were seen after 1-2 days at first; then after one year of usage, these symptoms began to appear after 8-10 days. In fact, the half-life of citalopram is 35 hours.

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Disappearance of the symptoms after taking the drug shows us the relation between the symptoms and citalopram. Here, the outstanding point is that the appearance of DS's time extension gets longer as the time passes; and the person used 20 mg citalopram after 8-10 days to stop the symptoms. Patient has to continue to use the drug unwillingly to get rid of the withdrawal symptoms.

## CONCLUSION

We can explain these cases with slow metabolism in the liver cytochrome enzyme system. CYP2C19 genetic polymorphism can change the half-life of citalopram and its metabolites, citalopram terminal half-life can get longer to 95 hours (3.96 days) in which individuals have PMDe/PMMe genotype and phenotype of CYP2C19. This situation is approximately two per thousand in a European or Asian population and five per thousand in Africans [15].

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