

Pruritus associated with abrupt mirtazapine discontinuation: Single case report

Brittany Spitznogle, PharmD, BCPS¹
Felicia Gerfin, PharmD, BCPP²

How to cite: Spitznogle B, Gerfin F. Pruritus associated with abrupt mirtazapine discontinuation: Single case report. *Ment Health Clin* [Internet]. 2019;9(6):401-3. DOI: 10.9740/mhc.2019.11.401.

Abstract

It is well known that antidepressants have the potential to cause withdrawal symptoms upon abrupt discontinuation. At the time of this case report, no literature has identified intense, body-wide pruritus as a result of abrupt mirtazapine discontinuation. However, there is literature to suggest that mirtazapine may be used as a treatment for pruritus at doses as low as 15 mg/d due to its high affinity for central and peripheral histamine H₁ receptors. Considering this information, it is suspected that the abrupt discontinuation of mirtazapine in the following patient case resulted in pruritus due to the reversal of antagonism at histamine receptors.

Keywords: mirtazapine, pruritus, antidepressants

¹ PGY2 Psychiatric Pharmacy Resident, Veteran Affairs Western New York Healthcare System, Buffalo, New York, ORCID: <https://orcid.org/0000-0001-9753-0187>; ² (Corresponding author) Mental Health Clinical Pharmacy Specialist, Veteran Affairs Western New York Healthcare System, Buffalo, New York, felicia.strom@va.gov, ORCID: <https://orcid.org/0000-0002-8652-9946>

Disclosures: None.

Background

Mirtazapine is classified as a tetracyclic antidepressant, which mechanistically acts as a central presynaptic alpha₂-adrenergic antagonist, resulting in an increased release of norepinephrine and serotonin.¹ Of significance, mirtazapine is also a potent antagonist of histamine H₁ receptors and serotonin 5-HT₂ and 5-HT₃ receptors as well as a moderate antagonist of peripheral alpha₁-adrenergic and muscarinic receptors.¹

It is well known that antidepressants have the potential to cause withdrawal symptoms upon abrupt discontinuation, especially when treatment duration has lasted for more than 3 weeks. Withdrawal symptoms can be somatic (ie, nausea, vomiting, diarrhea, headaches, dizziness, tremors, balance difficulties, sleep disturbances) and/or psycholog-

ical (ie, anxiety, irritability, mood lability, confusion, depersonalization, concentration difficulties).² At the time of this case report, no literature has identified intense, body-wide pruritus as a result of abrupt mirtazapine discontinuation. However, there is literature to suggest that mirtazapine may be used as a treatment for pruritus at doses as low as 15 mg/d due to its high affinity for central and peripheral histamine H₁ receptors.³ Considering this information, it is suspected that the abrupt discontinuation of mirtazapine in the following patient case resulted in pruritus due to the reversal of antagonism at histamine receptors.

Case

The patient is a 46-year-old, overweight white male with a past medical history significant for anxiety, migraines, and chronic pain. He has a documented allergy to DayQuil™ (urticarial, Procter & Gamble, Cincinnati, OH). He was referred by his psychologist and primary care provider to an outpatient, pharmacist-run mental health clinic for medication management of depression and anxiety. At his initial clinic appointment, the patient reported the following symptoms: poor appetite with 6.8-kg weight loss over 8-week period, insomnia, anergia, anhedonia,

irritability, feelings of guilt, difficulty concentrating, racing thoughts, restlessness, uncontrollable worry, avoidance, and isolation. Initial patient health questionnaire 9-item score was 20, indicating severe depression; initial generalized anxiety disorder 7-item score was 16, indicating severe anxiety. The patient denied history of any other mental health conditions or diagnoses and had never taken a psychotropic medication in the past. He denied history of substance abuse and reported drinking alcohol socially, on occasion, not in excess. At that time, the patient was only taking vitamin D supplementation and denied taking any prescription or over-the-counter medications. Following his initial clinic visit, patient tried and failed treatment with sertraline (titrated up to 50 mg daily; total treatment duration of 12 weeks) due to intolerable adverse effects, including nausea, constipation, and sexual dysfunction. Sertraline was tapered to discontinuation over a 2-week period without any notable withdrawal symptoms. Given the patient's primary complaints of depressed mood, insomnia, and poor appetite, he was then started on mirtazapine 7.5 mg at bedtime. He was instructed to increase the dose to 15 mg nightly after 2 weeks if tolerated. The patient reported titrating dose as instructed but self-discontinued mirtazapine 15 mg after approximately 2 weeks at that dose (4 weeks after starting mirtazapine) due to excessive daytime somnolence. The patient contacted clinic 1 week after self-discontinuation of mirtazapine, complaining of lower extremity itching that started within 48 hours of abruptly stopping the mirtazapine. He denied experiencing any other possible withdrawal effects. Over the following 2 weeks, pruritus spread from lower extremities to diffuse, body-wide pruritus; no urticaria, xeroderma, or lesions. The patient adamantly denied any changes to toiletry products, detergents, other medications, or diet. He was started on loratadine 10 mg daily for pruritus, which had modest effect. As of 5 months after mirtazapine discontinuation, pruritus had continued but to a much lesser extent. The patient was no longer using an antihistamine to control pruritus. Additionally, shortly after the time the mirtazapine was discontinued, the patient was started on escitalopram 10 mg daily, which he continued to tolerate well with adequate mood symptom control as of 5 months from initiation (time of case report).

Discussion

Withdrawal symptoms as a result of abrupt mirtazapine discontinuation and dose tapering have been reported in several case studies with mirtazapine doses ranging from 15 to 60 mg/d for a minimum treatment duration of 4 weeks.⁴ Most frequently reported withdrawal symptoms include dizziness, nausea, vomiting, paresthesia, insomnia, reduced need to sleep, anxiety, panic attacks, restlessness,

irritability, elated mood, pressure of speech, and increased energy.⁴ In this case, the patient took mirtazapine for a total of 4 weeks at a maximum dose of 15 mg/d. Uniquely, upon abrupt discontinuation, he experienced pruritus initially localized to his lower extremities, which then led to diffuse, body-wide pruritus. Given that this report is based on a single case, there are limitations that exist. In this report, the pruritus was subjectively reported by the patient to multiple providers, mostly via telephone visits; no objective findings were recorded. Additionally, the pruritus may have been a symptom of a dermatological, neurological, or systemic disease; however, prior medical evaluation and laboratory data (complete blood count, hemoglobin A_{1c}, lipid panel, thyroid function test, and comprehensive metabolic panel obtained 2 months prior to mirtazapine initiation) were within normal limits (patient was not evaluated for iron deficiency or malignancy due to normal laboratory studies and otherwise normal physical examination). It is also possible that the patient experienced psychogenic itch. According to Misery et al,⁵ patients who scored higher on depression measures reported higher degrees of pruritus when compared to those who were not depressed.

Of note, there have been published case reports of second-generation antihistamines, which are highly selective for the H₁ receptor, causing unbearable pruritus within 1 to 3 days after medication discontinuation.⁶ The patients described pruritus without rash or urticaria, and in some cases, pruritus lasted for several weeks.⁶ Although there are informal patient forums that identify "intense itching" as a result of mirtazapine discontinuation, this is the first peer-reviewed report of such a case.

Because pruritus is a subjective sensation and diagnosis is based solely on patient-reported symptoms, it is difficult to identify 1 causative agent. Considering that, prior to treatment, this patient had no complaints of pruritus and onset was reported within 48 hours of stopping mirtazapine, abrupt medication discontinuation may be considered a possible cause as indicated by the Naranjo adverse drug reaction probability scale (score of 3). Given mirtazapine's antagonistic effects on central and peripheral histamine H₁ receptors, it may be hypothesized that the withdrawal effect of pruritus resulted from the reversal of histamine receptor antagonism.^{1,3} As loratadine is selective for peripheral H₁ receptors, this may also explain why loratadine was only modestly efficacious for relief of the patient's pruritus.⁷

Conclusion

Withdrawal symptoms commonly occur after antidepressant discontinuation; however, there is limited available literature regarding withdrawal effects specific to mirta-

zapine outside of several case studies. Pruritus following mirtazapine discontinuation is a possible withdrawal symptom that has not been noted in previous reports. This unique case encourages health care professionals to be aware this reaction may occur and to consider tapering doses whenever possible.

References

1. Remeron (mirtazapine) [prescribing information]. Whitehouse Station (NJ): Merck Sharp & Dohme Corp; 2018.
2. Schatzberg AF, Haddad P, Kaplan EM, Lejoyeux M, Rosenbaum JF, Young AH, et al. Possible biological mechanisms of the serotonin reuptake inhibitor discontinuation syndrome. Discontinuation Consensus Panel. *J Clin Psychiatry*. 1997;58 Suppl 7:23-7. PubMed PMID: [9219490](#).
3. Kaur R, Sinha VR. Antidepressants as antipruritic agents: a review. *Eur Neuropsychopharmacol*. 2018;28(3):341-52. DOI: [10.1016/j.euroneuro.2018.01.007](#). PubMed PMID: [29456150](#).
4. Cosci F. Withdrawal symptoms after discontinuation of a noradrenergic and specific serotonergic antidepressant: a case report and review of the literature. *Person Med Psych*. 2016;1-2(2017):81-4. DOI: [10.1016/j.pmip.2016.11.001](#).
5. Misery L, Dutray S, Chastaing M, Schollhammer M, Consoli SG, Consoli SM. Psychogenic itch. *Transl Psychiatry*. 2018;8(1):52. DOI: [10.1038/s41398-018-0097-7](#). PubMed PMID: [29491364](#).
6. Ekhart C, van der Horst P, van Hunsel F. Unbearable pruritus after withdrawal of (Levo)cetirizine. *Drug Saf Case Rep*. 2016;3(1):16. DOI: [10.1007/s40800-016-0041-9](#). PubMed PMID: [27889900](#).
7. Loratadine. Lexi-Drugs. Lexicomp®. Riverwoods (IL): Wolters Kluwer Health, Inc [cited 2019 Aug 19]. Available from: <http://online.lexi.com>