Suicidality Emerging From Rapid Venlafaxine Discontinuation:

A Challenge–Dechallenge–Rechallenge Case Report

Milutin Kostic, MD, PhD; Martin Plöderl, PhD; Michael Hengartner, PhD; and Jelena Buzejic, MD

There is ongoing controversy about suicide risk associated with antidepressant use,[1,2] but much less is known about suicide risk related to discontinuation of antidepressants. Antidepressant withdrawal syndrome (AWS)[3] can be a burdensome syndrome, with well-known symptoms.[4,5] One possible explanation for this condition is the oppositional model of tolerance.[6]

Some study results are suggestive that suicidality can be part of AWS,[7,8] although the data are still inconclusive. We are aware of only 3 case reports of suicidal behavior with antidepressant discontinuation, which occurred after discontinuation of paroxetine,[9] venlafaxine,[10] and escitalopram.[11]

In this case report, we present a patient without a history of suicidal crisis who, in the span of 6 months, experienced 2 suicidal crises, each occurring directly following rapid discontinuation of venlafaxine. Both crises subsided with reintroduction of the drug.

Case Report

The patient was a 30-year-old woman, single, without children, and employed. She consulted our institution's outpatient service in September 2022, 8 days after she attempted suicide by drug overdose. She described the suicide attempt as feeling "as if I didn't do it; I cannot understand what got hold of me."

In 2020 she had started self-medicating her depressive and anxiety symptoms with marijuana. In 2021 she consulted a psychiatrist, who diagnosed major depressive disorder with intense symptoms of anxiety and borderline personality disorder, and she was started on venlafaxine, quetiapine, lorazepam, and, subsequently, lamotrigine. She immediately stopped any further use of marijuana. She had no past or current somatic comorbidities.

The first major deterioration occurred in April 2022 and coincided with the patient's abrupt discontinuation of venlafaxine (while she continued taking all other prescriptions) because of a shortage of it at the market. For 3 consecutive days she did not take venlafaxine, down from the prescribed 225 mg daily dose at the time.

For the first 2 days after discontinuation of venlafaxine, she felt unchanged. On the third day, after an argument with a family member, a feeling of "not being protected from depression" suddenly overwhelmed her, together with a feeling of inadequacy. She became upset with suicidal thoughts and wishes "to disappear since there was no place for her in this world, no peace of her own." This was the first time in her life she had experienced suicidality. That evening she managed to find venlafaxine and on the following morning was free of her previous complaints.

She continued with her prescribed medication until September 2022. She was stable, but her physical weight increased by 20 kg. Her psychiatrist started adjusting her antidepressant medication by tapering venlafaxine in order to switch to duloxetine. The plan was to taper 225 mg of venlafaxine within 7 days: 150 mg per day in the first 3 days, 75 mg in the next 3 days, and stopping venlafaxine on day 7. In addition to the antidepressant, she was also taking 75 mg quetiapine per day, 200 mg lamotrigine per day, and 3.75 mg lorazepam per day.

On the first day of the gradual dose reduction of venlafaxine, her mood lowered, with less interest in everyday activities and listlessness. Suicidal ideas emerged on day 7, the day she completely tapered venlafaxine. She described a feeling that "suddenly everything collapsed, like there was nothing left, no way out, only blackness, and I wanted to be gone." She began searching the internet for the most effective ways to kill herself. She wrote a farewell letter to her mother. That evening she took a substantial amount of medication—75 mg lorazepam and 1,500 mg quetiapine—after which she fell asleep. The next day, she woke up and felt very relieved at having survived. She contacted her psychiatrist, and they agreed to return to a venlafaxine 225 mg per day therapeutic protocol, which she started on the same day.

After 1 year, the patient is stable without suicidal ideations. She is no longer on treatment with lamotrigine and quetiapine and is now on a very slow taper of lorazepam and venlafaxine (current dose, 112.5 mg daily). With slow taper, new suicidal episodes were not reported.

Discussion

This case report adds to the small body of evidence suggesting that antidepressant discontinuation may also carry the risk of increased suicide risk in addition to AWS, which is increasingly acknowledged as a frequent and burdensome condition of varying severity.[3,12] A few other case reports have indicated that suicidal behavior may emerge after

discontinuation of antidepressants,[9–11] but to our knowledge, our case report is the first that fits a challenge–dechallenge–rechallenge paradigm. That is, suicidality was never an issue for the patient (baseline) but emerged after a first withdrawal of venlafaxine (challenge), immediately disappeared after taking venlafaxine again (dechallenge), and reemerged after the second withdrawal (rechallenge). This supports the assumption that abrupt or rapid cessation of venlafaxine was causally related to acute suicidal behavior. The experience of our patient is also in line with the literature, which classified venlafaxine among the antidepressants with the strongest AWS[13] and as one of the drugs associated with the greatest risk for suicide after discontinuation.[7]

Article Information

Published Online: January 22, 2024. https://doi.org/10.4088/JCP.23cr14930

J Clin Psychiatry 2024;85(1):23cr14930

Submitted: May 3, 2023; accepted October 24, 2023.

To Cite: Kostic M, Plöderl M, Hengartner M, et al. Suicidality emerging from rapid venlafaxine discontinuation: a challenge-dechallenge-rechallenge case report. *J Clin Psychiatry.* 2024;85(0):23cr14930.

Author Affiliations: Institute of Mental Health, Belgrade, Serbia (Kostic, Buzejic); Faculty of Medicine, University of Belgrade, Serbia (Kostic); University Clinic of Psychiatry, Psychotherapy, and Psychosomatics; Paracelsus Medical University, Salzburg, Austria (Plöderl); Zurich University of Applied Sciences (ZHAW), Zurich, Switzerland (Buzejic).

Corresponding Author: Milutin Kostic, MD, Institute of Mental Health, Kasaninova 3, Belgrade, Select 11000 Serbia (milutin.kostic@imh.org.rs).

Relevant Financial Relationships: None.

Funding/Support: None.

ORCID: Milutin Kostic: https://orcid.org/0000-0001-6986-303X; Michael Hengartner: https://orcid.org//0000-0002-2956-2969

Patient Consent: Consent was received from the patient to publish the report, and information has been de-identified to protect anonymity.

References

1. Hengartner MP, Plöderl M. Newer-generation antidepressants and suicide risk in randomized controlled trials: a re-analysis of the FDA database. *Psychother Psychosom.* 2019;88(4):247–248.
2. Hayes JF, Lewis G, Lewis G. Newer-generation antidepressants and suicide risk. *Psychother Psychosom.* 2019;88(6):371–372.
3. Massabki I, Abi-Jaoude E. Selective serotonin reuptake inhibitor 'discontinuation syndrome' or withdrawal. *Br J Psychiatry.* 2021;218(3):168–171.
4. Warner CH, Bobo W, Warner C, et al. Antidepressant discontinuation syndrome. *Am Fam Physician.* 2006;74(3):449–456.
5. Fava GA, Benasi G, Lucente M, et al. Withdrawal symptoms after serotonin-noradrenaline reuptake inhibitor discontinuation: systematic review. *Psychother Psychosom.* 2018;87(4):195–203.
6. Fava GA. May antidepressant drugs worsen the conditions they are supposed to treat? the clinical foundations of the oppositional model of tolerance. *Ther Adv Psychopharmacol.* 2020;10:2045125320970325.
7. Coupland C, Hill T, Morriss R, et al. Antidepressant use and risk of suicide and attempted suicide or self harm in people aged 20 to 64: cohort study using a primary care database. *BMJ.* 2015;350(feb18 32):h517.
8. Valuck RJ, Orton HD, Libby AM. Antidepressant discontinuation and risk of suicide attempt: a retrospective, nested case-control study. *J Clin Psychiatry.* 2009;70(8):1069–1077.
9. Bloch M, Stager SV, Braun AR, et al. Severe psychiatric symptoms associated with paroxetine withdrawal. *Lancet.* 1995;346(8966):57.
10. Stone TE, Swanson C, Feldman MD. Venlafaxine discontinuation syndrome and suicidal ideation: a case series. *J Clin Psychopharmacol.* 2007;27(1):94–95.
11. Waldvogel N, Akira A. Antidepressant discontinuation syndrome resulting in a suicide attempt: a case report. *J Clin Psychiatry.* 2022;83(6):22cr14562.
12. Hengartner MP, Davies J, Read J. Antidepressant withdrawal: the tide is finally turning. *Epidemiol Psychiatr Sci.* 2019;29:e52.
13. Horowitz MA, Framer A, Hengartner MP, et al. Estimating risk of antidepressant withdrawal from a review of published data. *CNS Drugs.* 2023;37(2):143–157.