

The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided. The patient described in this column is a composite with characteristics of several real patients.

Recognition and management of antidepressant discontinuation syndrome

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A 22-year-old woman presented to the emergency department during the flu season with flu-like symptoms that had persisted for 3 days and reported intense anxiety and sadness, dizziness with movement, insomnia, nausea, periodic “electric shock” sensations and seeing flashes of light. A week prior, she had stopped taking 150 mg venlafaxine. Her symptoms resolved when venlafaxine was reintroduced. It was then tapered over 4 weeks and switched to 5 mg vortioxetine. One year following remission, vortioxetine was discontinued over 2 weeks without onset of discontinuation symptoms.

Antidepressant discontinuation syndrome (ADDS) is a new entity in DSM-5 in the category of medication-induced movement disorders and other adverse effects of medication.¹ Symptoms generally begin 2–4 days after abrupt discontinuation of antidepressants taken continuously for at least 1 month.¹ ADDS is often seen during taper or after missed doses with short half-life agents, such as paroxetine and venlafaxine.^{2–4}

Up to 70% of patients prescribed antidepressants occasionally skip doses.⁵ For diagnosis, ADDS symptoms should not be present before dose reduction and should not be better explained by another psychiatric disorder.¹ Symptoms that fit the FINISH mnemonic (flu-like symptoms, insomnia, nausea, imbalance, sensory disturbances, hyperarousal), can be experienced by up to 40% of patients upon abrupt antidepressant discontinuation.^{2,6–8} The Discontinuation Emergent Signs and Symptoms Scale (DESS) can be used to quantify symptoms.² ADDS can also include worsening symptoms of the original illness and can be mis-

taken for a relapse.^{1,2} In addition, misdiagnosing the physical symptoms of ADDS can lead to unnecessary medical and laboratory workup.⁹

Patients must be informed of ADDS when starting treatment and of the differences between ADDS and withdrawal associated with addiction.¹⁰ Although withdrawal symptoms and ADDS could have neurobiological similarities, such as a “receptor rebound” phenomenon upon sudden discontinuation,^{2,7,11,12} there are important differences. Unlike antidepressants, use of drugs of abuse include reinforcing/euphoric effects of the drug and associated drug-seeking behaviour.¹ Symptoms of ADDS are associated with short half-life agents, and symptoms are usually mild and short-lived.¹

Risk for ADDS is highest with short half-life agents, high doses and rapid taper.^{1,10} The risk also appears to be higher for those who have taken antidepressants for 8 weeks or longer,¹³ experience anxiety symptoms when starting a selective serotonin reuptake inhibitor (SSRI), are taking other centrally acting medications (e.g., antipsychotics, antihypertensives, antihistamines), are children/adolescents, or have a history of ADDS episodes.^{2,10} ADDS has been reported with all monoamine oxidase inhibitors (MAOIs) and commonly presents with agitation, movement disorders, and sleep and speech problems.¹⁰ ADDS has most commonly been reported for amitriptyline and imipramine among tricyclic antidepressants (TCAs) and paroxetine and venlafaxine among SSRIs.¹⁰ Neonatal venlafaxine discontinuation syndrome upon maternal venlafaxine discontinuation before childbirth has been reported.¹⁴ ADDS with TCAs and SSRIs commonly presents with flu-like symptoms, insomnia and vivid dreams, and with additional “shock-like” sensations with SSRIs.¹⁰ Movement disorders have occasionally been reported with both TCAs and SSRIs.¹⁰ Symptoms of ADDS

have not been reported with abrupt discontinuation of agomelatine^{10,15,16} or vortioxetine.^{10,17}

Prevention of ADDS, particularly for short half-life agents, includes a gradual discontinuation over 4 weeks with a slow rate of taper at the end,^{2,6,7} and a longer taper for those on MAOIs. Importantly, patients need reassurance that ADDS is common, self-limited and often mild.² If symptoms are severe, restarting the original antidepressant or another antidepressant with a long half-life in the same class can be followed by gradual taper.² When ADDS symptoms persist despite slow taper,¹⁸ abrupt withdrawal options could be considered, particularly when patients prefer a short period of intense symptoms to a longer period of mild symptoms associated with a gradual taper.¹⁰ Importantly, there is limited evidence on ADDS management; some studies suggest benefits with fluoxetine for ADDS associated with venlafaxine¹⁹ or clomipramine²⁰ and anticholinergic agents in TCA withdrawal.²¹ Although one recommendation is to switch patients to long-acting antidepressants like fluoxetine before withdrawal of venlafaxine, there are no controlled studies to identify the best option (taper v. substitution).²²

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