The dark side of SSRIs

selective serotonin reuptake inhibitors

Learn how to recognize medical and surgical complications associated with these commonly used antidepressants. By Theresa J. Inott, RN, MSN

FORTY-EIGHT HOURS AFTER UNDERGOING transurethral resection of the prostate (TURP), Peter Althouse, 58, develops nausea and intermittent vomiting, followed by chills, dizziness, and tremors. He's anxious and irritable.

Concerned that Mr. Althouse is exhibiting signs and symptoms of a serious postoperative complication, you obtain blood specimens and send them to the lab. His complete metabolic profile and complete blood cell count are within normal limits, and additional diagnostic testing rules out a bacterial infection or respiratory complication.

Mr. Althouse has no history of alcohol or drug abuse. Two years earlier, however, he'd been prescribed paroxetine for major depressive disorder. Now when you question him further, he says he stopped taking the drug the day before his admission because he was told not to take anything by mouth after midnight.

Based on his clinical condition and history of abruptly stopping a selective serotonin reuptake inhibitor (SSRI), you suspect that Mr. Althouse is suffering from SSRI discontinuation syndrome.

More than 20 million American adults experience some form of a mood disorder. The most common drugs prescribed for these conditions are SSRIs, and many patients who take these medications, like Mr. Althouse, are admitted to medical or surgical settings for other conditions. In this article, I'll describe complications of SSRIs that you might see in a patient like Mr. Althouse, and how to intervene.
SSRI discontinuation syndrome

The most common complication of SSRIs in hospitalized patients is antidepressant discontinuation syndrome. Patients are at risk if they stop taking their prescribed SSRI, if the antidepressant is discontinued by their healthcare provider without tapering, or if they're made N.P.O.

SSRI discontinuation syndrome typically occurs 24 to 72 hours after the patient stops taking an SSRI. Although not life-threatening, it can cause distressing physical and emotional symptoms that can be mistaken for complications of an illness, procedure, or other medication. Signs and symptoms appear abruptly and last for 1 to 2 weeks if not identified and treated.

The most common signs and symptoms fall into four categories:
- gastrointestinal (GI), including nausea, vomiting, diarrhea, and indigestion
- neurologic, such as light-headedness, dizziness, vertigo, loss of balance, headache, tremors, involuntary muscle twitching, numbness, and electric-shock sensations
- somatic, including chills, rhinorrhea, fatigue, and lethargy that may mimic the flu
- psychological, such as anxiety, irritability, agitation, depressed or labile mood, hypomania, insomnia, and vivid dreams or nightmares.

The severity of signs and symptoms depends on how long the patient was taking the SSRI, the dosage, and the specific drug's half-life. For example, patients who've taken an SSRI for less than 6 weeks are less likely to develop signs and symptoms of SSRI discontinuation syndrome than patients whose brains have adapted over time to the medication. Also, patients taking higher doses of an SSRI are more likely to have discontinuation symptoms than those taking lower doses.

Medication half-life also affects the severity of serotonin reuptake discontinuation syndrome. The SSRIs with short half-lives, such as paroxetine, are more commonly prescribed because they typically cause less frequent and less severe adverse reactions. However, because of this short half-life, a patient is more likely to develop discontinuation symptoms if he misses a dose or stops taking the medication.

Because serotonin norepinephrine reuptake inhibitors (SNRIs) have similar mechanisms of action to SSRIs, patients who abruptly discontinue SNRIs also can develop discontinuation syndrome.

Most patients with mild signs and symptoms need only an explanation and reassurance. Moderate signs and symptoms can be treated symptomatically, for example, by administering a short course of medication to treat insomnia. For a patient with severe signs and symptoms of discontinuation syndrome, treatment consists of restarting his medication as soon as possible. It may be given via nasogastric tube if the patient can't take oral medications. Discontinuation symptoms typically subside within 24 hours of resuming the medication.

Mr. Althouse was restarted on paroxetine, but at half his usual dose. His signs and symptoms resolved within 24 hours. After 1 week, he resumed taking his normal dosage. Before discharge, teach him about discontinuation syndrome and why he shouldn't abruptly discontinue his medication without talking to his healthcare provider. If he's being tapered off an SSRI, he should notify his primary care provider if he develops flu-like signs and symptoms.

Serotonin syndrome

Unlike SSRI discontinuation syndrome, serotonin syndrome is a potentially life-threatening complication of SSRI therapy. It occurs when an over-accumulation of available serotonin results in excessive stimulation of serotonin receptors in the central and peripheral nervous systems.

Serotonin syndrome can be caused by concomitant administration of monoamine oxidase inhibitors (MAOIs) and SSRIs. However, this potentially lethal syndrome also can result from drug interactions that don't involve MAOIs (see Some causes of serotonin syndrome).

Signs and symptoms of serotonin syndrome emerge rapidly within minutes to hours after starting or increasing a serotonergic medication. When assessing the patient for possible serotonin syndrome, you can group signs and symptoms into three categories: mental status changes, autonomic hyperactivity, and neuromuscular symptoms. He may have a broad range of signs and symptoms, and the syndrome can progress rapidly.

Serotonin syndrome can also be categorized according to severity, as follows:
- mild, characterized by restlessness, diaphoresis, tachycardia, tremor, and myoclonus. This form of serotonin syndrome is common.
- moderate, characterized by signs and symptoms of mild serotonin syndrome plus agitation, decreased level of consciousness, hypertension, shivering, rigidity, and hyperthermia (temperature of more than 104° F [40° C]).
- severe, characterized by moderate signs and symptoms plus shock, generalized tonic-clonic seizures, and coma.

If you suspect that your patient has serotonin syndrome, discontinue the

Some causes of serotonin syndrome

Monoamine oxidase inhibitors aren't the only drugs that can trigger serotonin syndrome. Other drugs associated with the syndrome include:
- any class of antidepressants
- valproate, an anticonvulsant drug
- linezolid, an antibiotic
- the anesthetics meperidine, fentanyl, pentazocine, and tramadol HCl
- the antiemetics metoclopramide, ondansetron, and granisetron
- dextromethorphan, which can be found in over-the-counter cough suppressants

Other causes of serotonin syndrome include resuming previously high doses of an SSRI after having stopped taking the medication, and accidental or intentional overdose of an SSRI.
medication or medications that precipitated the syndrome and immediately notify his healthcare provider. Assess the patient frequently and intervene to control and alleviate the mental-status changes, autonomic instability, and neuromuscular effects of the syndrome.

Mild cases of serotonin syndrome usually can be managed with supportive care and benzodiazepines to control agitation. Patients with moderately severe signs and symptoms should receive interventions for cardiopulmonary and temperature abnormalities, and may need 5-HT 2a antagonist therapy. The atypical antipsychotics risperidone and olanzapine may be used; cyproheptadine, a potent serotonin antagonist, may be ordered to treat severe cases of serotonin syndrome.

Patients who are hypothermic should receive the same interventions as patients with mild and moderate cases, plus immediate sedation, neuromuscular blockers, and endotracheal intubation and mechanical ventilation. Avoid physical restraints, which may aggravate isometric muscle contractions; chemical sedation is preferred.

Recovery from serotonin syndrome is rapid; typically within 24 hours. However, for patients taking SSRIs with long half-lives, residual symptoms such as muscle aches may persist for up to 8 weeks. Before your patient is discharged, teach him about serotonin syndrome and which drugs to avoid while he’s taking an SSRI.

Other risks
If your patient is taking an SSRI at a therapeutic dosage, you’ll still need to be on the lookout for bleeding and hyponatremia, two less-common risks with SSRI therapy.4-7

Bleeding is a risk because platelets release serotonin to promote platelet aggregation. By reducing available serotonin, SSRI therapy inhibits coagulation (see SSRIs and bleeding risk). In vulnerable patients (for example, those also taking aspirin or other nonsteroidal anti-inflammatory drugs, older patients, or those with a history of bleeding), this can lead to hemorrhage.4-7

Several studies have reported that patients who take SSRIs are 2.5 to 3 times more likely to develop GI bleeding than patients not on SSRIs.7,9

One study found that patients on SSRIs who had orthopedic surgery lost twice as much blood during surgery than those not taking an SSRI and were more likely to need blood transfusions.10

If you’re caring for a postoperative patient who takes an SSRI, perform frequent focused assessments to detect any postoperative bleeding promptly. Watch especially for signs and symptoms of GI bleeding, such as hypotension, tachycardia, coffee-ground emesis, tarry stools, or frank bleeding.

Serotonin may have a function in regulation and release of antidiuretic hormone, so SSRIs can lead to syndrome of inappropriate antidiuretic hormone (SIADH). Hyponatremia as a result of SIADH, a rare adverse reaction to SSRIs, may occur during the first few weeks of SSRI therapy. Patients at highest risk for SIADH and hyponatremia are those over age 65, women, patients with comorbid conditions associated with hyponatremia, and those using medications causing fluid loss (such as diuretics).4,11

Closely monitor your patient’s fluid and electrolyte balance (particularly serum sodium levels), and watch for signs and symptoms of mild hyponatremia, including mild anorexia, headache, and muscle cramps. Without appropriate treatment, hyponatremia can worsen, leading to confusion, changes in level of consciousness, and seizures. If your patient develops hyponatremia, discontinue the SSRI, restrict fluid intake, and administer sodium replacement as indicated and prescribed.

Staying vigilant
Because many hospitalized patients have comorbid medical conditions or are taking multiple medications, the role of SSRIs in complications can be easily overlooked. By understanding how SSRIs fit in, you can help your patient get prompt, appropriate care if complications develop.

REFERENCES


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