Benzodiazepine Withdrawal: Potentially Fatal, Commonly Missed

Following benzodiazepine cessation, withdrawal symptoms may begin within 24 hours or take up to two weeks to develop

By Michael I. Greenberg, MD, MPH

Patients experiencing benzodiazepine withdrawal pose an important clinical problem for emergency physicians who see these cases frequently. Most of the literature on the subject comes from psychiatry, not emergency medicine.

A 23-year-old man was brought by paramedics from his home to a community hospital emergency department. His parents found him on his bedroom floor where he was seizing continuously. On arrival to the emergency department, he was manifesting tonic-clonic generalized seizures. Vital signs were essentially normal, and he was noted to be afibrile.

The history obtained from his parents indicated that he had no pre-existing medical problems, but had been seeing a psychologist on a weekly basis and a psychiatrist on a monthly basis. The only medication he had been taking was clonazepam daily for the past year as prescribed by his psychiatrist.

On presentation, the patient was intubated, and intravenous access was obtained. The patient was treated with intravenous diazepam up to a maximum of 90 mg, but the seizures continued. A CT scan of his head was normal as were all routine blood tests. Consultation with a neurologist was obtained, and the patient was treated with barbiturates, which were successful in stopping the seizure activity.

Another patient, a 30-year-old man, presented to the emergency department complaining of feeling “uneasy” and “agitated.” He was diaphoretic and pacing around the emergency department. This patient’s vital signs were normal, and he had no other complaints.

The patient was treated with intravenous diazepam that successfully controlled his agitation. He was discharged home with follow-up evaluation arranged with his family physician who had been treating him for an “anxiety disorder” with daily doses of Ativan.

Both of these patients were felt to be suffering from benzodiazepine withdrawal syndrome. This syndrome, as the name indicates, quite simply results when a patient stops taking a benzodiazepine drug. The circumstances under which this syndrome can develop are variable. Benzodiazepines are one of the most widely prescribed medications in the world today. First introduced in the 1960s, these drugs have significant anxiolytic, hypnotic, muscle relaxant, and anticonvulsant actions. However, they also are widely abused as illicit drugs.

Patients may or may not be taking these drugs under a physician’s supervision, and in either case, withdrawal may occur when the patient voluntarily stops taking previously prescribed drugs or when the patient is injured, unconscious, or severely ill and thus stops taking the drug. In either circumstance, the patient may develop withdrawal symptoms as blood levels of benzodiazepine compounds are reduced.

Similar to Sedatives

The signs and symptoms of benzodiazepine withdrawal may be similar to those associated with the withdrawal of other sedatives and hypnotics (barbiturates, etchylphenytoin, glutethimide, and meprobamate or alcohol). Following benzodiazepine cessation, withdrawal symptoms may begin within 24 hours or take up to two weeks to develop.

The average period of time between drug cessation and symptom onset is roughly three to four days. This time frame may be dictated by the activity and the half-life of any active metabolites formed from specific parent drugs. It is not unusual for patients withdrawing from such drugs to have mild symptoms such as disturbed sleep or agitation a few days before more severe symptoms develop as active metabolites accumulate.

The symptoms that may be associated with withdrawal from relatively low doses of benzodiazepines are listed in the table. While these symptoms may be considered somewhat nonspecific in the patient with known benzodiazepine use and abrupt cessation, the diagnosis of withdrawal may be readily apparent.

The symptoms that may be associated with withdrawal from relatively high doses of benzodiazepines include halluci-nations, psychotic behavior, altered mental status, and seizures. It is important, however, to remember that any of the symptoms mentioned may be associated with withdrawal from virtually any dose of benzodiazepine drugs.

The most common symptom associated with benzodiazepine withdrawal is a mild change in behavior. Seizures are not common following benzodiazepine withdrawal, but they do occur.

Status Epilepticus

As in the patient described above, status epilepticus can and does result from withdrawal, and may be life-threatening. Withdrawal from benzodiazepines is not usually associated with significant elevations in blood pressure and pulse as those that commonly occur in patients in alcohol withdrawal. The emergency clinician must be aware that in the face of a possible benzodiazepine withdrawal syndrome, other serious medical problems must be ruled out. These include intracerebral catastrophes, meningitis, and other neurologic emergencies must be considered.

There have been many proposals offered for effective treatment of benzodiazepine withdrawal syndrome. The first principle of treatment, of course, is to ensure an adequate airway with effective oxygenation and circulation. Intravenous access may need to be immediately obtained and the patient reassured and observed. Excellent supportive care will be essential in cases of benzodiazepine withdrawal.

The mild to moderately affected patient may be effectively treated with simple benzodiazepine replacement and in-hospital medication tapering over a period of several days. Some advocate the use of barbiturates for any patient withdrawing from benzodiazepines. Either approach should be effective.

The more severely affected patient may require more complex therapy, including the use of barbiturates as substitute agents for benzodiazepines. Other drugs such as valproate also have been proposed as potentially useful adjuncts in treating benzodiazepine withdrawal. Even in a severely effected patient, immediate benzodiazepine replacement is advocated pending the administration of barbiturates.

Some have described the use of a continuous benzodiazepine infusion to induce sedation, seizure control, and sleep in these patients. It is important to remember that the patient who is placed on such a continuous infusion must be monitored in an intensive care setting with compulsive one-on-one nursing care.

One special situation involving benzodiazepine withdrawal deserves mention. In a clinical setting, benzodiazepine withdrawal can be inadvertently induced by the injudicious administration of flumazenil. In such cases, larger than expected doses of benzodiazepine drugs may be needed to overcome the effects of the flumazenil and effectively treat the symptoms of withdrawal. The best way to avoid this situation is to avoid the use of flumazenil in any situation in which there is even a remote possibility of inducing withdrawal.

By Edwin Leap, MD

A tough old bird, with not a word, His clothing soaked in blood,
A chain saw cut his arm half off,
He lectured the world through the mud.

Turns out back in ’44,
He waded through the sea,
Amid the guns and mines and wire
That waited there at Normandy.

He wears a bit of shrapnel still,
And you can guess how his pain rates.
He’s crying crocodile tears,
“Some what’s a little cut?” he says.

“Myy buddies had it worse back then,
I think I broke my ankle, man,
I’m pretty sure I heard a pop.
This pain must be a twenty-five.
Please do something! Make it stop!”

He suffers like no one before,
But not a fracture can be found.
It wasn’t bullet, blade, or bomb.
His enemy was just the ground.

So what’s a doctor now to do?
The pain scale clearly says it all.
Morphine for the weeping lad.
But chain saw man gets Tylenol.

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Toxicology Rounds

The Painful Scale

By Michael I. Greenberg, MD, MPH

Its scores about a three often.

“My buddies had it worse back then,
And keeps on working mourn tonight.
Please do something! Make it stop!”

“I’m pretty sure I heard a pop.
This pain must be a twenty-five.
Please do something! Make it stop!”

He lectured the world through the mud.

Sequel to the Secon D Opinion

Tremors
Vomitting
Nausea
Headache
Agitation
Tension
Anxiety
Insomnia


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