

... CASE 31

A 54-year-old man comes to the emergency department with a chief complaint of "I'm having a hard time kicking the habit." The patient states that for the past 2 days, he has experienced a depressed mood, muscle aches, diarrhea, insomnia, sweating, and a fever. Three days ago he ceased using his drug of choice, which he used heavily for more than 4 years. On a physical examination, the patient is noted to have a watery nose and eyes, a **fever** of 100°F (37.8°C), and dilated pupils.

- **What is the most likely diagnosis for this patient?**
- **What drug can be used to alleviate the patient's symptoms?**

ANSWERS TO CASE 31: Opioid Withdrawal

Summary: A 54-year-old man discontinued use of his drug of choice 3 days previously. Since then, he has experienced dysphoric mood, diarrhea, muscle aches, sweating, and a fever. A physical examination shows pupillary dilation, lacrimation, rhinorrhea, and a fever of 100°F (37.8°C).

- **Most likely diagnosis:** Opioid withdrawal
- **Medication to help alleviate symptoms:** Methadone or any other opioid: clonidine

Analysis

Objectives

1. Recognize opioid withdrawal in a patient.
2. Understand the use of methadone in ameliorating opioid withdrawal symptoms.

Considerations

Shortly after he ceased using his drug of choice after years of heavy use, this patient began to experience classic signs and symptoms of opioid withdrawal. Whereas opiate intoxication causes apathy, psychomotor retardation, constricted pupils, and drowsiness, opiate withdrawal results in nausea and vomiting, muscle aches, lacrimation or rhinorrhea, diarrhea, fever, and dilated pupils. These symptoms can develop within hours or days of the last opiate dose depending on the half-life of the agent and the body's dependence status. In general, agents with a short half-life tend to induce a rapid, severe withdrawal effect, whereas opiates with a long half-life tend to be associated with a less severe, more gradual withdrawal course. The introduction of clonidine to treat the autonomic hyperactivity in the acute phase, followed by administration of a long-acting opiate such as methadone for maintenance, is effective.

APPROACH TO OPIOID WITHDRAWAL

Definitions

Autonomic hyperactivity: Symptoms of autonomic hyperactivity include tachypnea, hyperreflexia, tachycardia, hypertension, sweating, and hyperthermia.

Endogenous opioids: A class of natural peptides that bind to all types of human opioid receptors (μ , δ , and κ): endorphins are included in this class.

Fasciculation: Muscular twitching of contiguous groups of muscle fibers.

Lacrimation: Secretion of tears from the eyes.

Methadone: An opioid with pharmacokinetic properties (including a long half-life, reliable absorption and availability, administered by oral ingestion, and nonspecific binding to tissues) that make it a helpful substitute for more dangerous and addicting opioids such as heroin.

Opioids: A class of drugs that includes naturally occurring compounds derived from opium, as well as other synthetic drugs that act as similar receptors.

Rhinorrhea: Runny nose

Clinical Approach

Opioid withdrawal is just one of many recognized substance withdrawal syndromes. All these syndromes have in common the development of a substance-specific pattern of symptoms following cessation of use of the drug in question. The drug use is generally heavy and prolonged, and a **physiologic dependence** develops: thus a withdrawal syndrome occurs on its cessation. The symptoms of opioid withdrawal specifically include **sensitivity to touch and light, goose flesh, autonomic hyperactivity, gastrointestinal distress, joint and muscle aches, yawning, salivation, lacrimation, urination, diarrhea, and a depressed or anxious mood**. Although very uncomfortable, opiate withdrawal is rarely **life-threatening unless complicated by a severe preexisting physical condition**. An intense craving for the drug is present. For the diagnosis, these symptoms must cause significant distress or impairment in functioning. They cannot be caused by either a medical condition or another mental disorder.

Differential Diagnosis

The differential diagnosis for opioid withdrawal is generally straightforward because patients undergoing withdrawal are conscious, are usually able to give their history, and know when the last dose of their drug of choice was taken. Other withdrawal syndromes are not manifested in the same way. For example, patients undergoing alcohol and/or benzodiazepine withdrawal present with anxiety, restlessness, irritability, and insomnia, as well as hyperreflexia and tremor. As withdrawal progresses, tachycardia, hypertension, diaphoresis, hyperthermia, and muscle fasciculations are seen. In severe cases, seizures, delirium, and death can occur. Withdrawal from cocaine includes a "crash," including hypersomnia, hyperphagia, and depressed mood. Withdrawal from nicotine produces anxiety, depression, irritability, headaches, poor concentration, sleep disturbance, and increased blood pressure and heart rate. Opioid withdrawal generally does not cause tremors, confusion, delirium, or seizures. Patients are seldom lethargic or tired. If any of these symptoms are present, the concurrent or separate use of other drugs of abuse should be considered.

Treatment

A rule of thumb regarding opioid withdrawal symptoms is that the shorter the duration of action of the drug ingested, the more acute and intense the withdrawal symptoms. The longer the duration of action of the drug being used, the more prolonged, but mild, the symptoms are. An exception to this rule occurs when an opioid antagonist is given to a person who is dependent on a long-acting opioid. In this case, the withdrawal symptoms can be severe. **Clonidine** has been used to **decrease the autonomic symptoms of opioid withdrawal, such as hypertension, tachycardia, sweating, lacrimation, and rhinorrhea**. It does not, however, remove the subjective sensations or cravings for the drug. Blood pressure levels must be monitored carefully if clonidine is used. It is thought that its mechanism of action in the treatment of opioid withdrawal involves the noradrenergic neurons of the locus ceruleus. Of course, methadone can be used in a daily oral dose to ameliorate opioid withdrawal syndromes, although technically, the patient has not withdrawn from drugs in the opioid class.

Comprehension Questions

- [31.1] A 25-year-old man comes to the hospital with classic symptoms of opioid withdrawal. He is adamantly opposed to the use of methadone to relieve his symptoms, saying he "wants to kick this thing once and for all." Which of the following medications can be used to help ameliorate his symptoms while he goes through withdrawal?
- A. Sertraline
 - B. Haloperidol
 - C. Desipramine
 - D. Lorazepam
 - E. Clonidine
- [31.2] A 42-year-old woman is determined to "kick her heroin habit" at home without the use of methadone or any other prescription drug. Of the following over-the-counter medications, which is most likely to be of benefit to this patient as she goes through opioid withdrawal?
- A. Acetaminophen
 - B. Ibuprofen
 - C. Benadryl (diphenhydramine)
 - D. Pseudoephedrine
 - E. Dextromethorphan

- [31.3] A 32-year-old man with a heroin addiction has recently started treatment with methadone as he tries to quit his heroin habit. Three days after starting the methadone regimen, he has not developed any major symptoms and has not taken any heroin. However, he is experiencing some craving, diarrhea, and mild sweating. Which of the following is the most appropriate course of action?
- A. Increase the dose of methadone.
 - B. Decrease the dose of methadone.
 - C. Keep the dose of methadone the same and assure the patient that the symptoms will subside.
 - D. Write a prescription for clonidine to be taken along with the methadone.
 - E. Put the patient on a 1-week methadone taper program and refer him to Narcotics Anonymous.

Answers

- [31.1] E. Clonidine can be used to help ease the withdrawal symptoms of opioid withdrawal. It is not an opioid and does not have any addictive properties. Withdrawal from the opioid, however, is not as painless as it otherwise would be if an opioid such as methadone were used. Blood pressure levels should be monitored when clonidine is used. Selective serotonin reuptake inhibitor antidepressants, such as sertraline, are not used in treating acute withdrawal, although the tricyclic antidepressant, desipramine was tried for the reduction of craving in cocaine withdrawal. Lorazepam, a benzodiazepine, is commonly used in the treatment of alcohol withdrawal. Haloperidol, an antipsychotic, has no use in treating withdrawal.
- [31.2] B. Ibuprofen can help relieve the muscle cramps that are common to opioid withdrawal.
- [31.3] A. Clinical signs of withdrawal appearing very early in the treatment of heroin addiction with methadone are an indication that the dose is not sufficient to ameliorate all the withdrawal symptoms. Because the patient is at great risk of returning to the use of heroin at this point in the process, a dose adjustment upward to prevent craving is appropriate.

CLINICAL PEARLS

A mnemonic that is helpful in remembering the signs and symptoms of opioid withdrawal is SLUD—salivation, lacrimation, urination, and defecation.

Opioid withdrawal is extremely uncomfortable for the patient but generally is not life-threatening.

Clonidine and methadone (a long-acting opioid) are the two most common treatments for the relief of opioid withdrawal symptoms.

Loperamide (for loose stools) and promethazine (for nausea and vomiting) are useful adjunctive treatments for the symptoms of opioid withdrawal, as is ibuprofen for muscle and joint aches.

The presence of dilated pupils and anxiety are often the first signs of opioid withdrawal that can easily be seen in the physician's office.

Methadone maintenance programs swap one addiction for another, but the social and physical advantages gained make it one of the best choices for treatment of opiate addiction. Other substances of abuse should always be sought in the presence of heroin addiction.

REFERENCES

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- Goldman HH. Review of general psychiatry, 5th ed. New York: McGraw-Hill, 2000:220.