CONDITION

Amitriptyline and perphenazine overdose

Learn how an overdose of amitriptyline and perphenazine can affect the heart, brain, breathing, and muscles, and why immediate emergency care is essential.

WHAT IT IS
Serious poisoning from prescription medicine overdose

BODY SYSTEM
Heart, nervous system, breathing and muscles

MAIN SYMPTOMS
Severe sleepiness or confusion, abnormal heartbeat, seizures, slow or stopped breathing

WHAT CAUSES IT
Taking too much medicine

HOW IT IS DIAGNOSED
Clinical assessment and repeated ECGs

MAIN TREATMENT
Emergency supportive and ECG-guided care

CAN IT BE CURED?
Sometimes - timely treatment enables recovery

IS IT AN EMERGENCY?
Yes - any suspected overdose

LONG-TERM OUTLOOK
Many recover with timely treatment and monitoring

Overview

Amitriptyline and perphenazine are prescription medicines that have sometimes been combined in one product. Amitriptyline is a tricyclic antidepressant, or TCA. It changes the activity of chemical messengers involved in mood and pain. Perphenazine is a first-generation antipsychotic that affects dopamine, a chemical messenger involved in thinking, movement, and behavior.

Taking too much of either medicine can cause serious poisoning. In combination, they may affect consciousness, breathing, blood pressure, body temperature, muscles, and heart rhythm. Amitriptyline overdose is especially concerning because it can quickly interfere with the heart's electrical system and cause seizures.

A suspected overdose is an emergency even if the person feels well or the amount taken is

uncertain. Symptoms can develop or worsen rapidly. In the United States, call 911 for severe symptoms and contact Poison Help at 1-800-222-1222 for immediate guidance. Outside the United States, contact the local emergency service or poison center.

Do not make the person vomit. Do not give food, drinks, or home remedies unless a poison specialist or clinician tells you to do so. If possible, bring the medicine container or a photo of its label to the hospital.

Symptoms

Symptoms depend on the amount taken, the time since exposure, other substances involved, and the person's health. Someone may have a mixture of effects from both medicines.

Possible early or moderate symptoms include:

Amitriptyline can cause an anticholinergic syndrome . This means it blocks a nerve-signaling chemical called acetylcholine. The result may be dry skin, enlarged pupils, fast heart rate, urinary retention, confusion, high body temperature, or reduced bowel movement.

Perphenazine can cause extrapyramidal symptoms , which are medication-related movement problems. These may include painful muscle spasms, neck twisting, jaw tightness, eye-rolling, tremor, stiffness, or an intense need to keep moving.

Emergency symptoms may include:

Rarely, perphenazine may contribute to neuroleptic malignant syndrome , a dangerous reaction involving high temperature, severe muscle rigidity, changes in alertness, and unstable blood pressure or heart rate. These symptoms require immediate emergency care.

- Severe sleepiness, confusion, agitation, or unusual behavior
- Blurred vision and enlarged pupils
- Dry mouth, flushed skin, or reduced sweating
- Fast heartbeat
- Dizziness or low blood pressure
- Nausea or vomiting
- Trouble urinating
- Muscle stiffness, tremor, restlessness, or abnormal movements
- Slurred speech or poor coordination
- A seizure

- Fainting, collapse, or inability to wake
- Slow, shallow, or stopped breathing
- Severe confusion or extreme agitation
- A very fast, irregular, or unusually slow heartbeat
- Chest pain
- Severe weakness or signs of shock, such as pale or clammy skin
- High body temperature with severe stiffness or altered consciousness

Causes and risk factors

An overdose may happen when someone takes more medicine than prescribed, takes doses too close together, accidentally uses the wrong product, or intentionally takes a large amount. Children may be poisoned after finding medicine that was not securely stored.

Risk can also increase when amitriptyline and perphenazine are taken with alcohol, opioids like oxycodone or morphine , sleep medicines, anti-anxiety medicines, antihistamines like cetirizine or loratadine , or other drugs that cause sedation. Other antidepressants like sertraline or fluoxetine , antipsychotics, and medicines that affect heart rhythm may add to the danger.

Certain health conditions can make the effects harder to tolerate. These include heart disease, a history of abnormal heart rhythm, seizure disorders, breathing problems, liver disease, and older age. However, serious poisoning can occur in a person without any known health condition.

It may be difficult to estimate the amount taken. Different products contain different strengths, and symptoms do not reliably show whether an exposure is safe. For this reason, decisions about care should be made by emergency clinicians or a poison center rather than by waiting for symptoms at home.

Intentional overdose may occur during a mental health crisis. Emergency care should address both the physical poisoning and the circumstances that led to it. A calm, nonjudgmental approach can help the person share information needed for safe treatment.

Diagnosis

Clinicians first assess the airway, breathing, circulation, alertness, and body temperature. They ask what was taken, how much may be missing, when it happened, and whether alcohol or

other medicines were involved. Treatment may begin before all of this information is available.

An electrocardiogram, or ECG, is a key test. It records the heart's electrical activity. Amitriptyline can widen part of the ECG called the QRS complex and can cause other conduction changes. These findings may signal a higher risk of seizures, low blood pressure, or dangerous heart rhythms. ECGs may be repeated because the effects can change over time.

Blood tests may check glucose, electrolytes, kidney and liver function, and acid balance. Clinicians commonly test for other important overdoses, such as acetaminophen, when the substances taken are not fully known. A pregnancy test may be offered when relevant to treatment decisions.

Routine drug screens have limits. A positive result does not show how severe the poisoning is, and some tests may react to medicines other than amitriptyline. Blood concentrations of tricyclic antidepressants also do not replace the person's symptoms and ECG findings when judging severity.

Observation time depends on symptoms, ECG results, treatment needs, and the suspected exposure. A person with significant symptoms generally needs continuous heart and breathing monitoring.

Treatment and management

Treatment takes place in an emergency department, often with advice from a medical toxicologist or poison center. People with severe effects may need intensive care.

The immediate priorities are protecting the airway, supporting breathing, and maintaining blood circulation. Oxygen may be given. A breathing tube and ventilator may be needed if the person cannot protect the airway or breathe adequately.

Activated charcoal can bind some medicine remaining in the digestive tract. It is not appropriate for every exposure and can enter the lungs if a person is very drowsy or vomiting. It should be given only under professional direction when the airway can be protected.

Intravenous sodium bicarbonate is a central treatment for serious heart effects from amitriptyline, including QRS widening, certain abnormal rhythms, and low blood pressure related to sodium-channel blockade. Clinicians adjust this treatment using ECG findings, blood pressure, and blood tests. It is not a home treatment.

Seizures are generally treated with medicines that calm excessive brain activity, often from the benzodiazepine group. Persistent low blood pressure may require intravenous fluids and medicines that tighten blood vessels. Clinicians also correct low oxygen, abnormal electrolytes, or changes in blood acidity.

Abnormal movements or painful muscle spasms from perphenazine can be treated with medicines selected by the care team. High temperature requires careful evaluation because it may result from agitation, anticholinergic poisoning, seizures, or neuroleptic malignant syndrome.

Some usual heart-rhythm medicines may be unsuitable in TCA poisoning. Treatment choices should therefore be guided by clinicians familiar with toxicology. Intravenous lipid emulsion may be considered in selected life-threatening cases that do not respond to standard treatment, but it is not routine therapy.

Hemodialysis, which filters the blood through a machine, does not effectively remove tricyclic antidepressants because these medicines bind strongly to tissues and proteins. Supportive care, ECG-guided treatment, and time are more important.

If the overdose was intentional, a mental health assessment is usually part of care once the person is medically stable. This is intended to improve safety and connect the person with appropriate support.

Complications

The most serious complications involve the heart, brain, and breathing. Amitriptyline can cause dangerous ventricular heart rhythms, severe low blood pressure, cardiac arrest, seizures, and coma. Reduced breathing or loss of airway reflexes can lead to low oxygen levels.

Vomiting while deeply drowsy may cause stomach contents to enter the lungs. This is called aspiration and can injure the lungs or lead to pneumonia.

Long seizures, extreme agitation, severe stiffness, or very high temperature can damage muscles. Muscle breakdown may then affect the kidneys. Prolonged low blood pressure can reduce blood flow to the brain, kidneys, and other organs.

Perphenazine may cause ongoing movement symptoms after the immediate poisoning improves. Neuroleptic malignant syndrome is uncommon but can lead to muscle injury, kidney problems, and unstable heart rate or blood pressure.

Many people recover with timely treatment and monitoring. The likely course depends on the amount taken, how quickly care begins, ECG changes, complications, and other substances involved.

Follow up

Before discharge, the care team may review the medication list, heart findings, movement symptoms, and any complications. Follow-up may involve a primary care clinician, psychiatrist, cardiologist, neurologist, or another specialist, depending on what happened.

Routine follow-up is important for reviewing whether amitriptyline or perphenazine should be restarted, changed, or stopped. Do not restart either medicine after an overdose unless the prescribing clinician provides a plan. Follow-up can also address safer storage, supervised dispensing, or disposal of medicines that are no longer needed.

After an intentional overdose, timely mental health care and a practical safety plan are important. Family members or trusted supporters may be included with the person's permission.

Seek urgent medical advice after discharge for new palpitations, worsening dizziness, repeated vomiting, increasing confusion, fever, unusual stiffness, or new involuntary movements. Call emergency services for fainting, a seizure, trouble breathing, chest pain, severe weakness, or inability to wake the person.

Sources

- U.S. National Library of Medicine. DailyMed: Amitriptyline hydrochloride tablet-prescribing information. See the warnings and overdosage sections.
- U.S. National Library of Medicine. DailyMed: Perphenazine tablet-prescribing information. See the adverse reactions and overdosage sections.
- Lavonas EJ, Akpunonu PD, Arens AM, et al. 2023 American Heart Association Focused Update on the Management of Patients With Cardiac Arrest or Life-Threatening Toxicity Due to Poisoning. Circulation. 2023;148:e149-e184.
- Chyka PA, Seger D, Krenzelok EP, Vale JA. Position paper: Single-dose activated charcoal. Clinical Toxicology. 2005;43(2):61-87.
- Lavergne V, Gosselin S, Mowry JB, et al. Extracorporeal treatment for tricyclic antidepressant poisoning: Recommendations from the EXTRIP Workgroup. Seminars in Dialysis. 2014;27(4):381-389.
- Health Resources and Services Administration. Poison Help: What You Can Do. U.S. Department of Health and Human Services.