Antihistamine poisoning

Key words: antihistamine overdose, promethazine overdose, anticholinergic toxidrome.

We present the case of a 35-old man in whom a diagnosis of promethazine overdose was made after he presented to the emergency department with profound alteration of mental status. We review the clinical picture and cornerstones in the treatment of antihistamine overdose.

Introduction

Antihistamines are a class of pharmacological agents that include the first generation, centrally acting H1 receptor antagonists and the newer generation, non-sedating H1 blockers. The histamine antagonists are quite effective when used for this indication. The first generation (sedating antihistamines) are in considerable use in other indications as "cold medicines", premedication for surgery, sleep inducing and anti-motion sickness. They are widely available and potentially toxic. Overdose may be an important problem in emergency medicine.

We present a patient with profound alteration of mental status due to promethazine overdose and review the clinical picture and cornerstones in the treatment of antihistamine overdose.

Case Report

A 35 year-old man was brought to the emergency department by emergency medical services after he was found comatose. He was responsive only to nociceptive stimuli. The blood pressure was 100/55 mmHg; the pulse 120/minute; 14 respirations/minute; the blood glucose was 78 mg/dl, and O₂ saturation was 98%. The patient received 0.8mg naloxone I.V. without any response. He was given supplemental O₂, I.V. fluid and was transferred to this hospital. On arriving he was in coma; the pulse was 103/minute; the blood pressure 107/58 mm. Hg; the respirations were 16/minute; the rectal temperature was 37°C. The skin was hot, dry and flushed; the mucosae were dry. On neurological examination the patient was in profound coma, responsive only to nociceptive stimuli with movements of the 4 limbs; the Glasgow Coma Scale was 4; the pupils were about 3-mm. in diameter and were responsive to light. The gag reflex was markedly reduced; there were no signs of meningeal irritation; the tongue was not bitten and there was no sphincter incontinence. The rest of the physical examination was not remarkable. The bedside glucose examination showed 77 mg./dl. The O₂ saturation 99%; the ECG showed sinus tachycardia with narrow QRS and normal QT interval. Blood was drawn for laboratory tests. The patient received 0.8 mg naloxone and 1 mg. flumazenil without any change in mental status. Because of profound coma and depressed gag reflex, he was intubated; the blood results showed a normal blood count, normal glucose, urea and electrolytes. The blood gases were normal. The blood alcohol and acetaminophen levels were negligible. The carboxyhemoglobin was 1.9%. A urine specimen taken after catheterization was positive only for opiates. The profound coma, without respiratory acidosis and the negative response to naloxone were against the possibility of opiate overdose. To rule out any possible intracranial bleeding a noncontrast head CT was done and the results were normal. The patient

Alberto Kurzbaum, MD
Safot Gassan, MD
Mohanna Khateeb, MD
Lucy Lieberman, MD
Claudia Simsolo, MD

Department of Emergency Medicine and Intensive Care Unit, Poryia Government Hospital, Tiberias, Israel
presented a partial anticholinergic toxidrome with normal pupils where coma was the dominant manifestations instead of delirium. The patient got I.V. fluid and activated charcoal via nasogastric tube. In his clothes an official stamped paper from a psychiatric hospital was found. A telephone call to the doctor signing the paper confirmed that the patient was allowed to leave the hospital for a few hours and did not return. The same day he called his doctor and told him that he was going to commit suicide. The patient usually received promethazine 25 mg. 4 times a day. With the diagnosis of antihistamine overdose (due to promethazine) he was admitted to the Intensive Care Unit. There, after 6 hours, he was extubated, returned to normal consciousness when he admitted taking 20 tablets of promethazine. After psychiatric consultation the patient was referred to a psychiatric hospital.

Discussion

Promethazine is an antihistamine classified as a phenothiazine. However, it is not used clinically as a neuroleptic because its ability to antagonize dopamine is approximately one-tenth that of chlorpromazine. It is a H1 receptor-blocking agent. In addition to its antihistaminic actions it is useful as a sedative, antiemetic and antimotion sickness. It is a sedating antihistamine with considerable anticholinergic effect; sedation is evident in therapeutic doses and useful as premedication in surgical patients. The relief of motion sickness, nausea and vomiting appear to be related to central anticholinergic actions and may implicate activity on the medullary chemoreceptor trigger zone. Mild antitussive activity had been attributed to promethazine, but this effect probably results from anticholinergic and sedative actions. Because of this spectrum of actions, as with other sedating antihistamines, promethazine appears in many “cold medicines” and sleep inducing pills, both as prescription and over the counter (OTC) preparations. Because of their ease of availability, these drugs may be involved in cases of accidental (especially in children) or intentional overdose (1). Promethazine has potent anticholinergic activity. In overdose the peripheral and central manifestations of the anticholinergic toxidrome are prominent. The skin is hot, dry and flushed. The mucous membranes are dry. The eyes show mydriasis with loss of accommodation and blurred vision; hyperpyrexia may be present. Sinus tachycardia is one of the earliest signs of muscarinic blockade. Some antihistamines (such as diphenhydramine and chlorpheniramine) may have quinidine-like effects with altered conduction and arrhythmias and others, such as the non-sedating piperidine antihistamines (astemizole and terfenadine), may prolong the QT interval; this may predispose to torsade de points ventricular tachycardia. Intestinal ileus and urinary retention may be present. The central anticholinergic manifestations usually present as a toxic delirium where agitation may be prominent. A high percentage, instead, may appear as somnolence, lethargy and coma, catatonic stupor, or with acute dystonic extrapyramidal movements. Seizures are not a common manifestation. Evaluation and treatment has to be systematic as in any case of altered mental status. Those who are cooperative should receive activated charcoal. Those with who are unable to protect their airway should have endotracheal intubation prior to instillation of charcoal by nasogastric tube. Those with anticholinergic induced delirium may be treated by supportive therapy alone. Benzodiazepines may be used in severely agitated patients. Physostigmine may be considered in the cases of pronounced hallucinations and agitation unresponsive to high doses of benzodiazepines. But because antihistamine overdose carries a greater risk for seizures, usually this is not recommended. A recent study suggests that physostigmine is more effective and just as safe as benzodiazepines to control anticholinergic associated delirium (2). Prior to physostigmine use, an ECG must rule out a conduction disturbance that may be secondary to tricyclic antidepressant or some antihistamines overdose as the cause of the anticholinergic toxidrome.
As many cough and cold preparations combine antihistamines and antipyretics, it is recommended to check acetaminophen levels. Because of their ease of availability, increased awareness by family and emergency medicine physicians is needed to recognize this possible cause of overdose. The diagnosis should be based on the clinical picture that may not be clear in mixed ingestion.

Our patient presented with coma and an anticholinergic toxidrome. The pupils were not dilated, possibly because of opiate co-ingestion or as described in phenothiazine overdose (3). He did not respond to flumazenil that was described to antagonize the sedative effects of promethazine (4).

References