Swift Onset of Central Nervous System Depression and Asystole Following an Overdose of Guaifenesin

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Guaifenesin is an over-the-counter expectorant used for chest congestion and is available both in single-ingredient formulations and in combination with antihistamines, cough suppressants and decongestants. The documented side-effects of guaifenesin are generally mild. We present the case of a 23-year-old female who committed suicide by ingestion of guaifenesin along with small amounts of cetirizine, ethanol and sertraline. Approximately 2 h after ingestion, the patient experienced central nervous system depression followed by asystole. No anatomic cause of death could be determined at autopsy. The initial toxicology detected only ethanol, which was found at a concentration insufficient to cause death. Upon further analysis, guaifenesin was detected in femoral blood at 25.0 μg/mL, urine at >50.0 μg/mL, vitreous fluid at 9.2 μg/mL, brain at 17.0 μg/g and liver at 25.0 μg/g. This is the first reported human case that can be considered a death to which guaifenesin was the significant pharmacologic contributor. Guaifenesin is not detected by the primary screening methods employed by some labs and may be missed in toxicological analyses of overdoses unless specifically suspected.

Introduction

Guaifenesin (glyceryl guaiacolate), an over-the-counter expectorant used to enhance the clearance of mucus from airways and relieve chest congestion, is available both as a single-ingredient medication and in formulations with antihistamines, antitussives and decongestants (1–3). MedlinePlus, a service of US National Library of Medicine and National Institutes of Health, reports that there were 10 brands of single-ingredient guaifenesin and 66 combination guaifenesin in formulations approved by the FDA on the US market as of May 2011 (3).

The documented side-effects of elevated guaifenesin levels include headache, nausea and vomiting (3, 4). At high doses, guaifenesin causes depression of the central nervous system and is used as a muscle relaxant with sedative effects in veterinary medicine (1, 5–7). Little information about the toxic and fatal concentrations of guaifenesin is available. In veterinary medicine, the margin of safety for guaifenesin is reportedly three times the recommended maximum dose (6). Prior to this report, guaifenesin has been observed in one non-fatal anaphylactic reaction and one human polypharmacy death (2, 8). To our knowledge, ours is the first case report of a human guaifenesin overdose without significant polypharmacy.

Case Details

A 23-year-old woman with a history of suicide attempts and illicit drug use during a recent pregnancy reportedly consumed an unknown quantity of cetirizine (Zyrtec®), ethanol, guaifenesin (Mucinex®) and sertraline (Zoloft®) at about 01:00–01:15 AM in a stated attempt to commit suicide. Approximately 1 h after ingestion, the patient’s significant other called the hospital, and the patient could be heard in the background yelling that she did not want medical help. The significant other called 911 at 02:10 AM, and emergency services were dispatched at 02:16 AM. At 02:20 AM, the patient reportedly began slurring her words and exhibiting shallow respirations. Emergency services arrived at 02:29 AM; when asked what had been ingested, patient responded “Zoloft,” with no further statements documented. At 02:51 AM, the patient was unresponsive and breathing with anasarca, with blood pressure in the “normal range” and a heart rate of 104 b.p.m., rhythm sinus tachycardia. At 02:51 AM, the patient’s heart rate dropped to 32 b.p.m. in sinus bradycardia and rose to 60 b.p.m. with an intravenous push of 0.5 mg of atropine. During transportation, the heart rate dropped to 36 b.p.m., rhythm sinus bradycardia, and was not improved by an additional 0.5 mg push of atropine at 03:04 AM. Minutes later, there was emesis, with some observed in the endotracheal tube (ETT); ETT was removed to prevent aspiration, and bag valve mask respirations continued until arrival at hospital. The patient was re-intubated in the emergency room, and ventricular fibrillation was observed at 03:07 AM. Defibrillation was performed and, after shock, the patient’s rhythm was asystole. Epinephrine was administered via IV with no response, shortly followed by a push of lidocaine and an additional push of epinephrine at 03:11 AM. At 03:13 AM, the patient had a spontaneous return of circulation, heart rate 56 b.p.m., rhythm sinus bradycardia, for ~1 min before going back into asystole. A push of 1.0 mg epinephrine was administered at 03:16 AM, with no response. Cardiopulmonary resuscitation efforts were discontinued at 03:42 AM and death was pronounced.

At autopsy, no anatomic cause of death could be determined. No acute cutaneous or internal injuries were detected, nor was there any evidence of aspiration of vomit. Anaphylaxis was ruled out as a diagnosis as there was no evidence of an eosinophil response, the airway was free of edema and a review of clinical records gave no indication of anaphylaxis. Microscopic examination of tissues identified focal atelectasis and interstitial fibrosis in lungs, congested sinusoids in liver, congestion in kidneys and unremarkable findings in brain and heart tissue.

Information provided to Laboratory A for the initial toxicologic analysis listed cetirizine, ethanol and sertraline as the suspected contributors to the fatality. Case samples were screened as general unknowns using gas chromatography with nitrogen phosphorus detector (GC-NPD) as a primary screening method,
with confirmations of drugs present by gas chromatography-mass spectrometry (GC-MS). Laboratory A detected ethanol at 0.120 g/100 mL in femoral blood and 0.146 g/100 mL in vitreous fluid (see Table I). Neither cetirizine nor sertraline were detected in the initial toxicology.

For unknown and unexplained reasons, the pathologist then concluded that death was from acute ethanol intoxication and positional asphyxia.

The Sheriff’s Investigator (T. Johnson) reviewed the investigative information and challenged the diagnosis of positional asphyxia since the patient was breathing unassisted and spoke briefly when emergency services arrived.

A second toxicologic screen was performed by a separate laboratory, with instructions to screen for cetirizine and sertraline. Laboratory B detected 0.14 µg/mL of cetirizine by GC-MS analysis and 0.0038 µg/mL of sertraline via GC analysis of femoral blood, well-below toxic concentrations and below the cut-off values for the first toxicologic analysis (9). This analysis provided confirmation of prior use of the said drugs but no indication of significant intoxication.

Mucinex®, with the primary ingredient guaifenesin, was then considered as a possible source of the overdose after reviewing the case notes made by the Sheriff’s Investigator. Prior to this point in the investigation, neither laboratory was informed of suspected guaifenesin use. Upon specific assay, Laboratory A confirmed the presence of guaifenesin in postmortem fluid and tissue.

Guaifenesin was detected in femoral blood at 25.0 µg/mL, urine at >50.0 µg/mL (exact amount not quantified by lab), vitreous fluid at 9.2 µg/mL, brain at 17.0 µg/g and liver at 25.0 µg/g.

While the amount of guaifenesin ingested could not be determined, the decedent’s significant other estimated that the number of tablets he saw her take amounted to ten, though such a low quantity appeared unlikely considering the subsequent presentation.

In this case, guaifenesin was quantitated by high-pressure liquid chromatography and confirmed by GC-MS. Acetaminophen, dextrimethorphan, phenylephrine and pseudoephedrine, drugs commonly combined with guaifenesin in Mucinex® products, are all detectable by GC-NPD, but were not found in the toxicology screens performed.

Ethanol intoxication can contribute to central nervous system depression; however, the amount detected, 0.120 g/100 mL in femoral blood, while indicative of intoxication, is insufficient to represent a dose with a possible fatal pharmacologic outcome. Legal intoxication for driving in most states is defined as the presence of concentrations between 0.08 and 0.10 g/100 mL, with lethal concentrations classified as those exceeding 0.350 g/100 mL (9).

Prior to this report, guaifenesin toxicity was documented in a polypharmacy death involving concurrent chlorpheniramine and diphenhydramine intoxication, where guaifenesin was detected in heart blood at a concentration of 27.4 µg/mL, urine at 21.0 µg/mL and vitreous fluid at 7.0 µg/mL (2).

For practical purposes, this report is the first of death in which guaifenesin was a significant pharmacologic agent and no anatomic contributor to the mechanism of death could be determined.

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