Strychnine Overdose Following Ingestion of Gopher Bait

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Abstract

A 52-year-old male was discovered supine on his bed in a state of early decomposition. Commercial strychnine-treated gopher pellets were found in the home, and suicide notes were present at the scene. Biological fluids and tissues were tested for basic, acidic, and neutral drugs using gas chromatography–mass spectrometry. Concentrations of strychnine in heart and femoral blood were 0.96 and 0.31 mg/L, respectively. Vitreous fluid, bile, urine, liver, and brain specimens contained 0.36 mg/L, 1.17 mg/L, 2.92 mg/L, 4.59 mg/kg, and 0.86 mg/kg strychnine, respectively. No other drugs were detected in any of the samples. The cause of death was attributed to rodenticide poisoning, and the manner of death was suicide.

Introduction

Strychnine is a basic alkaloid with central nervous system stimulant and convulsant effects. The bitter-tasting white crystalline material is derived from ripe seeds of the native Indian Strychnos plant, S. nux-vomica. Between 1540 and 1960, strychnine was used medicinally in many cathartics, stimulants, and tonics. Poisoning was more frequent up until the late 1920s, at which time strychnine was removed from many over-the-counter tonics and laxatives. Today, its use is restricted to veterinary preparations and rodenticides. Household and commercial rodenticides typically contain between 0.3 and 3% strychnine by weight.

Strychnine prevents the uptake of glycine at inhibitory synapses, resulting in a net excitatory effect and diffuse muscle contractions. Following ingestion, onset of stimulant activity occurs within 15–30 min. Overwhelming convulsions, paralysis, and death follow heightened stimulation, awareness, and muscle spasms. Oxidative biotransformation occurs in the liver to unknown metabolites, and approximately 10–20% of the dose is excreted unchanged in the urine within 24 h (1). Human fatalities have been reported at doses in excess of 5–10 mg, but survival following higher doses has been documented (2).

In one report of accidental exposure, plasma and urine samples contained 0.2 and 6.9 mg/L, respectively, 28 h post-exposure (3). The half-life of strychnine is reported to be in the range of 10–12 h (4), and the volume of distribution is high (13 L/kg). Absorption from the gastrointestinal tract is rapid, and there is minimal protein binding (5). In two cases involving rapid death, strychnine concentrations in the liver were low (0.8 and 1.6 mg/kg) even though the blood concentrations (2.4 and 12 mg/L) were in the fatal range (6). Urinary strychnine concentrations of 37 and 4 mg/L were measured in two young males who survived after inhaling strychnine, believing it to be cocaine (4).

Case History

The 52-year-old male decedent was a disabled veteran with a history of depression and a prescription for amitriptyline. He was discovered supine on his bed in a state of early decomposition. He was last seen alive four days earlier. Multiple suicide notes were nearby, and a drinking glass in the kitchen contained a mixture of tan pellets and a green crystalline material. Subsequently, a box of commercial strychnine-treated gopher pellets was found in the home. At autopsy the pathologist identified approximately 100 mL of the mixture within the gastric lumen, severe pulmonary edema, and alveolar hemorrhage. Additional findings included severe atherosclerotic cardiovascular disease and sequela of systemic hypertension. Small portions of heart (500 g), liver (1490 g), spleen (210 g), brain (1430 g), and lungs (940 and 900 g) were retained for analysis.

Methods

Femoral blood, heart blood, vitreous fluid, urine, bile, brain, and liver were submitted for toxicological analysis. Femoral blood was tested for alcohol using gas chromatography with flame ionization detection. Common drugs of abuse were detected using enzyme-linked immunosorbent assay (Orasure
A general drug screen for acidic, basic, and neutral drugs was conducted using solid-phase extraction and gas chromatography–mass spectrometry (GC–MS) as follows. Tissue samples (2–3 g) were homogenized with 10 mL 0.15M sodium chloride solution prior to analysis. Samples, calibrators, and controls (2 mL) were fortified with 50 μL of methanolic internal standard solution consisting of 0.02 mg/L mepivacaine (Alltech, Deerfield, IL), 0.05 mg/L hexobarbital (Alltech), and 0.02 mg/L delorazepam (Sigma, St. Louis, MO). For quantitative determination of strychnine, calibrators were prepared by fortification of bovine blood with a stock solution of 0.1 mg/mL strychnine (Sigma). Two milliliters of phosphate buffer (100 mM, pH 6.0) was added, followed by sonication for 15 min and centrifugation for 15 min at 4500 rpm. The supernatant layer was transferred to a PolyChrom Cerex Clin II SPE cartridge (SPEWare, San Dimas, CA). Samples were drawn through the column using just enough pressure to maintain constant flow. Columns were then successively rinsed using 1 mL deionized water and 1 mL acetic acid (1M). Columns were dried for 5 min at full vacuum, followed by another rinse with 1 mL hexane. Acidic and neutral drugs were eluted using ethyl acetate (1 mL). Columns were rinsed once again using methanol (1 mL), followed by elution of basic drugs with ethyl acetate containing 2% concentrated ammonium hydroxide (1 mL). The basic, acidic, and neutral fractions were combined, and 30 μL of acidic methanol (1% concentrated hydrochloric acid in methanol) was added. Samples were evaporated to dryness under nitrogen and reconstituted in 25 μL of ethyl acetate. This extraction is routinely used in our laboratory for the isolation of basic, acidic, and neutral drugs. Appropriate sample dilutions were made in order to obtain quantitative values that were within the calibration range.

Samples were analyzed by GC–MS using an Agilent 6890 GC with a 5973 mass selective detector. The injector and interface were set at 250 and 280°C respectively. Separation of components in each 2 μL injection was achieved using a 30-m DB-5 capillary column (J&W Scientific, 0.25-mm i.d., 25 μm). Following an initial oven temperature of 160°C and hold time of 2 min, the temperature was increased at 30°C/min to 230°C. After a 2-min hold, the temperature was further increased to 290°C at a rate of 30°C/min. The final hold time was 5.67 min, and the total run time was 14 min. Helium was used as the carrier gas at a flow rate of 1.3 mL/min. Mepivacaine (m/z 98) was used as the internal standard for the quantitative determination of strychnine (m/z 334). Acquisition was in full scan mode (m/z 40 to 650), and quantitation ions are underlined.

### Results and Discussion

No alcohol was detected in the femoral blood. Drugs of abuse, including opiates, benzodiazepines, cocaine metabolite, cannabinoids, methadone, propoxyphene, barbiturates and amphetamines were not detected by immunoassay. Strychnine calibrators (0–1 mg/L) prepared in bovine blood yielded a linear calibration with an R² value of 0.998. Independent controls, prepared using a different stock solution, yielded quantitative values within acceptable range. Sensitivity of the procedure was excellent; the signal-to-noise ratio (m/z 334) for the lowest calibrator (0.07 mg/L) was 1776:1. The distribution of strychnine in various fluids and tissues are depicted in Table I. No other drugs were detected by GC–MS. A portion of the total ion chromatogram and the mass spectrum obtained using heart blood are depicted in Figure 1. Strychnine eluted at 14.13 min using the GC conditions described. The heart/femoral blood concentration ratio reported in this case was approximately 3. Central/peripheral blood concentration ratios of 1.8 and 15 have been reported by other authors (7,8). The concentrations of strychnine in femoral blood and vitreous fluid were in close agreement (0.31 and 0.36 mg/L, respectively).

Blood strychnine concentrations in a series of 15 fatalities were reported between 0.5 and 61 mg/L (4). Average strychnine concentrations in blood, brain, liver, and urine were 20, 14, 116, and 8.3 mg/L, respectively (4). The relatively low urinary strychnine (2.92 mg/L) in this case is consistent with low urinary concentrations in fatalities reported in the literature. Urinary concentrations in persons surviving strychnine overdose appear to be higher compared with fatalities, likely attributable

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Strychnine Concentration</th>
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<tbody>
<tr>
<td>Femoral Blood</td>
<td>0.31 mg/L</td>
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<tr>
<td>Heart Blood</td>
<td>0.96 mg/L</td>
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<tr>
<td>Vitreous Fluid</td>
<td>0.36 mg/L</td>
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<tr>
<td>Bile</td>
<td>1.17 mg/L</td>
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<tr>
<td>Liver</td>
<td>4.59 mg/kg</td>
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<tr>
<td>Brain</td>
<td>0.86 mg/kg</td>
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<tr>
<td>Urine</td>
<td>2.92 mg/L</td>
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Figure 1. Total ion chromatogram and mass spectrum for strychnine in heart blood extract. Elution order: cholesterol, cholesterol artifact, and strychnine.
to the delay in accumulation of drug in the bladder. The time to
reach peak urinary strychnine concentrations is not known, but
it appears likely that paralysis and death occur relatively quickly.
Most persons do not tolerate more than five convulsive episodes,
each of which may last between 0.5 and 2 min (2). The mecha-
nism of death is usually respiratory arrest secondary to spasm
of the respiratory muscles. Hypoxia, hyperthermia, rhabdomy-
olysis, and acute renal failure are complications from strych-
nine-induced convulsions. The cause of death was attributed to
rodenticide poisoning and the manner of death was suicide.

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Manuscript received April 17, 2003;
revision received July 11, 2003.