CASE REPORT

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A Case of Suicide by Ingestion of Sodium Nitroprusside

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ABSTRACT: The study reports a case of suicide by ingestion of sodium nitroprusside which resulted in acute cyanide poisoning. Analyses carried out on body fluid yielded the quantitation of total (5.00 mg/L) and free (3.30 mg/L) cyanide in blood and of methemoglobin (blood = 10.5%). At the scene, some solid reddish-brown material was found in a glass, which on toxicological analysis was found to contain sodium nitroprusside; about 9 g of the same substance was identified in stomach contents. The detection and quantification of cyanide and methemoglobin in biological samples from the case indicated that the lethal effect was due to both metabolic products (cyanide and methemoglobin).

KEYWORDS: forensic science, forensic toxicology, nitroprusside poisoning, cyanide, methemoglobin

Sodium nitroprusside ($Na_2Fe(NO)(CN)_5$ $2H_2O$) (nitrosylpentacyanoferrate, Niprite) (SNP) is a short-acting iron-nitrosyl hypotensive agent that produces peripheral vasodilatation and reduces peripheral resistance by acting directly on both veins and arteries (1,2). Both effects are attributable to the release of nitric oxide free radicals (3,5). SNP is used in the treatment of hypertensive crisis (2), malignant hypertension (1) and controlled hypotension in anaesthesiology (1), and as an antidote in acute ergotism (6). The chemical appears as a reddish-brown powder, easily soluble in water, and marketed in 5 mL amber-colored vials, each containing 50 mg of the drug; SNP solutions degrade quickly when exposed to light (7).

SNP is therapeutically administered only by slow intravenous infusion at the average adult dose of 3 μg/kg per minute, using a microdrip regulator; during treatment monitoring of the subject's blood pressure and flow rate is absolutely essential (2). It has recently been reported that SNP is also adsorbed at the gastrointestinal level (8).

In man, SNP quickly undergoes nonenzymatic biotransformation, reacting with hemoglobin with the production of methemoglobin and release of free cyanide. The latter highly toxic drug is subsequently transformed to thiocyanate (9). For this reason, in monitoring SNP administration in long-term therapy, plasma levels of cyanide and thiocyanate are used and the nitroprusside concentration is not measured (10).

The toxic effects of SNP are due to its metabolic products (methemoglobin and cyanide) (9). Due to its particular biotransformation and the considerable release of cyanide, several deaths involving the therapeutic administration of SNP have been reported in the literature (9,11–15). The blood cyanide concentration in these cases averaged about 5 mg/L (9). No studies have been found describing lethal cases of SNP poisoning after oral ingestion of the drug.

The symptoms of poisoning start 15 to 30 min after intravenous infusion, with deep hypotension, tonic contractions, vomiting, hyperventilation, and tachycardia, followed by bradycardia and drowsiness, and are similar to the symptoms of cyanide poisoning.

The detection of cyanide in biological specimens was originally carried out using colorimetric techniques with isolation in microdiffusion (16,17). Later, gaschromatographic (18,19), HPLC (20), and GC-MS (21) methods were applied. A specific method to detect cyanide in the presence of nitroprusside is also available (22).

Case History

The decedent was a 41-year-old white woman found dead in her kitchen. Near the body was a brown glass containing 5 g of a solid reddish-brown material and, on the kitchen table, a handwritten note containing words of suicidial intent. The rubbish bin contained a brown glass tube containing 0.120 g of a similar substance. The woman had family problems; she worked as a technician in a chemical laboratory and had free access to chemical reagents.

Autopsy Findings

External examination revealed bright red hypostasis and the absence of other signs. Autopsy showed that the surface of the stomach lining was blackened and eroded. The lumen contained 9 g of a semi-solid reddish-brown material; other organs showed no specific changes. Organs weighed as follows: brain 1190 g, heart 300 g, right lung 410 g, left lung 390, liver 1600 g, spleen 200 g, right kidney 150 g, left kidney 150 g. Histological findings showed massive pulmonary and cerebral edema. Death was attributed to massive pulmonary edema and cardiac arrest. The pathological investigation excluded causes of death not related to poisoning.

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Toxicological Analysis

Sampling and Storage

Biological fluids (blood and stomach contents) were collected during autopsy. One mL of blood and one g of stomach contents were sealed immediately in suitable vials. Several vials for each specimen were prepared in order to repeat analyses at least three times. The vials were stored at −20°C prior to analysis. Blood samples for the detection of methemoglobin were spiked immediately before being sealed, with sufficient amounts of buffer. Samples of nonbiological materials from the glass and tube found at the scene were also collected in the same manner. All the analytical procedures were performed in triple and the results reported were the average of three values.

Preparation of Samples

The procedure of Rodkey and Collison (22) was applied to detect and quantify cyanide in blood. The method of Kruszyna et al. (23) was used to identify methemoglobin. Three different methods, described below, were applied to detect sodium nitroprusside in stomach contents and in nonbiological samples.

Methods

Cyanide—Isolation and determination of free cyanide: 1.0 mL of blood was placed in a 50 mL flask stoppered with inlet and outlet tubes; the outlet tube was connected with a plastic absorption tube containing 2.0 mL of 50 mmol/L NaOH; 1.0 mL of 0.5 mmol/L H_2SO_4 was added by syringe to the reaction mixture, and a slow flow of nitrogen was then sent through the vessel to sweep the HCN into an NaOH trap. After removal of the stoppers from the absorption tube, the droplets of alkali on the walls were forced to the bottom by centrifugation. The tubes were cooled in an ice bath and 0.2 mL of Chloramine T-phosphate reagent were added. After 5 min, 3.0 mL of pyridine/pyrazolone were added and the mixture was kept at room temperature for 30 min. Absorbances of solutions were read at 620 nm with "blank" solutions as references. The concentration of free cyanide was calculated from the equation of Rodkey and Collison (22).

Determination of Total Cyanide—1.0 mL of blood was placed in a 50 mL flask and added with 0.3 mL of methemoglobin (50 g/L) and 1.0 mL of cysteine (5 mg/mL) solutions, both prepared as proposed by Rodkey and Collison (22); the flask was stoppered with inlet and outlet tubes, and the mixture was incubated at room temperature for 1 h. After this time, the outlet tube was attached to the absorption tube. Determination of cyanide was then carried out spectrophotometrically, as described previously. The resulting value represented total cyanide.

Calculation of Nitroprusside Concentration (SNP)—This was calculated following the equation: SNP = (total-CN − free-CN)/5. A factor of 5 was used because each mmole of nitroprusside yields 5 mmoles of combined cyanide (22). To convert the result in mg the number of mmoles/L of SNP obtained from the equation was multiplied by the number of mgSNP/mmoleSNP. The difference, total-CN − free-CN, represents the combined CN (CN released from nitroprusside during analysis).

Methemoglobin—0.1 mL of blood was added to 2.4 mL of phosphate buffer 0.1 mol/L. A twofold excess of CN was added to bind any methemoglobin present, and absorbance was read at 576 nm. A twofold excess of potassium ferricyanide was then added and absorbance was again measured. The concentration of methemoglobin was calculated according to the extinction coefficents resulting from the equations of Kruszyna et al. (23).

Detection of Sodium Nitroprusside in Stomach Contents and Nonbiological Samples.

a) 1 g of stomach contents, 1 g of material found in the glass, and all material in the tube found in the rubbish bin were added to 1 mL of distilled water. The solutions were diluted 1/1000 in water and submitted to the procedure previously reported for evaluation of free cyanide, total cyanide, and nitroprusside (23).
b) Separately, 700 mg of stomach contents and 700 mg of the material in the glass were added to 100 mL of distilled water. The solutions were directly submitted to spectrophotometric detection, which showed an absorbance peak at 395 nm, an absorbance shoulder at 510 nm, and a minimum at 370 nm. The absorbance curve was compared with that for nitroprusside standard (24).
c) 5 mg of the material in the glass and 5 mg of stomach contents were separately added to 2 mL of distilled water, 2 drops of acetone and 0.5 mL NaOH 2 N; an orange color developed; 2 mL of acetic acid were added and the color was seen to change to deep purple (24).

Results

Results from blood samples are listed in Table 1. The blood level of total cyanide was 5.0 mg/L, free cyanide 3.30 mg/L, and combined cyanide released from nitroprusside 1.7 mg/L. The concentration of nitroprusside was calculated at 4.073 μg/L according to the equation of Rodkey and Collison (22). Methemoglobin was 10.5%.

Results from nonbiological samples are listed in Table 2. The amount of nitroprusside calculated in the tube material was nearly 100% in weight (894 mg/g); that in the glass was a little less (871 mg/g). The amount calculated in stomach contents was 639 mg/g and that of nitroprusside ingested nearly 6 g. The methods previously reported under (b) and (c) qualitatively confirmed the presence of nitroprusside in the material (from from glass and stomach).

Toxicological screening for basic, acid, and neutral drugs in blood and stomach contents and the blood alcohol determination gave negative results.

Discussion

The results allowed us to identify and quantify cyanide and methemoglobin in blood and to calculate the presence of nitroprusside in blood, stomach contents, and nonbiological specimens found at the scene. Rodkey and Collison's procedure to evaluate total and free cyanide quantified both the real amount of cyanide released into the body prior to death and the amount of cyanide freed from nitroprusside during the analytical procedure as an expression

TABLE 1—*Results from blood samples.*

	Total CN*	Free CN*	Combined CN*	Methemoglobin†
Blood	5.0	3.3	1.7	10.5

* In mg/L.
† % of total.

TABLE 2—*Results from stomach contents and nonbiological samples.*

	Total CN*	Free CN*	Combined CN*	Nitroprusside*
Stomach Contents	420.9 (total 3788 mg)	150.5 (total 1354 mg)	270.4 (total 2434 mg)	639 (total 5751 mg)
Material from Tube	430.8	40.6	390.2	894
Material from Glass	425.2	45.1	380.1	871

*In mg/g.

of its presence. In blood, more than two-thirds of the cyanide was free, due to release from nitroprusside immediately after absorption and before death (in vivo release). The method of Kruszyna et al. to detect methemoglobin allowed only the measurement of this pigment derived from hemoglobin, without interference by the cyanide present in the samples. The values of free cyanide in blood (3.3 mg/L) and methemoglobin indicated that death was due to both toxic substances, particularly to cyanide.

Some findings made during pathological examination of the body (bright red color of hypostasis, blackened and eroded surface of stomach lining) confirmed this diagnosis. The results of toxicological analysis on nonbiological materials indicated that SNP was present in all specimens. The chemical showed considerable stability in the tube and glass, probably due to the particular conditions of preservation (in brown glass and at night). Results from stomach contents indicated partial release of cyanide from nitroprusside, probably due to the acidity of gastric fluid.

Conclusions

The whole set of anatomopathological and toxicological data allowed us to attribute death to acute poisoning by orally ingested nitroprusside. The overall toxic effect was due to the metabolic products of the chemical, cyanide, and methemoglobin.

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