JOURNAL OF FORENSIC SCIENCES

J Forensic Sci, January 2012, Vol. 57, No. 1
doi: 10.1111/j.1556-4029.2011.01907.x
Available online at: onlinelibrary.wiley.com

CASE REPORT

TOXICOLOGY

Elisabetta Bertol,[1] *Ph.D.; Lucia Politi,*[1] *Ph.D.; and Francesco Mari,*[1] *Ph.D.*

Death by Potassium Chloride Intravenous Injection: Evaluation of Analytical Detectability

ABSTRACT: Potassium chloride intravenous injection is used in suicide attempts and lethal procedures for state-sanctioned punishment. Owing to its relatively high concentrations in hemolyzed blood (25–80 mM) compared to serum (about 4 mM), it is difficult to conclude potassium poisoning by postmortem analysis of biologic samples. A 41-year-man was found dead with an injection sign on his foot and a syringe close to the corpse. No particular signs were noted during the autopsy. Blood, bile, and urine were submitted to xenobiotic screening procedures used in the laboratory. Syringe content was found positive to potassium ions. Blood potassium concentration was determined by ion-selective electrode measurement (range 3.0–150 mM). Blood was found positive for diazepam at therapeutic level. Potassium concentration was 160.0 (cardiac) and 87.3 mM (femoral blood). Our results show that potassium concentration was significantly higher in heart blood in a suicide case. Hence, the general issue of considering potassium poisoning hardly demonstrable by toxicology needs to be questioned and thoroughly studied.

KEYWORDS: forensic science, toxicology, potassium chloride, intravenous injection, suicide, potassium blood concentration

The most abundant intracellular cation, potassium, is fundamental in maintaining the osmotic balance between cells and interstitial fluid. Potassium can be used therapeutically in the treatment of muscular weakness, metabolic alkalosis, disorders of acid–base or fluid balance, gastric antacid, or urine acidifier (1,2), even in intensive care treatments. Beside the clinical practice, potassium chloride intravenous injection is reported as a means in suicide/homicide attempts or in lethal procedures for state-sanctioned capital punishment. Deleterious effects on the electric activity of the heart are the most important consequences of hyperkalemia, involving profound depression in impulse generation and conduction in all cardiac tissues and eventual asystole (1), which usually happens at potassium plasma concentration of 8–9 mM. On the other hand, as intracellular potassium represents 98% of total body potassium (3), its concentration in hemolyzed blood is relatively high (25–84 mM [2]) as compared to serum in physiologic conditions (about 4 mM). Owing to this reason, it is problematic to undertake potassium poisoning by postmortem analysis of biologic samples (4,5). Thus, death by potassium intravenous injection has been considered unperceivable by toxicological analyses when only hemolyzed blood is available. As a consequence and considering that suicidal self-poisoning cases are only rarely reported (6,7), literature is relatively scant.

In considerations of the results of the determination of blood potassium in a case of suicide by potassium poisoning, the meaning of blood potassium concentration is questioned and discussed. In particular, more thorough studies would be able to resolve the dilemma of endogenous versus exogenous potassium concentration in hemolyzed blood through the definition of a "baseline" of potassium level in the cadaveric specimen.

Case Report

A 41-year-old man, working as a nurse at the Hospital Intensive Care Unit (where he had access to all the drugs used, including potassium chloride 2 mmol/mL, 10 mL), was found dead at his workplace, and resuscitation protocol was used with no results.

At the external examination, the left sock was partially removed and a puncture sign was observed on his left foot (Fig. 1). Close to the corpse, a 20-mL syringe for intravenous injections was retrieved, while other paraphernalia (butterfly blood collection set with the tube full of blood and its plastic wrap) were found to have been discharged after using in the water in the toilet. This finding testifies that, in all likelihood, death was not immediate. At the autopsy and histological examinations, no other particular signs were noted.

Materials and Methods

The biologic specimens collected during the autopsy (blood, bile, and urine) were submitted to the screening procedures for drugs and poisons in use in the laboratory. Before analysis, all samples were kept at −20°C for a maximum of 3 weeks. No preservatives were used. Vitreous humor was not collected during the autopsy.

Blood, bile, and urine were analyzed by the general unknown screening based on solid-phase extraction (SPE) (Bond Elut Certify cartridges; Varian, Harbor City, CA): 2 mL each was submitted to an extraction for acidic and neutral substances and, separately, to an extraction for basic substances (from [8] with minor modifications). Before SPE procedure, the urine sample was submitted to enzymatic hydrolysis with overnight β-glucuronidase incubation.

[1]Division of Forensic Toxicology, Department of Anatomy, Histology, and Legal Medicine, University of Florence, Viale Morgagni 85, 50134 Firenze, Italy.

Received 6 July 2010; and in revised form 22 Sept. 2010; accepted 21 Nov. 2010.

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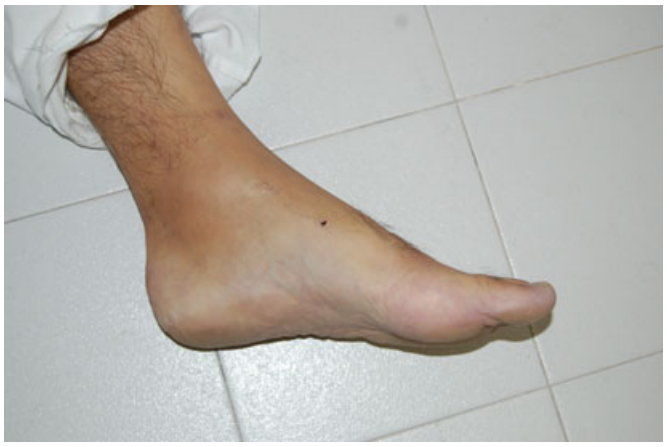

FIG. 1—*Left foot of the man with puncture sign.*

Nalorphine, eptabarbital, and pinazepam were used for internal stardardization. The extracted samples were injected with and without trimethylsilyl derivatization (using either *N*-methyl-*N*-trimethylsilyltrifluoroacetamide or methanol) in the gas chromatography mass spectrometry (GC-MS) system (Agilent 7890A and 5975C; Agilent Technologies, Palo Alto, CA) working in scan mode from 40 to 600 amu. Blood was also submitted to head-space gas chromatography for the detection of ethanol and other volatile compounds.

The urine sample was tested by an EMIT equipment (Siemens Viva-E®; Siemens Healthcare Diagnostics, Camberley, U.K.) for opiates (cutoff = 0.3 mg/L), cannabinoids (cutoff = 0.05 mg/L), cocaine metabolite (cutoff = 0.3 mg/L), amphetamines (cutoff = 0.5 mg/L), methylendioxy-methylamphetamines (cutoff = 0.5 mg/L), methadone (cutoff = 0.3 mg/L), barbiturates (cutoff = 0.3 mg/L), buprenorphine (cutoff = 0.005 mg/L), and benzodiazepines (cutoff = 0.2 mg/L).

Blood and urine also underwent the quantification procedure for benzodiazepines in use in the laboratory, by liquid–liquid extraction and GC-MS analysis in selected ion monitoring (three ions per compound: *m/z* 256, 283, 221) with pinazepam as internal standard (*m/z* 280, 307, 91). The extraction was performed using a mixture toluene/dichloromethane (9:1, 5 mL) after pH stabilization at 9.0 of 2 mL of the sample. The organic phase was evaporated, reconstituted in methanol (50 μL), and injected in the GC-MS.

The content of the 20-mL syringe found in proximity of the corpse was submitted to Feigl spot tests for inorganic ions and, in particular, for potassium (9). The tube and other paraphernalia were not tested because of the contamination with the water in the toilet before collection.

Finally, blood potassium concentration was determined by ion-selective electrode (ISE) measurement (Konelab™; Thermo Electron, San Jose, CA), which is linear over the range from 3.0 to 150 mM (calibrators at 3.0, 4.5, 6.0, 150.0 mM) according to the manufacturer's instructions. ISE analyzer uses a direct potentiometry technique for electrolyte measurement (10).

Results and Discussion

According to GC-MS screening procedure and library search, blood was found positive for diazepam and its main metabolite desmethyldiazepam. The blood sample was then submitted to benzodiazepines confirmation method, diazepam was confirmed, and its quantification resulted in 0.21 mg/L. This value is much lower than those reported in fatal intoxication cases (20 mg/L [2]) and recognizable as a low therapeutic concentration. Also, in good accordance with this result, the urine specimen tested positive for benzodiazepines at EMIT assay and GC-MS confirmation method permitted to quantify diazepam at 12.0 mg/L. Desmethyldiazepam was identified in both blood and urine.

No other drugs of abuse, pharmaceuticals, or poisons were found by the screening methods in blood or urine. The bile sample tested negative to the procedure. The investigations performed on the content of the syringe found in proximity of the corpse highlighted a high concentration of potassium, not quantifiable by Feigl tests (9).

By ISE analysis, potassium concentration was found at 160.0 mM in cardiac blood and at 87.3 mM in femoral blood. Both mean values were determined in triplicate, and also, in order to avoid measurement imprecision because of matrix effect, blood samples were analyzed after various dilutions in deionized water (1:2, 1:4, 1:8, and 1:16). Results of the different dilutions were consistent for both cardiac and femoral blood (standard deviation: 6.5% and 3.4%, respectively). It is interesting to note the significantly higher concentration of cardiac blood compared to femoral was probably due to celerity of death as expected in the case of potassium injection. This fact and the finding of injection paraphernalia discharged in the toilet bowl in all probability account for a very short period of conscious time after introduction of potassium in the vein and, as soon as injection bolus reached the heart, for a death faster than distribution in the vascular system.

During lifetime, potassium is kept inside the cell by the Na^+/K^+-ATPase pump and blood hemolyzation occurring after death might be considered responsible for high potassium concentration in autopsy blood. Owing to this reason, discrimination of endogenous potassium (of both intra- and extracellular origin) from exogenous potassium in hemolyzed blood is regarded as particularly difficult, and hence, fatal potassium poisoning has been considered difficultly discernible by analysis of hemolyzed postmortem specimen (2). In this respect, average potassium concentration in the dead was experimentally determined: 55 autopsy samples of femoral blood, randomly chosen from cases with no toxicological involvement in the cause of death and heterogeneous in consideration of gender, age, and weight, were submitted to potassium determination. All samples were completely hemolyzed because of storage conditions (−20°C for 1–4 months). Potassium concentration was found between 27.2 and 50.1 mM (median: 35.3 mM, mean: 36.2) in a relatively narrow range (standard deviation: 16.26%). According to our results, the baseline for potassium level in hemolyzed blood, including endogenous potassium of intra- and extracellular origin, is in the interval from 27.2 to 50.1 mM. This finding is in good accordance with the literature where potassium concentration in postmortem blood is in the range 25–84 mM (2).

Our analytical results sustain that heart and femoral blood of this case had much higher potassium concentration compared to both experimental results of nontoxicological deaths (27.2 and 50.1 mM) and the exogenous origin of a significant part of the potassium ions is therefore assumable.

Comparison of blood and vitreous humor potassium concentration could not be performed in this case, because vitreous humor was not collected during the autopsy. However, owing to the significance of vitreous humor data in potassium intoxications (11), further reports would be significant to corroborate the relevancy of blood data.

Finally, it is interesting to note the consistency of potassium concentration in heart blood of this case (160.0 mM) with the perimortem determination of 162 mM reported by Swanson (12) in a

case of execution by intravenous infusion of 100 mmol of potassium chloride.

Conclusions

Death by potassium intravenous injection is often considered undetectable by analytical toxicology when only hemolyzed blood is available, and consequently, literature is poor of analytical data. Our result shows how potassium concentration was significantly high in heart blood in a case of suicide by potassium chloride intravenous injection when compared to the average potassium concentration in the dead. This result might be of relevancy in the identification of death by potassium in cases without any circumstantial indications, and also, the general issue of considering potassium poisoning hardly demonstrable by toxicology laboratories needs to be questioned and thoroughly studied. In addition, histopathological studies might be a precious support in the definition of the cause of death (5), as well as exhaustive control of the death scene (13).

Finally, to discriminate potassium chloride exogenous administration, a baseline for potassium level in hemolyzed blood in the interval from 27.2 and 50.1 mM was proposed for the first time.

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Additional information and reprint requests:
Elisabetta Bertol, Ph.D.
Division of Forensic Toxicology
Department of Anatomy, Histology, and Legal Medicine
University of Florence
Viale Morgagni 85
50134 Firenze
Italy
E-mail: elisabetta.bertol@unifi.it