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Fatal intravenous injection of potassium: Is postmortem biochemistry useful for the diagnosis?

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ABSTRACT

Fatal cases of potassium overdoses have traditionally been considered indemonstrable due postmortem biochemical investigation limits (mainly potassium determination in postmortem serum and vitreous humor). Nevertheless, some authors have expressed a divergent opinion over the years based on the results of their own investigations. In this study, we investigated left vitreous, right vitreous, postmortem serum from peripheral blood, postmortem serum from cardiac blood, urine, pericardial and cerebrospinal fluid potassium concentrations in 21 forensic autopsy cases. One of these was a case of accidental, fatal intravenous potassium injection in a hospitalized patient. The other twenty cases were subjects with various causes of death unrelated to potassium administration and comparable postmortem intervals. Our aim was to assess whether postmortem biochemical investigations performed in several biological samples may be useful in diagnosing exogenous potassium administration. No statistically significant differences were observed between the measured concentrations in the fatal case of potassium intravenous administration and the control cases in any of the tested samples. Potassium concentrations in the investigated case of exogenous potassium injection were within the range of those measured in the control cases, irrespective of the tested biological sample. Our findings corroborate the conclusions of former authors who highlighted that circumstantial evidence provides the greatest diagnostic contribution in situations of suspected potassium poisoning. This is due to the objective limitations demonstrated by postmortem biochemical investigations in such cases, even when potassium measurements are carried out in several biological samples of satisfying quality and within a relatively short postmortem interval.

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1. Introduction

The potassium ion is an essential electrolyte present in all tissues and body fluids in mammals. Its plasma levels are normally maintained within narrow limits (typically, 3.5–5.0 mEq/l) by multiple mechanisms that collectively make up potassium homeostasis [1,2].

Strict maintenance of equilibrium between intracellular and extracellular potassium concentrations is essential for a broad array of vital physiologic processes. These include resting cellular-membrane potential as well as the propagation of action potentials in neuronal, muscular, and cardiac tissue, along with hormone secretion and actions, vascular tone, systemic blood pressure control, gastrointestinal motility, acid–base homeostasis, glucose and insulin metabolism, mineralocorticoid action, renal concentrating ability, and fluid and electrolyte balance [2,3].

The importance of potassium homeostasis is highlighted by the well-recognized finding that patients with hypokalemia or hyperkalemia experience an increased death rate from any cause. Serious acute cardiac arrhythmias and conduction abnormalities possibly resulting in sudden death are the most important manifestations of hyperkalemia (defined as serum potassium levels greater than 5.5 mEq/l), involving profound depression in impulse generation and conduction in all cardiac tissues as well as eventual asystole. This usually occurs at potassium plasma levels of 8–9 mEq/l [1–5].

Although fatal intravenous injections of potassium in the hospital setting are rare, they may occur due to pharmacy errors in solution preparation, nursing errors in medical administration, or intentional injection. In the forensic setting, potassium

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measurement in blood or postmortem serum is considered unsatisfactory because cell lysis releases intracellular potassium. This means that death by potassium intravenous injection is often considered undetectable when only hemolyzed blood is available. In addition, vitreous potassium is considered unreliable as an indicator of antemortem plasma potassium and therefore of minimal value in the diagnosis of exogenous potassium administration. This is due to the fact that potassium leaks from the retina rapidly after death. Furthermore, specimen contamination with retinal cells is also a recognized source of falsely raised vitreous potassium concentrations [3,6–9].

We investigated left vitreous, right vitreous, postmortem serum from peripheral blood, postmortem serum from cardiac blood, urine, pericardial and cerebrospinal fluid potassium concentrations in order to assess whether postmortem biochemical investigations performed in several biological samples may be useful in diagnosing exogenous potassium administration. A case of fatal intravenous potassium injection due to a nursing error in medical potassium administration was chosen as a starting point in our study. This was a hospitalized patient who underwent medico-legal investigations immediately after death. We also studied a series of control cases with various causes of death and comparable postmortem intervals who similarly underwent medico-legal investigations immediately after death.

2. Materials and methods

2.1. Study design and study populations

The present study was designed as a single center study. All collected cases had underdone medico-legal autopsies as requested by the inquiring authorities (the public prosecutor). Laboratory analyses were performed as part of the medico-legal investigations.

A total of 21 forensic autopsy cases (15 males and 6 females) with a mean age of 39.6 years (range 23–73 years) were selected and included in this study.

One of these was a case of accidental, fatal intravenous potassium injection in a hospitalized patient.

Due to a nursing error, the patient received 30 mmol potassium chloride in 10 ml solution with direct intravenous administration and was found dead in his bed 30 min post potassium injection.

The corpse was immediately transferred to the local medico-legal center and was not refrigerated. The postmortem interval, defined as the interval between death and the first biological sample collections (vitreous humor, cerebrospinal fluid and postmortem serum from femoral blood), was 4 h and 45 min. Collected and analyzed postmortem samples for potassium measurement included left vitreous humor, right vitreous humor, postmortem serum from peripheral blood, postmortem serum from cardiac blood, urine, pericardial and cerebrospinal fluids.

The other twenty cases were subjects with various causes of death unrelated to potassium administration. These subjects had not been treated with potassium at the time of death nor had any medical history of hypo- or hyperkalemia. Personal data were collected from clinical patient databases and medical records obtained from general practitioners and local health services. Intervals between death and biological sample collections ranged from 5 to 7 h. The corpses were not refrigerated prior to postmortem examination. Case inclusion criteria consisted of postmortem interval (not exceeding 7 h) and availability of all biological samples during autopsy.

The causes of death included hanging, drug intoxication, and natural diseases (sudden deaths in subjects with various degrees of coronary atherosclerosis, with or without acute coronary thrombosis and/or myocardial infarction). Cases with known or suspected ocular diseases, localized trauma or head injury involving the orbital area were excluded as were those in which the vitreous were contaminated with blood and/or tissue.

2.2. Postmortem investigations

Medico-legal autopsies, histology, toxicology and postmortem biochemical investigations were performed in all cases. Medical records and clinical histories as well as police reports pertaining to each case were consistently reviewed before conclusions were made. Conventional autopsies were jointly performed by two forensic pathologists (at least one board-certified) as in accordance with both local standards and international guidelines for medico-legal autopsies. Conventional histology was systematically performed and included hematoxylin–eosin (HE) stain of brain, heart, lung, liver and kidney samples. Systematic toxicological analysis based on the use of chromatographic techniques and mass spectrometry was systematically carried out.

Biochemical investigations systematically included potassium determination in all collected fluids, measured by indirect potentiometry with ion-selective electrodes.

2.3. Sample collection

Biological samples for biochemical investigations were collected as soon as possible after corpse arrival at the morgue (vitreous humor, cerebrospinal fluid and postmortem serum from femoral blood) and during postmortem examination (pericardial fluid, urine and postmortem serum from cardiac blood). All samples were transferred to the laboratories immediately post collection and analyzed immediately.

Undiluted vitreous humor samples (between 1 and 3 ml) were obtained by aspiration using a sterile needle and syringe. Right and left vitreous samples were collected separately through a scleral puncture at the lateral canthus and gently aspirated from the center of each eye. In all cases, vitreous appeared clear without veils or strands. After collection, vitreous samples were immediately centrifuged at $3000 \times g$ for 15 min. The separated supernatant was collected and stored in preservative-free tubes. No specimens were excluded due to insufficient sample volume. No specimens were excluded due to contamination by tissue fragments.

Undiluted cerebrospinal fluid samples were collected by aspiration using a sterile needle and syringe by suboccipital puncture immediately prior to autopsy. All samples appeared clear without veils or strands. No specimens were excluded due to blood contamination. All samples were immediately centrifuged at $3000 \times g$ for 15 min. After centrifugation, the separated supernatant was collected and stored in preservative-free tubes. No specimens were excluded due to insufficient sample volume.

Femoral blood samples were collected from the femoral vein(s) immediately prior to autopsy. Blood was drawn by aspiration using a sterile needle and syringe after clamping the vein(s) at the proximal end and lifting the lower limb(s) for several minutes. Femoral blood was immediately stored in serum separator tubes and centrifuged immediately post collection at $3000 \times g$ for 15 min. After centrifugation, the separated supernatant (postmortem serum, between 1 and 5 ml) was collected and stored in preservative-free tubes. Postmortem serum hemolysis was evaluated by direct observation and recorded as follows: 0, no hemolysis; 1, slight; 2, moderate; and 3, severe hemolysis. All samples were pink tinged, suggesting the presence of slight hemolysis. No specimens were excluded due to insufficient sample volume.

Undiluted samples of pericardial fluid were collected during autopsy immediately post pericardium incision using a sterile needle and syringe. All samples appeared clear and were

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