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Case Report

Pentobarbital in the context of possible suicides: Analysis of a Case

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ABSTRACT

Pentobarbital is a barbiturate, acting as a central nervous system depressant (CNS), being used for its anticonvulsant, sedative, hypnotic and anaesthetic properties. Barbiturates were replaced by benzodiazepines, leading to a decrease in poisoning cases with these compounds. However, pentobarbital is still used in many countries as an anaesthetic in veterinary medicine. Due to its properties, this compound is sought after by people who wish to commit suicide, acquiring it on the black market.

The authors present an unusual fatal pentobarbital intoxication case, in a 37 years-old male salesperson, with no known connection with the veterinary field, being more difficult to obtain this compound.

Toxicological results in cardiac blood revealed the presence of pentobarbital (111 mg/L), ethanol (0.94 g/L), diazepam (33 ng/mL), nordiazepam (50 ng/mL), oxazepam (3.3 ng/mL), temazepam (5.3 ng/mL), and metoclopramide. No illicit drugs were detected.

Pentobarbital analysis in urine and gastric content was also positive, as well as its presence in the glass powder and in the bottle residue sent to the laboratory.

In the present case, it was possible to conclude that the death was a suicide due to pentobarbital intoxication in association with other depressants of the CNS (benzodiazepines and ethanol).

It is important to search pentobarbital in routine toxicological analyses, since it is one of the drugs most frequently mentioned by entities defending "painless death", advising the simultaneous use of metoclopramide for emesis avoidance.

1. Introduction

Barbiturates, derivatives of barbituric acid, are one of the oldest classes of general central nervous system (CNS) depressants. Various barbiturates are still available, indicated as sedative-hypnotics, anticonvulsants, in migraine therapy, and for reduction of cerebral oedema secondary to head trauma. The general barbiturate structure has multiple modification sites to produce the various therapeutic barbiturate analogs [1]. The characteristic signs and symptoms of barbiturate poisoning are the depression of the CNS and of the cardiovascular systems. Severe intoxication led to coma, followed by death, frequently due to cardio respiratory arrest [2]. The use of barbiturates as sedative-hypnotic agents has declined over time, being replaced by safer drugs, such as benzodiazepines and leading to a decrease in clinical prescriptions [1,2]. However, even though barbiturates are legally available only under prescription, the street use of these compounds still continues [2].

Pentobarbital is a short-acting barbiturate that was first synthesized in 1928, being available both as a free acid and as a sodium salt, this last one being freely soluble in water [3,4]. It has been used as a sedative-hypnotic agent and to relieve intracranial pressure in head trauma cases [1,5]. Accidental and volunteer overdoses caused by short-acting barbiturates in humans have become rare, since these molecules became commercially unavailable as sleeping drugs/hypnotics [6]. In many countries, Pentobarbital is no longer used in human therapeutics. However, it

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is still used in veterinary medicine and for animal euthanasia purposes, as an anaesthetic. In some countries where euthanasia is legal, pentobarbital is frequently used in assisted suicide [7–9].

We report a deliberate overdose with Pentobarbital, associated to the intake of benzodiazepines, metoclopramide and ethanol.

2. Case report

A 37 years-old male salesperson was found dead at home, sitting on the couch. He had not been seen by anyone for 4 days. At the death scene, a glass with a spoon containing a white powder residue, and a bottle also with a white powder residue were found close to the body (Fig. 1). A metoclopramide box was also found at the scene. There was no written note found.

The autopsy was carried out 24 h after the discovery of the corpse, at the Forensic Pathology Service of the North Branch of the Portuguese National Institute of Legal Medicine and Forensic Sciences (INMLCF). Histological examinations were required, as well as toxicology analysis. For toxicological investigations, cardiac blood (preserved with sodium fluoride), urine, and gastric content were collected at the autopsy, and were sent to the Forensic Toxicology Laboratory. The glass and the bottle, both containing a white powder residue, and the "Primperam" box were also sent for toxicological analysis.

Ethanol analysis, illicit drugs and therapeutic drugs were required after medico-legal autopsy.

3. Material and methods

3.1. Toxicological analyses

Ethanol was analysed by Head-Space/Gas Chromatography with flame ionisation detection (GC/HS-FID). The screening of medicines was carried out on a GC/MS technique with a simple quadrupole mass analyzer. The screening of illicit drugs (opiates, cocaine and metabolites, amphetamines, methamphetamines, and cannabinoids) and of benzodiazepines was performed by EIA immunoassays. The confirmation and quantification of benzodiazepines and pentobarbital was performed by Liquid Chromatography–Mass Spectrometry (UPLC/MS–MS) after a solid phase extraction (SPE) procedure with Oasis HLB columns (3 cc, 60 mg). Table 1 describes the UPLC/MS/MS main conditions.

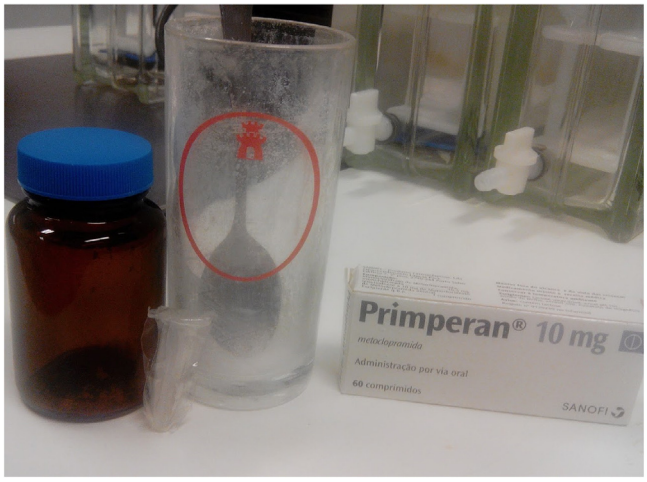

Fig. 1. Material sent to the laboratory.

3.2. Materials, standards and chemicals

Pure Pentobarbital and deuterated internal standard (Pentobarbital-D_5) were purchased from Lipomed AG (Arlesheim, Switzerland). Each standard, dissolved in methanol (1 mg/mL), was stored at −20 °C.

All solvents were analytical or HPLC grade and were purchased from E. Merck (Algés, Portugal). The mobile phase for Liquid Chromatography was LC–MS grade and filtered with a 0.20 μm Schleicher & Schuell filter and degassed in an ultrasonic bath for 15 min just before use.

3.3. Sample preparation for pentobarbital quantification

Control and calibration standards were prepared by spiking drug-free whole blood samples (100 μL) with standards at concentrations ranging from 0.1 to 10 mg/L. A SPE procedure with Oasis HLB columns (3 cc, 60 mg) was used to isolate pentobarbital, using 100 μL of sample (cardiac blood, urine and gastric content).

3.4. Pentobarbital quantification by UPLC–MS/MS

Pentobarbital analysis was carried out on a Waters Acquity UPLC separation module (Waters, Milford, MA, USA). The chromatographic separation was performed through a Waters Acquity UPLC HSS T3 column (100 × 2.1 mm, 1.8 μm), at 35 °C, using a gradient elution with formic acid 0.1% and acetonitrile at a flow rate of 0.5 mL/min. The UPLC system was combined with a TQD detector (triple quadrupole mass spectrometer, Waters, Milford, MA, USA) equipped with an electrospray ionization source, operating at negative mode. System operation and data acquisition were controlled by MassLynx™ software (version 4.1 SCN 919). Pentobarbital confirmation analysis was obtained through Multiple Reaction Monitoring (MRM) with two transitions (225.1 m/z–42.1 m/z and 225.1 m/z–182.2 m/z) for the analyte, and one for the internal standard, pentobarbital-D_5 (230.2 m/z–42.0 m/z) (Fig. 2).

4. Results and discussion

Toxicological results in cardiac blood revealed the presence of pentobarbital (111 mg/L), ethanol (0.94 g/L), diazepam (33 ng/mL), nordiazepam (50 ng/mL), oxazepam (3.3 ng/mL), temazepam (5.3 ng/mL), and metoclopramide (qualitative result), but no illicit drug was detected. The analysis of urine and gastric content also revealed positive results for pentobarbital. The chemical analysis of the powder residues in the glass and in the bottle sent to the laboratory revealed the presence of pentobarbital.

Pentobarbital has disappeared in human medicine several years ago and has, therefore, become rare as a suicide drug [10]. In fact, in recent years, suicide poisoning with drugs used for animal euthanasia is not usual [11], but there are some described cases in the literature [10,12–15], where the reported concentration of pentobarbital in blood was lower than the concentration found in our case.

In a suicide case of pentobarbital intraperitoneal injection, the authors detected pentobarbital in femoral and cardiac blood (36 and 15 mg/L, respectively) [10]. Another study reported a suicide case with pentobarbital oral administration with a peripheral blood concentration of 21.4 mg/L [12]. Cantrell et al. reported two fatal self-poisoning cases with pentobarbital, and their results revealed a peripheral blood concentration of 8.6 mg/L and 27 mg/L. The authors also reported pentobarbital intoxication in a victim that had a complete recovery (pentobarbital blood concentration of 24.4 mg/L in the first day of analysis) [13]. Another study reported a suicide by pentobarbital injection with