Case Report

Concentrations of Heroin, 06-Monoacetylmorphine, and Morphine in a Lethal Case Following an Oral Heroin Overdose

Pok P. Rop*, Monique Fornaris, Thierry Salmon, Joelle Burle, and Mireille Bresson
Laboratoire de Police Scientifique, 97, boulevard Camille Flammarion–13248, Marseille 04, France

Abstract

A case of lethal overdose by heroin ingestion is presented. The concentrations of drugs were measured several hours after death. Heroin, 06-monoacetylmorphine, and morphine were identified and quantitated in blood, urine, and gastrointestinal contents by gas chromatography–mass spectrometry and high-performance liquid chromatography. Concentrations of heroin, 06-monoacetylmorphine, and morphine were 109, 168, and 1140 ng/mL, respectively, in blood and 17, 12, and 425 ng/g, respectively, in gastrointestinal content. In urine, however, only morphine was detected at 3650 ng/mL.

Introduction

Heroin (diacetylmorphine) is an ester compound. It is known to be unstable in vivo and in vitro. It is readily absorbed into the body after oral administration or injection. In organisms, heroin is rapidly hydrolyzed to 06-monoacetylmorphine and morphine. Because of its rapid hydrolysis, heroin is difficult to detect. The drug can be detected in blood 2 min after an intravenous dose of 4 to 5 mg, but it declines to a blood concentration of less than 10 ng/mL within 10 to 15 min (1). After smoking 3.5–10.5 mg of heroin base, peak concentrations were achieved within 5 min and ranged from 14 to 140 ng/mL (2). The estimated minimum lethal dose is 200 mg, but addicts may be able to tolerate up to ten times as much drug (3).

Several papers summarize fatal intoxication of heroin. Relation drug concentration and fatality were also established but were only expressed as morphine because heroin is decomposed rapidly and the main break-down product formed is morphine. Other drugs, such as codeine, pholcodine, ethylmorphine, and dihydrocodeine are also metabolized to morphine (4–6). In several fatal cases where a heroin overdose was strongly suspected to be the cause of death, heroin and 06-monoacetylmorphine were absent. There is the risk of overlooking the cause of death. This report represents the first case of a fatality in an oral heroin overdose that we encountered. It documents the analytical findings of heroin, 06-monoacetylmorphine, and morphine in blood, gastrointestinal contents, and urine.

Case History

A 40-year-old man had a long history of heroin abuse and drug trafficking. He was placed in a detention center where he received medical care. The prisoner was suspected to have dealings with other drug traffickers in order to obtain heroin while in the center. Every evening before being locked up in his cell, he was searched for drugs. One evening during the search, he tried to hide a sachet of heroin by swallowing it. He was observed and questioned by the guard. According to his declaration, it was a capsule of bromazepam (Lexomil®). He was found dead in his cell the next morning. An autopsy was performed shortly after the body was discovered. Toxicologic analyses on blood, urine, and gastrointestinal contents are described.

Experimental

Instrumentation

The analyzed compounds were identified by gas chromatography–mass spectrometry (GC–MS). The system was a Hewlett-Packard 5890 series II GC with a 5971 mass selective detector. The mass selective detector was used in the electronic impact mode. The ionization voltage was 70 eV. The DB-5 MS capillary column (15 m × 0.25-mm i.d., 0.25-μm coating, J&W Scientific, Folsom, CA) was connected to the mass selective detector. Helium flow was 30 mL/min through the column. The temperature program was as follows: 70°C for 1 min, increased 25°C/min to 170°C, then to 290°C at 5°C/min. The injector and detector temperatures were 280 and 300°C, respectively. Derivatization of morphine and 06-monoacetylmorphine was realized with N,O-bis-trimethyl-
silyl trifluoroacetamide–trimethylchlorosilane (BSTFA–TMS) at 70°C. Like heroin, 06-monoacetylmorphine can be analyzed without derivatization. Heroin, 06-monoacetylmorphine, and morphine were then quantitated by high-performance liquid chromatography (HPLC) based on our previously described method (7) with some modifications. The previous method used electrochemical detection for measuring 06-monoacetylmorphine and morphine. In this work, ultraviolet detection at 220 nm was employed because heroin was electrochemically inactive.

Sample preparation

The sample (i.e., blood, 1 mL; urine, 1 mL; or gastrointestinal contents, 1 g) was taken into a 5-mL glass tube. Three milliliters of distilled water and 10 μL of nalorphine hydrochloride (internal standard) in methanol (0.1 μg/μL) were added. After vortex mixing for 1 min, the mixture was pipetted into a Toxi-Tube® extraction tube (Toxi-Lab, Irvine, CA). The tube was
gently shaken for 3 min and centrifuged at 2500 rpm for 5 min. The organic extract was transferred into a conic tube and evaporated to dryness. The residue was reconstituted with 100 μL of methanol. Twenty microliters of this solution was injected into the chromatograph.

Sample standards were prepared from the blank samples (blood and urine) and aqueous solution (gastrointestinal content) spiked with drugs to obtain standard calibrations of 10, 50, 100, 500, and 1200 ng/mL of each drug. Extration was performed as described previously.

Drug (heroin, 06-monoacetylmorphine, and morphine) concentrations in analyzed samples were calculated by comparing the peak-area ratio of the drug with that of nalorphine (internal standard) against the standard calibration curve.

### Results and Discussion

Qualitative analysis of the decedent's blood gave a GC-MS pattern consistent with heroin, 06-monoacetylmorphine, and morphine (Figure 1).

Bromazepam, which was suspected to be the cause of intoxication, was not found. For quantitative analysis, the relationship between the area ratios and the concentrations of each analyzed drug was linear in range from 10 to 1200 ng/mL. The limit of determination with UV detection at 220 nm was approximately 10 ng/mL for heroin, 5 ng/mL for 06-monoacetylmorphine, and 3 ng/mL for morphine.

A summary of the quantitative results of HPLC appears in Table 1. A chromatogram of the blood extract is shown in Figure 2.

The pharmacokinetics of heroin in patients with chronic pain were studied by Inturrisi et al. (1). After an oral dose of 52.3 mg of heroin, neither heroin nor 06-monoacetylmorphine could be detected. Under clinical conditions and after constant infusion of heroin hydrochloride (20 mg per 180 min), blood concentrations at steady-state for heroin, 06-monoacetylmorphine, and morphine were reported at 57, 15, and 30 ng/mL, respectively. Heroin and 06-monoacetylmorphine were measured in a blood sample taken 5 min into the infusion, and morphine could only be measured after 45 min.

The decedent ingested an unknown quantity of heroin, which caused his death. Heroin and 06-monoacetylmorphine remained and were detected, which showed that a massive dose was absorbed. The concentrations of heroin, 06-monoacetylmorphine, and morphine measured in his blood were 109, 168, and 1140 ng/mL, respectively. These concentrations were 2-, 11-, and 38-fold, respectively, higher than those found in steady state. The moment of death was probably at the time the peak morphine concentration was achieved, which was during the night.

Morphine plasma concentrations in therapy are usually in the range of 10 to 70 ng/mL (3). Spiehler (9) established free morphine concentrations in blood in morphine overdoses using artificial intelligence computer software. A blood morphine concentration greater than 240 ng/mL was considered characteristic of a morphine overdose. In the presented study, the
morphine concentration (free drug), 1140 ng/mL, was about 16 times greater than the highest therapeutic plasma level and 5-fold higher than an overdose concentration. It was in the blood postmortem range of 10–1400 ng/mL (3).

In addition to heroin, the subject was also taking the following prescription drugs: alimemazine, tropatepine, and zopiclone. Only traces of these drugs were detected in the blood. A test for ethyl alcohol in the blood was also negative. Furthermore, heroin and 66-monoacetylmorphine were both detectable in gastrointestinal contents (Table I), which strongly suggested that heroin was involved. Neither prescription medication nor alcohol contributed to this death. This death was certainly caused by an overdose resulting from massive ingestion of heroin. The high concentration of morphine in urine, 3650 ng/mL, provided evidence of recent usage of heroin or other opiates.

Conclusion

The present study is the first case that we have encountered that documents postmortem concentrations of heroin, 66-monoacetylmorphine, and morphine following an oral heroin overdose.

References


