

FATAL POISONING BY ALCOHOL AND HEROIN*

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Drug abuse with alcohol consumption have been on the rise in Split-Dalmatian County for a while now. This article reports two separate cases with three deaths due to fatal combinations of heroin and alcohol. The first case of poisoning is related to a young couple, a 30-year-old man and a 28-year-old woman, who were found dead in a car, surrounded by cans of a variety alcoholic drinks. Two needles were found beside the bodies as well. The victims were registered drug abusers who had been in withdrawal programs. The second case was a 29-year-old man who was found dead in a house. Three fresh injection marks were visible on his right arm, and two needles were near his body. He was not known as a drug addict, but he had tried to commit suicide recently.

Carboxyhaemoglobin was found in blood samples of both victims from the first case. The concentration was 25 % and that could contribute to their death. In both described cases blood alcohol concentration was higher than 1.60 g kg⁻¹. Toxicology tests were positive for heroin, meconin, acetaminophen, 6-acetylmorphine, codeine, noscapine and papaverine. Ethanol, being a respiratory depressant, combined with morphine drastically increases the risk of rapid death due to respiration failure.

KEY WORDS: *death, fatal intoxication, intravenous injection, toxicology*

Recent years have seen an increase in illicit drug consumption in Croatia. In Split-Dalmatian County the number of drug addicts and of fatal poisonings has increased since the beginning of the 1990s (1). The most common poisonings are by heroin (2).

Morphine is an opiate analgesic which itself is abused, but is more frequently found as a metabolite of heroin (diacetyl morphine). After administration, heroin rapidly hydrolyses in whole blood to 6-monoacetylmorphine (6-MAM) with a half-life from less than 20 min to ~3 min after parenteral administration. This process probably continues after death. Morphine is amphoteric and moderately lipid-soluble (3). Although fatal outcome due to injection of heroin is widely recognised and documented, post-mortem morphine concentrations show large individual variations (4). These could be explained by

differences in samples used, differences in tolerance and the time interval between injection and death. Victims may be influenced by other drugs, and a negative correlation between morphine concentration and alcohol concentration has been shown in both unconscious and deceased drug addicts, indicating an additive effect of alcohol to heroin toxicity (4).

The objective of this study was to find out whether or not toxicological analysis of multiple samples could be of any support in determining the cause of death.

MATERIALS AND METHODS

In order to establish drug distribution, multiple samples were collected at autopsy and stored at

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4 °C until analysis. All solvents and chemicals were analytical-grade-purity products of Merck Darmstadt, Germany. Solid-phase extraction was performed using Amberlite XAD-2, polyaromatic adsorbent resin (Supelco; SIGMA ALDRICH, Taufkirchen, Germany) (5). Pentafluoropropionic acid anhydrides (PFPA), Bis (trimethylsilyl) trifluoroacetamide (BSTFA) with 1 % trimethylchlorosilane (TMCS) were obtained from Sigma Chemical Co. (St. Louis, MO, USA) and used in the analysis of drugs of abuse as a variety of derivatisation reagents (6).

The toxicological analysis was performed using a Shimadzu GC-2010 with ion trap mass spectrometer (mass selective detector, MSD). The chromatographic column was RTX-5MS (5 % diphenyl + 95 % dimethyl polysiloxane, 30 m, and 0.25 mm i.d, with a film thick 0.25 µm). The initial column temperature of 90 °C was held for 3 min, then programmed to 270 °C at 20 °C/min, and held for 25 min. Ultra-pure-grade helium was used as the carrier gas at a flow rate of about 1.5 mL min⁻¹.

Blood-alcohol concentration (BAC) was measured using a Shimadzu 2010 gas chromatograph with headspace and flame ionisation detector (FID). Ter-Butanol was used as standard solution.

Absorbancies at 541, 560 and 576 nm were measured by a spectrophotometer (Ultrospec 2000. Pharmacia Biotech (Biochrom) Ltd. Cambridge, England) to evaluate the amount of carboxyhemoglobin (COHb) (7).

Case 1

This winter, a young couple was found dead in a car in the suburb of Split. Syringes and cans of a variety of alcohol drinks were found around the bodies. Both man and the woman had a history of drug abuse, were registered by the police, and their families claimed that they were included in withdrawal programs at the time.

Blood, urine, tissue samples and syringes were collected for toxicological analysis. Routine screening for pharmaceutical drugs was negative. Heroin, meconin, papaverine and caffeine were found in both syringes. Meconin was found in all samples. Monoacetylmorphine was determined only in the woman's urine, bile and hair, while noscapine was detected in the man's hair (Tables 1-2). The man's blood alcohol mass fraction was 1.60 g kg⁻¹ and urine alcohol mass fraction 2.93 g kg⁻¹. The woman's blood alcohol mass fraction was 1.81 g kg⁻¹ and urine

Table 1 Heroin and its distribution in the syringe, fluids and tissues of the woman in Case 1.

Sample Compound	Syringe	Blood	Urine	Bile	Liver	Kidney	Hair
Meconin	+	+	+	+	ND	ND	ND
Caffeine	+		+	+	+	+	+
Heroin	+	ND	ND	ND	ND	ND	ND
Monoacetylmorphine	ND	ND	+	+	ND	ND	+
Papaverine	+	ND	ND	ND	ND	ND	ND

+ = positive

ND = not determined

Table 2 Heroin and its distribution in the syringe, fluids and tissues of the man in Case 1.

Sample Compound	Syringe	Blood	Urine	Bile	Liver	Kidney	Hair
Meconin	+	+	+	+	+	+	+
Caffeine	+	ND	+	+	+	+	ND
Heroin	+	ND	ND	ND	ND	ND	ND
Noscapine	ND	ND	ND	ND	ND	ND	+
Papaverine	+	ND	ND	ND	ND	ND	ND

+ = positive

ND = not determined

alcohol mass fraction 2.48 g kg⁻¹ (Table 3). Blood concentration of COHb was 25 % in both.

Case 2

A 29-year-old man was found dead in a house due to overdose. Allegedly, he had attempted suicide on an earlier occasion. Three fresh injection marks were found on his right arm, while two needles were near the body.

Toxicological testing of the syringe was positive for heroin, theophylline, meconin, acetaminophen, monoacetylmorphine, codeine, noscapine, papaverine and caffeine. Morphine concentration was much higher in tissue samples from the three injection marks than in other samples (according to the signal from GC/MS and sample weight) (Figure 1A). Meconin was found in blood, urine and bile samples, while codeine and monoacetylmorphine were found in blood (Figure 1 B-E and Tables 4-5). Blood alcohol mass fraction was 1.67 g kg⁻¹ and urine alcohol mass fraction was 2.03 g kg⁻¹ (Table 3).

DISCUSSION

Autopsy and histological findings in both presented cases pointed to drug poisoning as the cause of death, which was confirmed by toxicological analysis. Heroin (diacetylmorphine) is rapidly hydrolysed to 6-monoacetylmorphine which in turn is hydrolysed to morphine following intravenous administration in humans (8). Blood level of morphine depends on the route of administration, dose, body weight, time elapsed since the last dose, and individual pharmacokinetics (9). Heroin is mainly excreted in the urine as free and conjugated morphine. Our results strongly suggest that deaths had occurred shortly after injection, since no significant amounts of morphine had been excreted (except for the woman in Case 1). The reason for rapid death could have been the lack of heroin tolerance in injected persons (10).

The main mechanism of heroin-related death is respiratory depression. Ethanol itself can cause death by a combination of respiratory, cerebral and cardiac

Table 3 Blood and urine alcohol mass fraction (g kg⁻¹) in Case 1 and Case 2.

Case		Alcohol / g kg ⁻¹	
		Blood	Urine
Case 1	woman	1.81	2.48
	man	1.60	2.93
Case 2		1.67	2.03

Table 4 Heroin and its distribution in the syringe and tissue from injection marks in Case 2.

Sample Compound	Syringe1	Syringe2	Tissue sample from injection mark 1	Tissue sample from injection mark 2	Tissue sample from injection mark 3
Meconin	+	+	+	+	+
Acetaminophen	+	+	+	+	+
Caffeine	+	+	+	+	+
Heroin	+	+	+	+	+++ ‡
3-acetylmorphine	+	+	ND	ND	ND
6-acetylmorphine	+	+	ND	ND	ND
Codeine	+	+	+	+	+
Noscapine	+	+	+	+	+
Papaverine	+	+	+	+	+

+ = positive

ND = not determined

‡ concentration was much higher than in an other samples from injection mark (according to the area under peaks)

Table 5 Heroin and its distribution in fluids and tissues in Case 2.

Compound	Blood	Urine	Bile	Liver	Kidney
Meconin	+	+	+	ND	ND
Acetaminophen	+	ND	ND	ND	ND
Caffeine	+	+	+	+	+
3-acetylmorphine	+	ND	ND	ND	ND
6-acetylmorphine	+	ND	ND	ND	ND
Codeine	+	ND	ND	ND	ND
Noscapine	+	ND	ND	ND	ND

+ = positive

ND = not determined

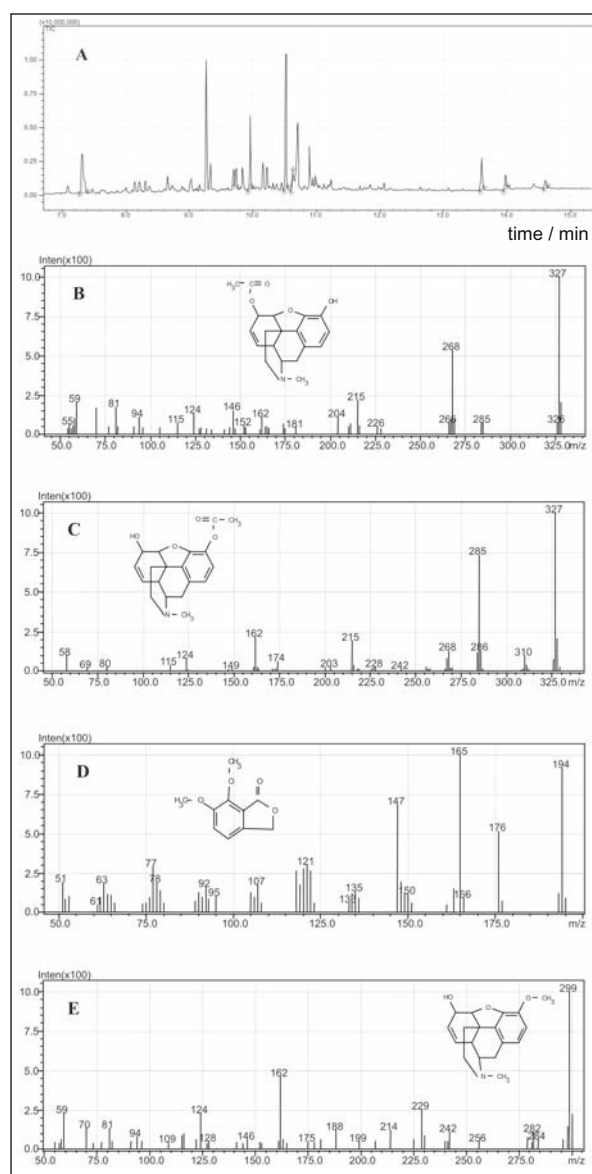


Figure 1 Total ion chromatogram of fresh injection marks (A) and characteristic spectra of 6-acetylmorphine (B), 3-acetylmorphine (C), meconin (D) and codeine (E)

depression (11). The effects of the consumption of opiates and alcohol together are therefore additive and drastically increase the risk of sudden or rapid death due to respiration failure. They also increase the risk of overdose in experienced drug abusers.

Blood morphine levels have been reported to be substantially lower in cases where alcohol is detected than in cases where it is not, although the clinical significance of this finding remains unclear (12-15). Darke S. and Zador D., reported similar findings by Chan et al., with mean blood morphine levels of 0.43 mg L^{-1} and 0.52 mg L^{-1} , respectively, and observed that mean blood morphine level declined with increased blood alcohol (10).

Collection of tissue samples from injection marks and of control tissue samples has been recommended to establish the cause of death. Improved classification and reporting might include documenting the cause of death as, for instance, morphine only or combined effects of heroin and alcohol.

The COHb concentration of 25 % found in blood of the young couple was sufficient for some clinical symptoms, but not for death (the lethal concentration is above 50 %), which suggests that this level could only contribute to the death (16). The couple was exposed to fumes from the car exhaust, but criminal investigation could not confirm their intention to commit suicide.

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Sažetak**KOBNA INTOKSIKACIJA ALKOHOLOM I HEROINOM**

U posljednje vrijeme u Splitsko-dalmatinskoj županiji konzumiranje opojnih droga uz alkohol je u porastu. Ovim radom prikazali smo dva slučaja s tri smrtno stradale osobe koje su bile kobne žrtve kombinacije alkohola i heroina. U prvom slučaju, mladi par, u dobi od 30 i 28 godina, pronađen je u automobilu okružen limenkama raznih alkoholnih pića. Dvije šprice nađene su kraj tijela. Žrtve su bili registrirani ovisnici i na programima odvikavanja u organiziranim tretmanima. Drugi slučaj bio je 29-godišnji muškarac pronađen mrtav u napuštenoj kući. Na njegovoj desnoj ruci primijećene su tri svježe ubodne rane, a dvije šprice pronađene su kraj tijela. Nije bio poznat kao ovisnik o drogama, ali je nedavno pokušao samoubojstvo. Karboksihemoglobin nađen je u uzorcima krvi objiju žrtava iz prvog slučaja. Koncentracija je bila 25 %, što je moglo pridonijeti njihovoj smrti. U oba opisana slučaja maseni udjel alkohola u krvi bilo je veći od 1.60 g kg⁻¹. Toksikološke analize bile su pozitivne na heroin, mekonin, acetaminofen, monoacetil morfin, kodein, noskapin i papaverin. Alkohol, i sam kao depresor respiracije, zajedno s heroinskom smjesom značajno povisuje rizik od nagle smrti kao posljedice zatajenja disanja.

KLJUČNE RIJEČI: *kobno trovanje, intravensko ubrizgavanje, smrt, toksikologija*

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