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A case of high opiate tolerance: implications for drug analyses and interpretations

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Summary. A case of driving under the influence of extremely high concentrations of codeine and ethylmorphine is reported. A high blood concentration of morphine was also found, which in this case was probably a metabolic product of codeine and ethylmorphine. This illustrates that when morphine is found in blood, the sample should also be analysed for other opiates in order to avoid misinterpretations.

Key words: Codeine – Ethymorphine – Morphine – Metabolism

Zusammenfassung. Es wird über einen Fall berichtet, bei welchem der Fahrzeugführer unter dem Einfluß extrem hoher Konzentration von Codein und Ethylmorphin stand. Im Blut wurde auch eine hohe Konzentration von Morphin gefunden, welche in diesem Fall wahrscheinlich ein Stoffwechselprodukt von Codein und Ethylmorphin war. Dies zeigt, daß bei Auffindung von Morphin im Blut die Probe auch auf andere Opiate untersucht werden sollte, um Fehlinterpretationen zu vermeiden.

Schlüsselwörter: Codein – Ethylmorphin – Morphin – Metabolismus

Introduction

Opiates are among the most common drugs of abuse, in particular heroin and morphine. Opiates are also among the most frequent causes of drug-related deaths [1].

Case history

A known drug abuser was apprehended by the police on suspicion of driving under the influence of alcohol or drugs. The suspect was brought to a physician for blood sampling and clinical examination, and his conclusion was that the suspect showed medium to strong impairment due to drugs. The suspect admitted a history of drug abuse including the use of LSD and amphetamine and admitted having used diazepam (30 mg) and an unknown amount of cough mixture (type not specified) some time before apprehension.

Analytical procedures

The blood sample was screened for amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine metabolites and opiates by immunological methods [2]. Codeine, ethylmorphine and morphine were subsequently confirmed and quantified using gas chromatography-mass spectrometry [3]. Other drugs were quantified using high-performance liquid chromatography and/or gas chromatography.

Results and discussion

The findings are presented in Table 1. Several drugs were found, but largely in agreement with the information on drug intake given by the suspect. The cough mixture must have been a type containing codeine phosphate (6.6 mg/ml) and ethylmorphine chloride (2 mg/ml). However, morphine was found in addition to codeine and ethylmorphine. Th opiate concentrations were extremely high, codeine and morphine were present in higher concentrations than in some fatal cases and probably indicated a high tolerance to opiates.

In order to exclude the intake of heroin, it might be suggested that 6-monoacetylmorphine (MAM) should have been analysed. As in most other forensic laboratories, MAM is in our laboratory only analysed in urine samples, which in this case was not available. The presence of MAM in urine indicates heroin intake, but the

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Table 1. Drug concentrations in the blood sample of the suspect

Drug	Concentration	
	μmol/l	mg/l
Amphetamine	0.7	0.09
Diazepam	2.1	0.60
N-desmethyldiazepam	2.3	0.62
Flunitrazepam	0.03	0.01
Codeine	8.6	2.6
Ethylmorphine	3.7	1.2
Morphine	1.0	0.29

absence of MAM may not be used to exclude heroin intake because urine MAM levels may be too low to be detected, even in some cases of fatal heroin intoxications (Wethe, personal communication). MAM can also be analysed in blood samples [3], but the blood MAM levels are very low [3], and may in many cases to be too low to be detected.

It is well known that codeine is metabolized to morphine [4]. After oral administration of codeine, 5%–15% of the excreted material is in the form of free or conjugated morphine [4]. In a study of 10 fatal codeine intoxications with blood codeine levels above 0.5 mg/l, the morphine-codeine blood concentration ratio ranged from less than 0.02–0.10, with a mean of 0.046 (Gjerde, unpublished observations). It has also been found that in humans ethylmorphine is metabolized to morphine, and that the morphine-ethylmorphine blood concentration ratio ranged from 0.02–0.15 in 4 subjects 1–3 h after intake of ethylmorphine (Ripel et al., personal communication). In the present case the blood concentration ratio between morphine and codeine + ethylmorphine of 0.08 indicated that the morphine found was probably a metabolic product of codeine and ethylmorphine.

If intake of morphine or heroin had been suspected, and the blood sample had been analysed only for morphine, the result might have been interpreted as morphine or heroin use. This illustrates that even when a high blood concentration of morphine is found, the blood sample should also be analysed for other opiates in order to avoid misinterpretations.

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