COMPREHENSIVE TOXICOLOGICAL ANALYSES IN A CASE OF UNEXPECTED FATAL CODEINE INTOXICATION

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Introduction

Codeine, a commonly prescribed opioid analgesic and antitussive, is widely used either alone or in combination with other medications. Despite its therapeutic benefits, codeine can induce adverse effects such as drowsiness, constipation, nausea, and respiratory depression, particularly at higher doses or in susceptible individuals.

Case Report

This work presents an unusual fatal codeine intoxication involving a 60-year-old woman, found dead at home by his husband, when he came back home for lunch. In that morning, he left her sleeping in the bed. She had diarrhoea in the previous 48h, was obese, and suffer of asthma and psychiatric illness. Her usual prescribed medications included the antidepressants escitalopram and triticum, the anticonvulsant oxcarbazepine (used primarily to treat epilepsy and bipolar disorder), the anxiolytic lorazepam, the antipsychotic quetiapine, the asthma control montelukast and the atorvastatin used to treat hypercholesterolemia. There was no history of ingestion of any formulation containing codeine. Autopsy showed no evidence of trauma. A slight cardiac hypertrophy related with a hypertensive cardiopathy was observed macro and microscopically. Fragments of white pills were found in stomach and a dark liquid content until the jejune.

Material and Methods

Samples preparation:

- Solid phase extraction (Oasis® MCX);
- Microwave derivatization (MSTFA/TMCS);
- Gas Chromatography- Mass Spectometry (GC-MS) analysis.

Instrumental methods:

- Immunoassay screening;
- Ethanol screening by Gas Chromatography-Flame Ionization Detector with HeadSpace injection (GC-FID-HS);
- Analysis of prescription substances by Ultra-High-Performance Liquid Chromatography-Mass Spectometry (UHPLC-MS-MS);
- Analysis of drugs of abuse and unknown substances by GC-MS.

Table 1. Monitored ions for codeine and IS (GC-MS).

Substance	Ions	Internal Standard	Ion
Codeine	371 178 196	Codeine-*d*3	374

Results and Discussion

Table 2. Codeine concentrations in the specimens analysed.

Specimen	Codeine (ng/mL)	Discussion
Peripheral blood	5309	Suggests recent consumption
Cardiac blood	7545	
Urine	205918	Indicates substantial drug excretion before death
Liver	9935	Confirms extensive metabolism
Gastric content	197428	Confirms ingestion prior to death

Table 3. Morphine concentrations.

Specimens	Morphine (codeine metabolite) (ng/mL)
Peripheral blood	190
Cardiac blood	616

Table 4. Prescription medication concentrations in the peripheral blood.

Specimen	Other Substances	Concentration (ng/mL)
Peripheral blood	Atorvastatin	15
	Citalopram/desmethylcitalopram	150/70
	Oxcarbazepine	100
	Paracetamol	28871
	Quetiapine/Norquetiapine	32/105
	Trazodone/mCPP	219/10
	Lorazepam	90
	Desalkylflurazepam	38

Conclusions

The autopsy was negative except for a hypertensive cardiopathy, that was not severe enough to justify the death. On the other hand, toxicological results showed unexpectedly codeine in the blood, stomach, liver, and urine, in high concentrations. The pills fragments found in the gastric content reinforce its ingestion before death.

Taking into account all these facts, the cause of death was attributed to codeine ingestion, although in an unknown formulation. The manner of death remains unascertained, as suicide could be a possibility according to her psychiatric antecedents, as well as an accident, if codeine had been taken to treat the diarrhoea she had.