Discovery of two corpses after lethal intoxication by oral application of transdermal fentanyl patches

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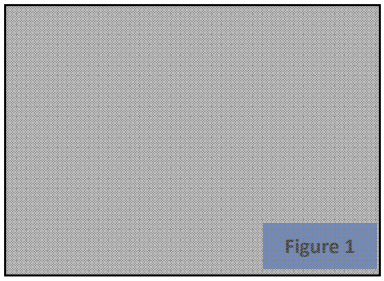
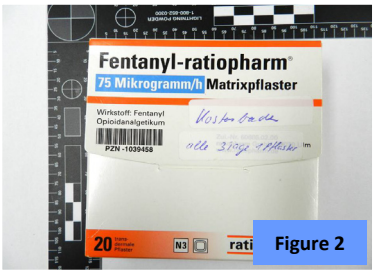


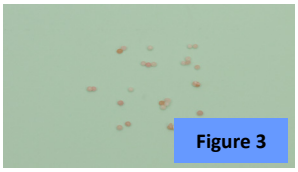
Introduction

The discovery of more than one corpse on site generally raises the suspicion of an unnatural death. They are often caused by homicide, extended suicide or carbon monoxide intoxication. However, intoxications by consumed drugs or medicines with more than one dead person are rare. In the case presented two male adults were found dead and the cause and manner of death had to be clarified.

The two men were known as drug and alcohol consumers. They returned to the aunt's flat in a drunken and "stoned" condition. On the next morning they were found dead by the aunt, one lying over the other (see figure 1).

Several packages of fentanyl patches that were prescribed the aunt (figure 2), were found nearby the bodies and the brother of one of the deceased reported on repeated sucking and chewing of fentanyl patches.





Autopsy findings

Autopsies were performed 45 hours and 47 hours, respectively, after discovery of the bodies. In both cases unspecific signs of intoxication (cerebral oedema, lung oedema, excessive contents of the urinary bladder, acute congestion of the organs) were found. The stomach content of one of the deceased showed small globular, transparent particals (see figure 3).

Results and Discussion

Autopsy yielded unspecific findings of an intoxication like cerebral and pulmonary oedema, filled urinary bladder and blood congestion in visceral organs in both deceased. No patches were found on the skin of the bodies. Blood alcohol concentrations were 1.18 ‰ (subject 1) and 1.26 ‰ (subject 2). Femoral serum concentrations of 30 and 38 ng/mL fentanyl as well as 22 and < 5 ng/mL norfentanyl were found which are suitable to induce severe respiratory depression in opiate naïve users. In hair the concentrations were 35 and 70 pg/mg fentanyl as well as 1 and 5 pg/mg norfentanyl (hair length of subject 1: 1.5 cm, subject 2: 5 cm), which would be compatible with a continued low level opioid abuse. Stomach content tested positive for fentanyl.

Besides fentanyl and norfentanyl in hair, methylphenidate (50 pg/mg), loperamide (50 pg/mg), tramadol and O-desmethytramadol could be detected in trace amounts in subject 1, methadone, cocaine, benzoylecgonine and cocaethylene could be detected in trace amounts in subject 2. These results pointed to a moderate abuse of drugs of both subjects [1]. The rather low level of fentanyl, norfentanyl and other opioids (loperamide, tramadol, methadone) in the hair samples lead to the suggestion that both subjects had not developed a pronounced opioid tolerance.

By discovery of several corpses in one room, carbon monoxide should always be taken into consideration as cause of death. The level of carbon monoxide-haemoglobin in heartblood was low – 1% (refered to total haemoglobin) (subject 1) and 2% (subject 2) – particularly among smokers (urine tested positive for nicotine and cotinine in both subjects).

Urine alcohol concentrations were 3.28 ‰ (subject 1) and 1.87 ‰ (subject 2). Thus at least subject 1 was in the elimination phase [2] and both subjects may had developed a significant alcohol tolerance.

Whereas in subject 2 no further drugs could be detected, subject 1 showed a current abuse/use of several drugs besides fentanyl. Additional findings in the femoral serum of subject 1 were as follows: 26 ng/mL methylphenidate, 5.4 ng/mL THC, 0.8 ng/mL 11-OH-THC, 17 ng/mL THC-COOH, loperamide below 1 ng/mL, and tetrazepam below 10 ng/mL. Urine tested positive for ibuprofen and paracetamol.

Conclusion

In both cases death could be explained by combined fentanyl and ethanol intoxication [3]. Fentanyl was obviously applied orally. Both subjects were most likely not opioid tolerant, although hair samples showed a history of mild drug abuse.

References

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Methods

LC-MS/MS analysis

Sample preparation for LC-MS/MS-analyses was performed as follows:

1 mL serum (according to an alkaline liquid-liquid extraction (LLE))
+ ISTD: 10 ng D_5-fentanyl/-norfentanyl for quantitation of fentanyl/norfentany.
20 ng D_5-MDEA for quantitation of methylphenidate
50 ng D_5-diazepam for quantitation of tetrazepam
100 ng D_3-doxepin for quantitation of loperamide
+ 0.5 mL borate buffer (pH 9)
+ 1.5 mL chlorobutane
→ 2 min mixing, 10 min centrifugation at 4000 rpm, evaporation of organic phase with N_2 at 40 °C
→ Residue was resolved in 25 µL solvent A/B (80:20) (v/v).

approx. 25 mg hair
+ ISTD: 10 pg/mg D_5-fentanyl/-norfentanyl for quantitation of fentanyl/norfentany.
100 ng D_3-Doxepin for quantitation of methylphenidate and loperamide
+ 2 mL methanol
→ 4 hours ultrasonication, evaporation of organic phase with N_2 at 40 °C, resolved in 2 mL phosphate buffer (pH 6), SPE extraction, evaporation of SPE-extract with N_2 at 40 °C
→ Residue was resolved in 25 µL solvent A/B (50:50) (v/v).

LC-MS/MS analysis (cont.)

LC settings: QTrap 2000 triple-quadrupole linear ion trap mass spectrometer fitted with a TurboIonSpray interface (AB Sciex, Darmstadt, Germany) and an Agilent 1100 Series HPLC system (G1312A Bin Pump, G1313A autosampler, G1379A degasser, Agilent, Santa Clara CA, United States). Separation was performed on a polar-endcapped phenylpropyl reversed phase column (Synergy Polar-RP 50 mm × 2 mm, 4 µm) with an equivalent guard column (4 mm × 2 mm) (Phenomenex, schaffenburg, Germany) and gradient elution using solvent A (0.1% formic acid (v/v) with 1 mmol/L ammonium formate) and solvent B (acetonitrile: 0.1% formic acid 95:5 (v/v) with 1 mmol/L ammonium formate) with the following 15 min gradient: 0–1 min: 20 % B; 1–10 min: 20–95 % B linear; 10–11 min: 95 % B; 11–12 min: 95–20 % B linear; 12–15 min: 20 % B. The total flow rate was set to 0.4 mL per minute. 20 µL of the extracted samples were injected.

Alcohol analysis

Blood and urine alcohol was detected by routine HS-GC-FID and ADH-procedure.

CO-Hb analysis

Photometry analysis of carbon monoxide-haemoglobin was performed based on a procedure of Heilmeyer and Hüfner [4].

GC/MS Screening

Urine samples were analysed by two step direct liquid-liquid extraction and by acidic hydrolysis followed by basic liquid-liquid extraction and acetylation [5].

Analyses were performed on an 7890A gas chromatograph equipped with a 7683B series injector, and a 5975C inert XL series mass selective detector in split-less mode with an HP-5-MS-0.25µm capillary column (Agilent, Waldbronn, Germany). The MS was operated in the scan mode with electron impact ionisation.

Quantitative GC/MS analysis of cannabinoids

1 mL serum
+ ISTD: 5 ng D_3-THC, 5 ng D_3-11-OH-THC, 25 ng D_3-THC-COOH
+ 2 mL 0,1 M acidic acid
→ 2 min mixing, SPE extraction, evaporation of SPE-extract with N_2 at 65 °C
→ Residue is resolved in 25 µL MSTFA and 25 µL ethylacetate.

Analyses were performed on an 7890A gas chromatograph equipped with a 7683B series injector, and a 5975C inert XL series mass selective detector in split-less mode with an HP-5-MS-0.25µm capillary column (Agilent, Waldbronn, Germany). The MS was operated in the SIM mode with electron impact ionisation.