LABORATORY OF FORENSIC CHEMISTRY AND TOXICOLOGY

ILLICIT FENTANYL INTOXICATION: A CASE REPORT

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AIMS & INTRODUCTION

Fentanyl is a central nervous system depressant opioid. It is prescribed for chronic, severe pain due to cancer, nerve damage, major trauma, among other causes. It is also illegally synthesized and used as a recreational drug. Non-pharmaceutical fentanyl is frequently referred as illicitly manufactured fentanyl (IMF). IMF is often mixed with heroin and/or cocaine, with or without the user's knowledge, in order to increase the drug's effect. Since 2013, fentanyl and its analogues have been associated to deaths both in Europe and through all states of USA, and the misuse of opioids prescriptions and illegally manufactured sources is a well-documented and rising phenomenon. Therefore, nowadays, there is an increasing concern about the relationship between this substance and the alarming increase in the number of opioid-related overdoses.

The authors present the first case in the North of Portugal where Fentanyl was detected in post-mortem samples, as a result of an illicit use. A 31-year-old man was found dead in a hotel room, with a plastic bag on his head, wrapped with a nylon cord and duct tape, with an MP4 player in the pants pocket with the headset connected. The corpse showed signs of dehydration and all the findings pointed to a suicidal etiology. Empty blisters of Alprazolam were found at the crime scene, along with a mirror with traces of a white powder and two small transparent plastic bags, one of them also containing a white powder. Cardiac blood samples were sent to the toxicology lab to search for ethanol, drugs of abuse and medicines, as well as to analyse the mentioned powders.

MATERIAL & METHODS

EXTRACTION PROCEDURE

Whole blood samples were subjected to solid phase extraction using Oasis HLB® 3 cc columns, following the procedure described in table 1.

Tabe 1. Extraction Procedure

Sample load	1000 µL diluted in 3,5 mL of water
Rinsing	2 mL Methanol 5%
Drying	10 minutes
Elution	2 mL Methanol

Tabe 2. GC-MS conditions.

GC	AGILENT 6890N
MS	AGILENT 5973N
Autosampler	AGILENT 7683
Chromatographic column	J&W Scientific 5-ms, 30 m x 0,25 mm x 0,25 µm 150ºC for 1 min, to 290ºC at 5ºC/min during 8 min
Detector	Direct interface; Internal Ionization by IE ; $T_{transferline}$: 280ºC $T_{quadrupol}$: 150ºC; SIM mode (**245**, 320, 335),dwell time 0,1 sec/scan; $T_{ionization}$: 230ºC.

Tabe 3. Analytical parameters.

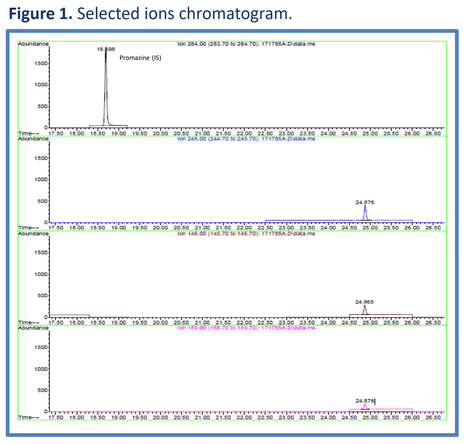
LOD/LOQ	Work range	Dilution factor
3 ng/mL	[3-50] ng/mL	4
Accuracy of low internal quality control (5 ng/mL)	**Accuracy of high internal quality control (40 ng/mL)**	**IS Deviation**
-17.6%	-2.8%	3.9%

The white powders were directly analysed by GC-MS-single quad, without extraction procedure.
The used conditions are described in table 2.

ANALYTICAL METHOD

Fentanyl identification and quantification in post-mortem blood samples was performed using a GC-MS-single quad (m/z: 245, 146, 189), with Promazine as Internal Standard (m/z: 284) (Fig. 1).

Figure 1. Selected ions chromatogram.



RESULTS AND DISCUSSION

Autopsy findings revealed bloody reddish foam on the surface of the bronchial section and tissue microscopic exam revealed lesions of deep pulmonary vascular congestion with initial signs of disseminated intravascular coagulation, none of them allowing the distinction between death by suffocation or by opioid intoxication.

The value found for fentanyl in the cardiac blood sample is enormous. In an extensive published review of postmortem fentanyl literature, deaths involving the rapid administration of fentanyl or the administration of large doses of fentanyl were found to have incomplete fentanyl distribution throughout the body tissues and fluids.

Cardiac Blood

Fentanyl: 158 ng/mL

Alprazolam: 123 ng/mL

Thus, non-equilibrium pharmacokinetics results in higher fentanyl heart blood concentrations than femoral blood values simply due to relative blood flow through the various vessels and organs prior to death. The fact that fentanyl is a basic, lipophilic drug, with a moderate volume of distribution (3 to 8 L/kg), also supports the contention.

With average published ratios for fentanyl reported as ranging from 1.1 to 2.8, it can be concluded that, even so, the assumed concentration found in the femoral blood would also be very high.

White Powder 1

Fentanyl

White Powder 2

Fentanyl

After GC/MS analysis, both powders were positively identified as fentanyl.

CONCLUSIONS

Until 2013, sporadic outbreaks of fentanyl and fentanyl analogs contaminating heroin supplies caused some deaths in heroin users. Since then, fentanyl has caused deaths in every state of USA and Europe and fentanyl and its analogs have completely infiltrated the heroin supply. In 2014, the first illicit pills containing fentanyl, fentanyl analogs, and other novel synthetic opioids were detected. In 2016 more than 20,000 deaths occurred in the USA due to overdoses of fentanyl and analogues.

In Europe, since the first reported detection of fentanyl in 2012, a total of 24 new fentanyl cases have been reported to the EMCDDA. The majority of these have been reported since the beginning of 2016, including 6 in 2017 until September, none of them in Portugal.

In Portugal, it's the first time that Fentanyl is detected in post-mortem samples associated to illicit use and the autopsy report suggests that, taking into account all the evidences, everything points to a death in a suicide context, with no injuries suggesting intervention of third parties in death. However, combining the toxicological results with autopsy findings, as well as the police information, it is not possible to exclude death by fentanyl intoxication.

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