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CASE REPORT

Madness with five dollars: Two new cases of non-lethal poisoning flakka (α-PVP)

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Summary We reported the case of two young men, known to be polydrug abusers, arrested in possession of plastic bags of crystals and capsules (total about 300 grams) suspected to be narcotics or new psychoactive substances (NPS). Placed in custody, they will quickly hospitalize for their bad condition (tachycardia, dysarthria, great excitement) where blood samples are taken. Hair samples will be taken for the two subjects, respectively, 1 month and 4 months after hospitalization. Analyses of seized materials, blood and hair samples were requested by the justice and sent to the laboratory for identification and document the drug exposure. Identification of seized materials was performed with gas chromatography-mass spectrometry (GC-MS) using commercial and free specialized mass spectra libraries. Blood toxicological analysis was performed by gas chromatography with flame ionization detection (GC-FID), high performance liquid chromatography-diode array detection (HPLC-DAD), gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-mass spectrometry (LC-MS/MS). Several hair segments were analyzed by LC-MS/MS. Alpha-pyrrolidinopentiophenone or alpha-pyrrolidinovalerophenone (α-PVP, also known as street name ''flakka'') and pyrrolidinoheptiophenone (PV8, also known as α-PHpP or α-PEP) were identified in seized materials. Toxicological analysis in peripheral blood revealed the presence of α-PVP (100 and 70 ng/mL, respectively), 2-oxo-PVP (50.4 and 22.7 ng/mL, respectively), PV8, diazepam and metabolites for the two subjects. Hair analysis demonstrated the presence of α-PVP (0.88 and 0.19 to 1.99 ng/mg, respectively), 2-oxo-PVP, morphine, cocaine and metabolites, amphetamine, MDMA, methadone and EDDP and suggested a repeated consumption of these substances.

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Introduction

These last years, new psychoactive substances (NPS) have invaded the drug market. They are designed to cause similar effects to drugs of abuse and are considered as ''legal'' alternative for some of them, hence the name of legal high and purchasing is very easy on specialized websites. In France, the synthetic cathinone chemical family is the most represented in drug seizures in the years 2014 and 2015. Alpha-pyrrolidinopentiophenone (alpha-pyrrolidinovalerophenone or α-PVP) has been available in the European Union (EU) since at least February 2011 and has been detected in 28 Member States, Turkey and Norway. In most cases it has been seized as a powder, but other forms including tablets have been detected. Multi-kilogram quantities of α-PVP have been seized at European borders, which usually originate from China. This includes the seizure of more than 280 kg in 2015 [1]. Illicit production and tableting sites within the EU have also been seized [1]. The substance α-PVP is sold online as a ''research chemical'' but also as ''bath salts'', ''plant food'' or ''insect repellers'' and was seized for the first time in France in 2011 as the PV8 (α-PHpP, α-PEP or pyrrolidinoheptiophenone) was seized in 2014 [2]. The substance α-PVP is a stimulant drug chemically related to MDPV (methylenedioxypyrovalerone). Both are pyrovalerones. Pharmacological description and health risks are described in the literature [3,4]. User reports indicate that it can be swallowed, insufflated, administered sublingually, and vaporized [1,3,4]. Many cases of intoxication, violent aggressive behavior and madness attacks were described in 2015 in the USA (Florida), widely reported in the international press. Presence of α-PVP is reported in polydrug overdoses and sometimes where the drug was found to be a significant contributory cause to the death. A total of 116 deaths associated with α-PVP (including 2 in France) were reported in Europe between 2012 and 2015 and 205 acute intoxications (including 10 in France) were reported in Europe in the same period [3]. Much of the synthetic cathinones are classified as drug of abuse in France since the decree of 27 July 2012 with for the first time, a new approach called ''generic'' classification with a single text [5].

Despite increasing use of such compounds in France, only few intoxications or fatalities concerning flakka have been reported with complete analytical data.

This case report documents two severe intoxications with this synthetic cathinone and the concentrations measured in blood and hair.

Case report

In December 2015, a seizure of crystals and capsules containing a white powder is performed on 2 men, who are placed in custody at the police station for drug trafficking.

During the interrogation, one of them says he had consumed products called α-PVP and described the effects usually felt by injection:

> *''After the injection, I have a flash for about 10 minutes, after I feel buzzy for 12 hours then it starts to feel like black holes''.*

Nevertheless, quickly after the arrest, they started to have disturbing clinical signs before their transfer to emergencies.

The subject 1 is a 27-year old man addicted on multiple drugs (alcohols and many psychoactive substances) which readily admits taking α-PVP. He indicates having injected 10 mg of α-PVP several times for 4 days having smoked it for 3 weeks. In the police station, he presents discomfort with short clonies and dysarthria. He indicates that he has self-injected 10 mg of α-PVP several times for 4 days having smoked it for 3 weeks. On admission to the emergency department, he presents tachycardia, is normotensive, and has no fever. He has no disturbance of consciousness but dyskinesias and a major agitation. The CPK value is increased to 1800 IU/L (N: 5—170). He is treated symptomatically by Valium, Skenan, Tercian, Lepticur and then transferred to a psychiatric hospital for the rest of the treatment.

The subject 2 is a 34-year old man, also addicted to multiple drugs (cannabis, amphetamines, Valium and Skenan); during his custody, he said he had not taken any drugs in the last 12 hours, yet his state of consciousness gets progressively worse and he was transferred for sleepiness to the emergency department. At the admission, the Coma Glasgow Scale is 14; he has tachycardia, and is normotensive. He is hospitalized for a neurological monitoring. Clinical signs improve spontaneously without treatment other than perfusion. Then, he is transferred in infectious diseases department for the treatment of an abscess at the injection site.

For these 2 patients, blood toxicology samples were collected on admission to the emergency department. Capillary samples will be later made for analysis: one month later (3 cm) for case 1 and four months later (20 cm) for case 2. The powder contained in capsules and bags seized during the arrest were also submitted for analysis.

Material and methods

Seized materials analysis

A sample of the contents of each bag: capsule contents for the bag 1 (Fig. 1) and 20 mg of crystals for the bags 2 and 3 (Figs. 2 and 3) were dissolved in methanol. The analyses were performed using a gas chromatograph (HP 6890 GC System, Agilent Technologies, USA) coupled to a mass spectrometer (quadruple mass analyzer Agilent 5973, Agilent Technologies, USA). The injector was maintained at 280 °C. Sample injection (1 μL) was in splitless mode. Components separation was conducted on a HP-5MS capillary column (30 m length, 0.25 mm inner diameter, 0.25 μm film thickness, Agilent Technologies USA). Helium was used as a carrier gas. The mass detector was set to positive electron impact mode (EI) and the electron beam energy was 70 eV. The mass detector was operating in a full scan mode in the range of 29—600 amu. The acquisition and results analysis were conducted with MSD ChemStation (Agilent Technologies, USA). Identification of substances was supported by comparison of its mass spectrum with spectra of standards included in commercial and free specialized libraries (e.g. SWGDRUG Mass Spectral Library version 2.3 and Cayman Spectral Library [CSL]) [6,7].