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A non-fatal intoxication and seven deaths involving the dissociative drug 3-MeO-PCP

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ABSTRACT

Introduction: 3-methoxyphencyclidine (3-MeO-PCP) appeared on the illicit drug market in 2011 and is an analogue of phencyclidine, which exhibits anesthetic, analgesic and hallucinogenic properties. In this paper, we report data from a non-fatal intoxication and seven deaths involving 3-MeO-PCP in Sweden during the period March 2014 until June 2016.
Case descriptions: The non-fatal intoxication case, a 19-year-old male with drug problems and a medical history of depression, was found awake but tachycardic, hypertensive, tachypnoeic and catatonic at home. After being hospitalized, his condition worsened as he developed a fever and lactic acidosis concomitant with psychomotor agitation and hallucinations. After 22 h of intensive care, the patient had made a complete recovery. During his hospitalization, a total of four blood samples were collected at different time points. The seven autopsy cases, six males and one female, were all in their twenties to thirties with psychiatric problems and/or an ongoing drug abuse.
Methods: 3-MeO-PCP was identified with liquid chromatography (LC)/time-of-flight technology and quantified using LC-tandem mass spectrometry.
Results: In the clinical case, the concentration of 3-MeO-PCP was 0.14 μg/g at admission, 0.08 μg/g 2.5 h after admission, 0.06 μg/g 5 h after admission and 0.04 μg/g 17 h after admission. The half-life of 3-MeO-PCP was estimated to 11 h. In the autopsy cases, femoral blood concentrations ranged from 0.05 μg/g to 0.38 μg/g. 3-MeO-PCP was the sole finding in the case with the highest concentration and the cause of death was established as intoxication with 3-MeO-PCP. In the remaining six autopsy cases, other medications and drugs of abuse were present as well.
Conclusion: Despite being scheduled in January 2015, 3-MeO-PCP continues to be abused in Sweden. Exposure to 3-MeO-PCP may cause severe adverse events and even death, especially if the user does not receive life-supporting treatment.

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1. Introduction

The arylcyclohexylamine 3-methoxyphencyclidine (3-MeO-PCP) is an analogue of the dissociative anesthetic phencyclidine (PCP); also known as “Angel dust” (Fig. 1) [1]. PCP was withdrawn from the market in 1965 due to adverse psychological effects in patients post-operatively, including agitation, violent behavior, paranoid delusions, disorientation, delirium and hallucinations [1,2]. However, it soon became a popular recreational drug in the US and Canada. Usage declined in the early 80s but is now rising again [1,3].

3-MeO-PCP was first synthesized in 1979 and became available online as a research chemical in April 2011 [1]. It was first reported to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) by the United Kingdom in March 2012 [4]. In November 2013, the Swedish Poison Information Center registered its first call

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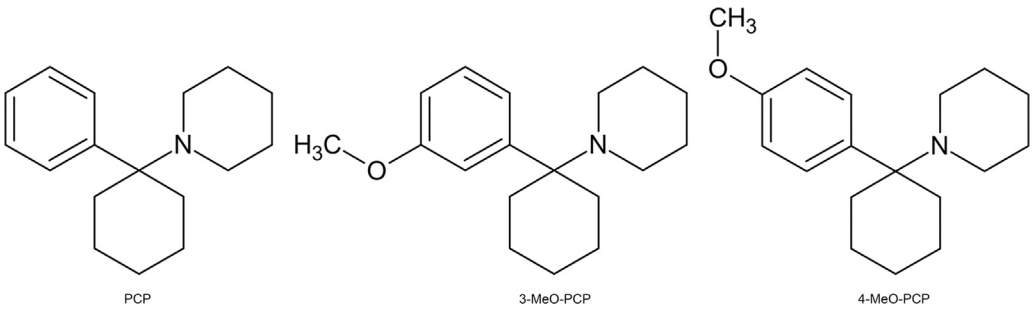

Fig. 1. The chemical structures of PCP, 3-MeO-PCP and 4-MeO-PCP.

related to 3-MeO-PCP [5] and on the 16th of January 2015 it was scheduled [6].

PCP acts primarily as a non-competitive *N*-methyl-D-aspartate (NMDA) receptor antagonist [7,8]. According to a study by Roth et al. [9], 3-MeO-PCP is a more potent NMDA receptor antagonist than PCP. It also has appreciable affinity for the sigma$_1$ receptor, which PCP lacks, and the serotonin transporter.

3-MeO-PCP is available as powder or tablets and is commonly administered orally but can also be injected, snorted or smoked [1,5]. Rectal administration has also been reported [5]. According to users [1,10–13], abuse dosages are usually 5–20 mg; 3–5 mg generating threshold activity and 10–20 mg strong dissociative effects. The duration of the effects has been reported to be ~4.5 h, with onset within 30 min of an oral intake and a peak at approximately 2 h [10–13].

4-methoxyphencyclidine (4-MeO-PCP) or methoxydine is a positional isomer of 3-MeO-PCP [1]. It was synthesized some ten years before the 3-methoxy analogue and was the first dissociative research chemical to be offered online. 4-MeO-PCP exhibit lower binding affinity for the NMDA receptor compared to PCP and 3-MeO-PCP [9].

In this paper, we report a non-fatal intoxication and seven deaths involving 3-MeO-PCP and also give some insight to its clinical characteristics, toxicokinetics and pathology.

2. Case descriptions

2.1. Clinical case

Paramedics were called to the house of a depressed and suicidal 19-year-old male drug addict due to erratic behavior. Upon arrival the patient was awake and sitting up. Electrocardiogram revealed a sinus rhythm. His respiratory rate was 22 breaths per minute, pulse 130 bpm, blood pressure 147/104 mmHg, oxygen saturation 96% on air, and blood glucose 5.4 mmol/L. The patient was catatonic and had a Glasgow Coma Scale score of 11 (E4V1M6). Pupils were dilated but reactive to light. A straw and a snuffbox containing a plastic bag with a white powder were found in his pocket. The bag was labeled “PCP”.

When arriving at the emergency department (ED) at 00:47, observations revealed respiratory rate 16 breaths per minute, pulse 95 bpm, oxygen saturation 98%, blood pressure 151/85 mmHg, temperature 37.2 °C and blood glucose 5.4 mmol/L. Creatinine was 82 μmol/L and glomerular filtration rate was 90 mL/min. During the next hour the patient developed pyrexia with a temperature of 38.5 °C and lactic acidosis (pH: 7.31, P-Lactate: 8.5 mmol/L). The patient also became agitated and started hallucinating and was treated with diazepam and haloperidol. At approximately 2 a.m. in the morning, the patient began to snore and oxygen saturation dropped to 92%. Therefore, he was sedated with propofol, intubated and moved to an intensive care unit (ICU). Shortly after arriving at the ICU, the patient became afebrile and continued to be so during the remainder of his time in the ICU. Likewise, his blood pressure, pulse, pH and lactate level normalized and the patient could be extubated at 09:45 in the morning. Table 1 shows the precise timing of the various events in the clinical case.

2.2. Autopsy case 1

A 27-year-old male was found dead at home in the bathtub. He had a history of substance abuse and regularly ordered hallucinogenic drugs online. Autopsy revealed some swelling of the brain, pulmonary edema, lots of urine in the bladder and burns on head, arms, torso and legs due to hot water from the shower.

2.3. Autopsy case 2

A 21-year-old suicidal male that lived with two friends was found unresponsive in bed after snoring loudly during night and early morning. He was pronounced dead after almost an hour of cardiopulmonary resuscitation. The deceased was a known addict and before he passed away he had been drinking alcohol, taking Subutex and possibly other drugs. Autopsy revealed brain edema, pulmonary edema, a patent foramen ovale and discrete coronary atherosclerosis.

2.4. Autopsy case 3

A 27-year-old male was found dead sitting on a chair in his apartment. The deceased had been suffering from psychiatric problems for a long time but according to relatives he was not suicidal. Several pharmaceuticals were found at the scene. Autopsy revealed congestion of the liver and lungs.

Table 1
Timeline and concentrations of 3-MeO-PCP in whole blood in the non-fatal intoxication case.

Day 1	22:00	Habitual state
Day 1	23:50	Ambulance arrives
Day 2	00:19	Ambulance leaves
Day 2	00:47	Arrives at the ED
Day 2	00:49	First sampling Concentration 3-MeO-PCP: 0.14 μg/g
Day 2	02:00	Intubated
Day 2	03:15	Arrives at the ICU, second sampling Concentration 3-MeO-PCP: 0.08 μg/g
Day 2	06:00	Third sampling Concentration 3-MeO-PCP: 0.06 μg/g
Day 2	09:45	Extubated
Day 2	18:00	Fourth sampling Concentration 3-MeO-PCP: 0.04 μg/g
Day 2	21:05	Discharged from the ICU
Day 3	11:30	Discharged from psychiatric ward

ED: emergency department; ICU: intensive care unit.

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