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Methcathinone: A new postindustrial drug

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Abstract

Methcathinone, a methyl derivative of cathinone, is an illicit drug also known as ephedrone. It is a stimulant found in the "khat" plant, *Catha edulis*, which can easily be synthesized from pseudoephedrine. Its intoxication is difficult to diagnose and cure properly for two reasons: (i) target consumers are usually "well-educated people" aware of the risks and precautionary measures and (ii) intoxication by cathinone derivatives of synthetic or natural (derived from the khat) origin induce misleading symptoms. As a result, documented reports of methcathinone intoxication that are based on reliable analyses are rare. This paper describes a case of reiterated coma due to an overdose of methcathinone dissolved in alcohol that was taken with bromazepam. A 29-year-old woman was admitted to an emergency department for a coma of toxic origin. Medical files showed that it was her second such episode to occur that month. Moreover, the family indicated signs of depression, incoherent behaviour and intake of "amphetamine-like" drugs. Clinical examination revealed a Glasgow coma score of 9, symmetrical reactive pupils with mydriasis and no convulsions. The patient presented with rapid respirations and her blood pressure was 93/53 mmHg. The ionogram and the blood gas analyses were normal, while the blood alcohol level was 0.167 g/dL. Urinalysis revealed the presence of benzodiazepines and a high concentration of amphetamines (methcathinone: 17.24 mg/L, ephedrine: 11.60 mg/L and methylephedrine: 11.10 mg/L). In addition, serum analysis revealed bromazepam (8.89 mg/L), methcathinone (0.50 mg/L) and methylephedrine (0.19 mg/L). This case showed that the consumption of bromazepam and alcohol altered the typical clinical symptoms of cathinone derivative intoxication, namely hypertension and convulsions. Methylephedrine, an impurity resulting from the alkylation of a primary amine, can be considered a chemical tag indicating fraudulent synthetic origin of the drug. This case describes a documented example of new addictive behaviour of "well-educated" people involving the intake of methcathinone, a postindustrial psychostimulant intentionally combined with an anticonvulsant benzodiazepine. However, this specific case suggests that in spite of a very high bromazepam concentration in presence of the potentiator alcohol, the vital respiratory function would be probably maintained, thanks to the association with methcathinone.

Keywords: Methcathinone; Ephedrone; Illicit drug

1. Introduction

Methcathinone is an illicit drug also known as ephedrone, which is a methyl derivative of cathinone, a stimulant found in the khat plant, *Catha edulis*. It can be easily manufactured via the oxidation of pseudoephedrine (Fig. 1) [1]. However, a difference between the clinical effects related to intoxication by cathinone derivatives from synthetic and natural (derived from the khat) origin may be observed [2]. The initial concentration of unreacted methcathinone precursor, namely pseudoephedrine, could be the reason for the differences in adrenergic stimulating effects on the α and β adrenergic receptors that are associated with synthetic methcathinone [3]. Although methcathinone and cathinone are structurally similar to adrenaline and norephedrine, respectively, they act

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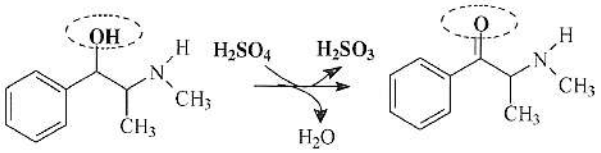


Ephedrine Methcathinone

Fig. 1. Synthesis of methcathinone.

indirectly by activating central and peripheral catecholaminergic pathways, as observed with ketophenylamines [4]. As a result of khat poisoning, a moderate increase in blood pressure and heart rate along with headaches, which are probably due to cerebral vascular vasoconstriction, may be observed [5]. Methcathinone can trigger neuropsychiatric syndromes, such as psychomotor agitation, tremors and insomnia. Documented reports of methcathinone intoxication that are based on reliable analyses are rare since it is not systematically screened for in toxicological analyses [6].

This paper describes a case of coma due to an overdose of methcathinone taken in conjunction with bromazepam and alcohol.

2. Case report

At 10:00 p.m., a 29-year-old woman was admitted to an ED in Paris suburbs for a coma of toxic origin. Medical history showed that it was the second such episode to occur in the month prior. In both cases, the patient consumed Lexomil® (bromazepam) dissolved in alcohol. Moreover, the family indicated signs of depression, incoherent behaviour and an intake of "amphetamine-like" drugs mixed with rum and whisky.

Clinical examination revealed a Glasgow coma score of 9 and symmetrical reactive pupils with mydriasis. The patient presented with rapid respirations. Her blood pressure was 93/53 mmHg.

Chest examination was normal. The electrocardiogram showed a sinusal heart rate (HR) of 92 bpm without any further ECG abnormalities. The rest of the examination was unremarkable.

Laboratory findings were normal, in particular the blood gas analyses, the blood-glucose level, the hydroelectrical, renal and enzymatic and muscular check up. The toxicological analyses revealed a blood alcohol level of 0.167 g/dL and the presence of benzodiazepines in the urine (pH 5.4). Additionally, a high concentration of amphetamines was detected in the urine by fluorescence polarisation immunoassay (FPIA) (automate Axsym, Abbott Laboratories, USA). The amphetamines were identified in the urine by high-pressure liquid chromatography coupled with UV detection (HPLC/UV) (automate Remedi, Biorad Laboratories, USA) at the following concentrations: methcathinone (17.24 mg/L), ephedrine (11.60 mg/L) and methylephedrine (11.10 mg/L). Serum analysis by HPLC (automate Remedi, Biorad Laboratories, USA) detected the following at the listed concentrations: bromazepam (8.89 mg/L), methcathinone (0.50 mg/L) and methylephedrine (0.19 mg/L).

The patient was kept in a quiet room for hemodynamic and neurological monitoring. As her clinical status evolved quite favourably over the course of the next 24 h, she was sent to a psychiatrist.

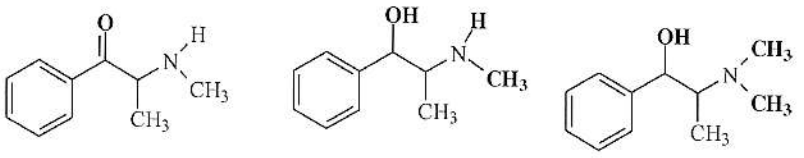
3. Discussion

Although the blood alcohol level of the patient was 0.167 g/dL, the assumption of an ethylic coma was excluded because the ionogram and blood gas analyses were normal. Additionally, we noted the lack of hypoglycemia as well as the absence of anionic and basic deficits related to an acetate outbreak. Therefore, the coma was attributed to methcathinone poisoning associated with bromazepam. On one hand, the bromazepam concentration of 8.89 mg/L approached a toxic level and showed a significant intake of this benzodiazepine [7]. It should be noted that bromazepam concentration reaching 8.89 mg/L in the presence of alcohol potentiator is the highest non-fatal level ever reported. Possibly, methcathinone might have contributed in the maintenance of the vital respiratory function. Indeed, the presence of rapid respirations instead of respiratory distress eliminated the hypothesis of a coma due solely to benzodiazepine overdose. On the other hand, the high level of methcathinone in the urine as well as its high concentration in the serum, rapid respirations without acidosis, mydriasis and behaviour disorders, suggested methcathinone poisoning [8]. The typical clinical symptoms of methcathinone intoxication, namely hypertension and convulsion, may have been masked by the concomitant intake of benzodiazepines (which would have anticonvulsant and hypotensive effects) and alcohol (which would contribute a vasodilating effect). In fact, the use of benzodiazepines is indicated in the treatment of intoxication by cathinone derivatives [9]. Some other authors found low blood pressure in cases of intoxication by phenylalkalamines mixed with other substances that affect the autonomic nervous system [10]. This is why drawing the etiologic diagnosis of coma due to methcathinone intoxication was delayed for 1 month.

It is of note that the toxicological screening of the urine sample by HPLC revealed the presence of ephedrine, the major urinary metabolite of methcathinone (over 55% compared to the unchanged native form in the urine) and whose elimination rate increases with acidic pH, as was seen in our patient [4,11,12].

Methylephedrine is a chemical impurity produced during the methylation of its primary amine (phenylpropanolamine) leading to monomethylamine (pseudoephedrine) and dimethylamine (methylephedrine) (Fig. 2) [13,14]. Thus, we can consider methylephedrine as a chemical tag of fraudulent chemical synthesis [1].

Using FPIA for phenylkylamine detection was very helpful in the setting up of the diagnosis but required



Methcathinone Ephedrine Methyl-ephedrine

Fig. 2. Chemical structure of detected phenylalkylamines.

separative and spectroscopic methods for confirmation [1,15].

4. Conclusion

We report a case of a 29-year-old woman who presented in a coma with mydriasis and rapid respirations due to intentional methcathinone intoxication associated with bromazepam and alcohol. The addition of alcohol and bromazepam altered the typical clinical symptoms of intoxication by cathinone derivatives, namely hypertension and convulsion.

This case shows new addictive behaviours in "well-educated" people involving the intake of methcathinone, a postindustrial psychostimulant intentionally combined with an anticonvulsant benzodiazepine.

Toxicological effects of methcathinone are not widely known. Additionally, these effects can be mistakenly attributed to having come from the synthetic precursors of methcathinone. In cases of synthetic ketophenylamine intoxication, high concentrations of pseudoephedrine with home-made methcathinone, without further extractions, may often cause dramatic adrenergic effects (malignant hypertension along with stroke) as documented in the medical literature.

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