4-CHLORO-2,5-DIMETHOXY AMPHETAMINE (D0C) - A RARELY REPORTED RAVE SCENE DRUG OF ABUSE

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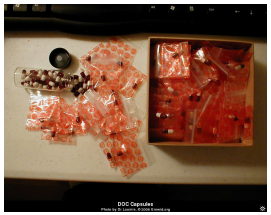
Introduction

- Recreational drug use in the UK is common, and amongst the highest in both Europe and the developed world. [1]
- Many recreational drugs such as amphetamines, MDMA ('ecstasy') and cocaine are controlled under specific legislation, for example in the UK this is the Misuse of Drugs Act (1971).
- More recently other drugs such as gamma-hydroxybutyrate (GHB) have been classified under these specific regulations when it has become known that there are problems associated with their use.
- However, new synthetic compounds such as 1-benzylpiperazine, Foxy Methoxy and other hallucinogenic amphetamines, continue to be developed and/or marketed to replace them. [2-4]
- 4-chloro-2,5-dimethoxy amphetamine (DOC) is a synthetic ring-substituted phenethylamine amphetamine derivative. Therefore, in the UK, it is controlled by the generic Misuse of Drugs legislation.
- There have been no previous reports of adverse effects associated with DOC use in the medical literature, although there has been one report of the adverse effects of DOC use previously on the internet site Erowid. [5]

Case Report Initial Presentation

- A 20-year-old-male with no significant past medical history collapsed having tonic-clonic seizures at a 'rave party'.
- His friends reported that he had taken DOI (4-iodo-2,5-dimethoxyamphetamine); additionally they confirmed that the patient had co-ingested a cocktail of ethanol and other recreational drugs of abuse.
- He was intubated at 'the scene' by the paramedic crew in view of his reduced level of consciousness. On arrival in the ED he had a sinus tachycardia (152 bpm) and blood pressure of 144/57 mmHg; he was apyrexial (temperature on arrival 36.8ºC).
- His pupils were dilated (6 mm) and were non-reactive to light. The remainder of his neurological examination was normal, and in particular there was normal tone and reflexes and no evidence of clonus.
- His initial electrocardiogram (ECG) confirmed his sinus tachycardia, with normal QRS duration and corrected QT interval (QTc).
- An arterial blood gas showed a metabolic acidosis.
- Initial biochemistry and haematological investigations were normal, apart from a reduced corrected calcium of 2.02mEql/L (NR 2.20-2.63mEql/L), elevated random blood glucose of 173mg/dL, neutrophilia of 10.5 x 10^6 and a low serum albumin of 30g/L (NR 35-50g/L)
- There was biochemical evidence of rhabdomyolysis with an initial creatinine kinase of 1314 iU/L and a normal troponin T.
- In view of his reduced level of consciousness and previous seizure, a CT scan of his brain was performed, which was normal.



Case Report Subsequent Progress

- Following initial stabilisation in the ED, he was admitted to the ICU for ongoing management, where he developed a low grade pyrexia (37.6º), and became cardiovascularly unstable with a systolic blood pressure of 98 mmHg and a heart rate of 92 bpm. His blood pressure improved with intravenous (IV) fluid resuscitation (500 ml coloid and 500mL crystalloid) and he did not require any inotropic support.
- Although he was covered with broad spectrum intravenous (IV) antibiotics (Cefuroxime and Metronidazole) for possible aspiration pneumonia, there was no biochemical or radiological evidence of significant sepsis and cultures remained negative.
- The patient responded well to fluid resuscitation and remained heamodynamically stable during the rest of the ICU admission.
- His creatinine kinase concentration peaked at 4924 iU/L and there was no associated renal dysfunction.
- His initial metabolic acidosis corrected with intravenous fluid resuscitation, and it is most likely that this was due to his tonic-clonic seizures prior to admission to the ED.
- He was extubated 22 hours following admission to and was discharged from hospital with no long term sequelae.

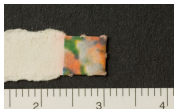
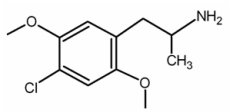


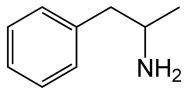
Figure 1. Paper tab obtained by TICTAC Communications and found to contain DOC.

Chemical Structure of

DOC



Amphetamine



Toxicological Analysis

- Routine toxicological analysis of urine samples using full scan gas chromatography-mass spectrometry (GC/MS) following liquid/liquid extraction, identified presence of: DOC, MDMA and MDA. There was no alcohol or other illicit drugs detected.
- MDMA and MDA were quantified in a serum sample – concentrations 0.57mg/L and <0.05mg/L respectively. The MDMA concentration was in the range associated with toxicity.
- DOC was confirmed in both specimens using single ion monitoring (SIM). The method was run in positive electron impact ionisation mode (EI) and the following ions were monitored m/z: 44 for DOC and 91 for pyribenzamine (internal standard).
- Quantification of DOC could not be performed due to lack of a commercially available pure reference standard. The standard used for confirmation of DOC in the serum sample was supplied by TICTAC Communication, who identified the compound from the associated paper tab (Figure 1) using NMR spectroscopy and liquid chromatography-mass spectrometry (LC/MS/MS).
- A further sample of case material identified as containing DOC, was supplied by a Swedish Forensic Laboratory and found to be identical to the compound in the paper tab and biological samples.

Conclusions

- We have described a case of poly-drug use, including DOC, with toxicological screening that confirmed the presence of DOC in plasma samples.
- Routine toxicological screening is generally not undertaken in patients with recreational drugs of abuse toxicity, since it will usually have no immediate impact on the clinical management of that individual patient. However, where this is undertaken with the appropriate expertise, often novel drugs of abuse are detected. [1]
- A more widespread use of 'routine' toxicological screening programmes could be useful to demonstrate the evolving epidemiological trends in recreational drugs of abuse availability and toxicity. [6]
- Some of the discovered compounds, such as DOC described here, may already be covered under current generic legislation due to their chemical similarity to other already classified drugs. However, others may represent true novel drugs of abuse, which will need further investigation to determine the appropriate degree of legal enforcement concerning their possession and/or supply.

References

1. United Nations Office on Drugs and Crime. 2007 World Drug Report. United Nations Publication E. 07.XI.5 (ISBN 978-92-1-148222-5). www.unodc.org/
2. Wood DM, Dargan PI, Button J, Holt DW, Ovaska H, Ramsey J, Jones AL. Collapse, reported seizure--and an unexpected pill. Lancet. 2007; 369: 1490
3. Babu K, Boyer E, Hernon C, Brush D. Emerging Drugs of Abuse. Clinical Pediatric Emergency Medicine. 2005; 6: 81-84
4. Wilson J, McGeorge F, Smolinske S, Meatherall R. A foxy intoxication. Forensic Sci Int. 2005; 148: 31-36
5. Eurowid news report (last accessed 5th September 2007). http://www.erowid.org/chemicals/doc/doc_article1.shtml
6. Staack RF. Piperazine designer drugs of abuse. Lancet. 2007; 369: 1411-1413