CASE REPORT

Ecstasy induced hepatitis mimicking viral hepatitis

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Abstract

Three cases of jaundice after ingestion of 3,4-methylenedioxymetamphetamine (MDMA), known as 'ecstasy', are reported and the complications associated with the misuse of this drug, which was initially misrepresented as 'safer than alcohol' are described. Ingestion of 'ecstasy' should be considered when investigating unexplained jaundice in younger patients.

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Keywords: ecstasy, 3,4-methylenedioxymetamphetamine (MDMA), adverse effects, jaundice.

MDMA (3,4-methylenedioxymetamphetamine), known as 'ecstasy', is a synthetic amphetamine derivative developed in 1914 as an appetite suppressant. It was never marketed – but was 'rediscovered' in the early 1970s as an adjunct to psychotherapy. Discarded as a psychiatric drug, it re-emerged as a 'recreational' drug in the 1980s. Initially claimed to be 'safer than alcohol', its recognised adverse side effects include trismus, anorexia and nausea, hyperthermia, and a tachycardia with hypotension. The pharmacological effects of the drug are compounded by physical exertion, and its popular use in Britain as a 'dance drug' has shown it to be dangerous,¹ sometimes with fatal consequences.²⁻⁴

Case reports

Case 1

A 24 year old male insulin dependent diabetic car mechanic was admitted with progressive, painless jaundice.

While 'out' with friends three days before admission, he became unwell with agitation, nausea, and profuse sweating. It transpired that his beer had been 'spiked' with ecstasy. He was taken home, where his blood sugar was 17 mmol/l on fingerprick (Boehringer Mannheim) testing. The symptoms settled over the ensuing hours, but over the next two days he became lethargic, anorexic, and nauseated, vomiting several times. On the third day his parents noticed him to be jaundiced and he was admitted to the infection unit for investigation. There was no history of intravenous drug abuse, homosexual activity, recent foreign

travel, blood transfusion or contact with known hepatitis patients.

On examination he was jaundiced but afebrile and clinically well. There was no organomegaly or stigmata of chronic liver disease. Serum bilirubin, aspartate aminotransferase, and alkaline phosphatase values rose progressively with peaks at 346 $\mu\text{mol/l}$ ($N < 22$), 950 U/l ($N < 31$), and 251 U/l ($N < 105$) respectively on the fifth hospital day. Serological tests for hepatitis A, B, and C virus, cytomegalovirus and Epstein-Barr virus were negative. The smooth muscle antibody was positive, but antinuclear and antimitochondrial antibodies negative. Over the next month the patient's clinical and biochemical hepatitis slowly resolved. Four months after his admission his liver function tests had returned to normal and he remained seronegative for hepatitis B and C virus. The smooth muscle antibody had become negative.

Case 2

A 22 year old male student was admitted with a short history of progressive painless jaundice. For some 10 days he had felt lethargic with generalised pruritis and abdominal discomfort after meals.

Admitting to 10-15 units of alcohol over a weekend, he denied intravenous drug abuse – although he had 'dabbled' with cannabis and 'magic mushrooms' as a schoolboy. Four weeks before his admission he had ingested an unknown amount of ecstasy. Three years previously, while in the intensive treatment unit after a fall from a cliff, he received a blood transfusion. There was no history of recent foreign travel or of promiscuous or homosexual practises. There had been no contact with a known case of hepatitis. On examination he was jaundiced but afebrile and clinically well. The liver was palpable 3 cm below the costal margin, but not tender. There was no splenomegaly or stigmata of chronic liver disease. Serum bilirubin was 137 $\mu\text{mol/l}$, aspartate aminotransferase 748 U/l, and alkaline phosphatase 216 U/l. Serological tests for hepatitis A, B, and C virus, cytomegalovirus and Epstein-Barr virus proved negative. Copper and caeruloplasmin concentrations were normal and the nuclear and smooth muscle antibodies negative. During his stay in hospital his clinical and biochemical jaundice progressively worsened. The serum bilirubin and aspartate aminotransferase values peaked on the ninth day at 371 $\mu\text{mol/l}$ and

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Figure 1: Swollen hepatocytes. Haematoxylin and eosin, original magnification $\times 4000$.

Figure 2: Inflammatory infiltrate in portal tracts. Haematoxylin and eosin, original magnification $\times 1600$.

1410 U/l respectively. Treatment was started with prednisolone (40 mg daily) and the serum bilirubin concentration rapidly decreased to 67 $\mu\text{mol/l}$ and aspartate aminotransferase to 278 U/l. The corticosteroids were stopped after 10 days. During the next three months the patient's liver function tests gradually returned to normal values and he remained seronegative for hepatitis B and C virus.

Case 3

A 23 year old toolman was admitted to hospital with a one month history of malaise, anorexia, and generalised pruritis. Systematic enquiry further disclosed vague right upper quadrant abdominal discomfort, and the passage of pale stools and dark urine. He admitted to taking four 'ecstasy' tablets and between 5 and 10 units of alcohol per week for the past year – but denied intravenous drug abuse, homosexual activity, recent foreign travel or blood transfusion.

On examination he was icteric, and biochemical tests requested by his general practitioner showed a serum bilirubin of 75 $\mu\text{mol/l}$, aspartate aminotransferase 639 U/l, alkaline phosphatase 265 U/l and γ -glutamyltransferase 395 U/l. These improved to 61 $\mu\text{mol/l}$, 468 U/l, 174 U/l, and 268 U/l respectively by the time of admission seven days later. Serum copper and caeruloplasmin concentrations were normal. Nuclear, mitochondrial, and smooth muscle antibodies were absent and there was no serological evidence of hepatitis A, B or C, cytomegalovirus or Epstein-Barr virus. Liver biopsy was performed four days after admission, and showed hepatitis characterised by lobular disarray with numerous swollen hepatocytes (Fig 1) and acidophil bodies, particularly evident in zone 3. Kupffer cells appeared prominent and were laden with large amounts of ceroid pigment. Most of the portal tracts

contained a dense infiltrate of inflammatory cells, predominantly lymphocytes, but with frequent plasma cells and eosinophils (Fig 2). In some areas there was evidence of 'spillover' of inflammatory cells into the periphery of lobules. The patient's liver function tests continued to improve without specific treatment and were normal five weeks after hospital admission. Serological tests remained negative for hepatitis B and C six months after the illness.

Discussion

The synthesis of MDMA requires minimal knowledge of chemistry and most of the MDMA available in Great Britain is produced by clandestine laboratories in the Netherlands.⁵ Experience of young people in Britain with use of the drug evolved between 1984 and 1989,⁶ and through its adoption by the new culture of all night dancing sessions, called 'raves', an estimated half a million young people had taken the drug by 1992.⁷ Enquiries to the National Poisons Information Service at Guy's Hospital, London, about MDMA increased from 5 to 10 per month in 1991 to 30 to 50 per month in 1992.⁴ In Britain alone, at least 15 young people have died after the ingestion of MDMA, mostly after taking a 'recreational dose' of the drug combined with vigorous dancing at all night dance sessions.⁷ The ensuing high body temperature with hypotension and a tachycardia can result in cardiac arrhythmias, disseminated intravascular coagulation, rhabdomyolysis, acute renal failure, and death. In this context acute hepatic failure has also been reported.^{2,4}

The subacute idiosyncratic toxic hepatitis seen in this report has been described in published reports in nine cases,^{4,8,9} and is believed to be induced by MDMA or one of its metabolites, a contaminant in MDMA manufacture,

Clinical course, peak bilirubin, peak aspartate aminotransferase (AAT), peak alkaline phosphatase (ALP), and peak γ -glutamyltransferase (γ GT) in three patients with MDMA induced hepatitis

Case	Interval between MDMA ingestion and peak values	Peak bilirubin	Peak AAT ($\mu\text{mol/l}$)	Peak ALP (U/l)	Peak γ GT (U/l)	Progress and outcome (U/l)
1	1 tablet 8 days previously	346	950	251	457	Resolution in 3 months
2	Unknown amount 5 weeks previously	371	1410	223	134	Resolution in 3 months
3	Regular use 4 tablets per week up to 3 weeks previously	75	639	265	395	Resolution in 5 weeks

or by an additive in tablet or capsule formulation. This form of hepatitis can develop after incidental (case one and two) or during regular ingestion (case three) of the substance. Analytical confirmation of MDMA was not possible because misuse had occurred some time previously. However, Henry⁴ and Shearman⁸ describe recurrent hepatitis after repeated exposure to MDMA, providing strong evidence for the aetiological role of this drug.

None of our patients gave a history of heavy alcohol intake or of intravenous drug misuse and, although the clinical presentation would have been compatible, none had evidence of viral hepatitis. The interval between ingestion of the drug and the initial symptoms varied; from three days (in case one) to four weeks (in case two). Pruritis was present in two of the patients.

The degree of hepatic dysfunction in the patients reported in published works was severe in most cases and lead to death in one patient and to liver transplantation in another.⁴ The peak bilirubin concentrations in our patients varied from 75 $\mu\text{mol/l}$ to 371 $\mu\text{mol/l}$ and the peak aspartate aminotransferase from 639 to 1410 U/l in case three and two respectively (Table). Liver biopsy, where performed

(Shearman *et al.*,⁸ Gorard *et al.*⁹ and case three in this report), showed evidence of acute hepatitis with lobular disarray and centrilobular drop out of hepatocytes. Recovery from the hepatic insult takes place over a variable amount of time, from three weeks to three months.

Hepatotoxicity should be recognised as a clear complication of MDMA misuse and the increasing number of cases reported, makes it worth exploring 'ecstasy' as an aetiological agent when investigating young people presenting with painless jaundice.

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