IRISH MEDICAL JOURNAL JULY 1993 VOLUME 86 NO4

Original papers

Ecstasy abuse in Ireland

CREGG MT, TRACEY JA
Poisons Information Centre, Beaumont Hospital, Dublin 9.

Abstract

Since the late 1970s, ecstasy (MDMA) has enjoyed increasing popularity as a recreational drug. We report a dramatic increase in reports of ecstasy ingestion to the National Poisons Information Centre from zero in January 1991 to thirty seven in June 1992. We have analysed these thirty seven cases retrospectively for age and sex distribution, clinical details and outcome. The patients involved were predominantly male (80%) and aged 10-30 years, the highest incidence being in the 16-25 year old age group. Thirty two (86%) patients were symptomatic. Symptoms in most cases were relatively mild. One death was reported due to congestive heart failure. The symptoms most frequently reported include dilated pupils, agitation, excitement, hallucinations, tachycardia, palpitations, CNS depression, incontinence and psychiatric symptoms.

Introduction

Ecstasy (MDMA, 3,4-methylenedioxymetamphetamine) is a semi-synthetic amphetamine derivative which was developed as an appetite suppressant in 1914, but was never marketed as such. In the early 1970s it was used in psychotherapy to facilitate therapeutic communication and to improve patient self-esteem.[1,2] Since the late 1970s ecstasy (also known as "XTC", "Adam", "MDM" and "M and M") has enjoyed increasing popularity as a recreational drug. In July 1985 MDMA was classed as a Schedule 1 drug with "high potential for abuse and without accepted medical use".

The effects of MDMA are usually euphorigenic. It produces a heightened sense of self-awareness, enhanced sociability, benevolence and sustained energy. Ecstasy is often taken in Britain[3] and Ireland as a "dance drug" at "rave" parties where its use is associated with extreme physical activity which may compound the toxic effects of the drug. In Britain at least seven deaths have followed use of ecstasy as a "dance drug".[3] The increasing number of calls we are receiving at the Poisons Information Centre about ecstasy ingestion prompted us to review the cases which have been reported to date.

Methods

This study retrospectively analysed all reports of ecstasy ingestion to the Poisons Information Centre between January 1991 and June 1992. We recorded patient age, sex and clinical details at the time of each call. We obtained the outcome of serious cases from the hospitals involved and the coroners report for any fatalities.

Results

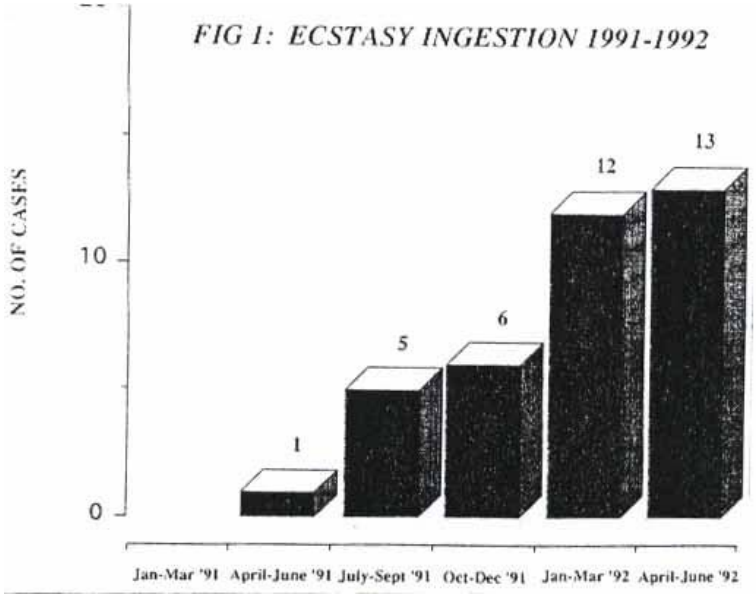
Incidence – Ecstasy abuse has become more popular in Ireland within the past 18 months. Reports of ecstasy ingestion to the Poisons Information Centre have increased dramatically from zero in January 1991 to 37 in June 1992 (Fig. 1).

Age and sex distribution – The patients involved were predominantly male (80%) and spanned a range of ages from 10-30 years. The highest incidence was seen in the 16-25 year old age group (Fig.2).

Clinical details – In this study most patients had only mild symptoms following ecstasy ingestion. A wide variety of symptoms (summarised in Table 1) were reported. Eight patients had no symptoms, 18 patients reported only one symptom and 11 patients had two or more symptoms. The most common complaints were agitation, excitement, hallucinations, palpitations and psychiatric symptoms. The most common findings were dilated pupils, tachycardia, hypertension, CNS depression and incontinence, One fatality was reported during the study period. This occurred in a 17 year old male and was attributed to congestive heart failure. Since completion of the study one further fatality has been reported to the Poisons Information Centre. This occurred in a 19 year old male.

Table 1 – Signs/symptoms reported following ecstasy ingestion

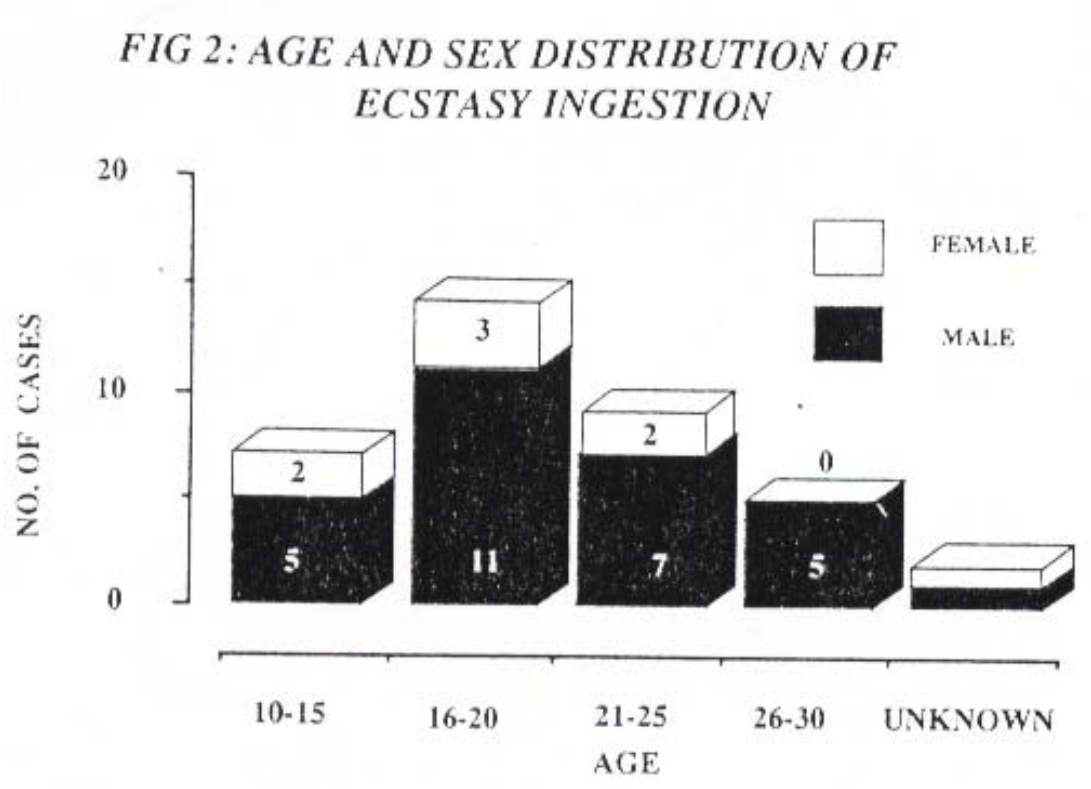
Sign/symptom	No of cases	% of cases
Agitation	9	24
Hallucinations	5	13.5
Excitement	4	13.5
Psychiatric symptoms	3	8.1
Palpitations	2	5.4
Dilated pupils	2	5.4
Hypertension	2	5.4
Incontinence	2	5.4
Tachycardia	2	5.4
Coma	2	5.4
Aggression	1	2.7
Vomiting	1	2.7
Trismus	1	2.7
Hypokalaemia	1	2.7
Muscle spasm	1	2.7
Slurred speech	1	2.7
Drowsiness	1	2.7
Convulsions	1	2.7
Depression	1	2.7
Cardiorespiratory arrest	1	2.7
Death	1	2.7



Discussion

The exact mechanism of MDMA toxicity remains unclear. Its structural similarity to endogenous catecholamines results in stimulation of both sympathetic and central nervous systems.[4] Animal experiments suggest it can cause long-term depletion of serotonin in the CNS.[5] In overdose, MDMA acts as a sympathomimetic agent, stimulating both alpha- and beta adrenergic receptors[6], leading to a sympathetic overdrive. Deaths which occur soon (<24 hrs post ingestion) are usually due to cardiac arrhythmias, seizures and CNS depression. Late deaths (24-48 hrs post ingestion) seem to result from a syndrome resembling mallignant hyperthermia.[3]

It appears that MDMA may have cardiovascular actions similar to its parent amphetamines including increased cardiac output, hypertension and induction of arrythmias. Dowling[7] studied a series of five deaths following ingestion of MDMA or MDEA (MDMA's legal replacement, 'Eve'). He attributed the death of a previously healthy eighteen year old to ventricular fibrillation following MDMA ingestion. The death reported during the study period was attributed to congestive heart failure in a previously healthy seventeen year old male. These may be examples of idiosyncratic reactions or may suggest a low toxic/therapeutic ratio for MDMA. It is also proposed that MDMA may induce or augment potentially fatal arrhythmias in individuals with predisposing cardiac disease.[7]



Hyperthermia is a frequent complication of ecstasy ingestion, particularly in fatal overdoses. Henry and co-workers[8] suggested hyperthermia seen in MDMA overdose represents a failure of thermoregulation due to interaction of at least three factors: a central effect of the drug (which may be serotonergic), marked physical activity and inadequate fluid replacement. Reviewing seven fatalities following ecstasy ingestion in England, they described a clear pattern of toxicity characterised by hyperthermia, DIC, rhabdomyolysis and acute renal failure. The ecstasy-induced death of a nineteen year old male reported to the Poisons Centre since the completion of this study followed exactly this profile of toxicity (i.e. hyperthermia, DIC and complete renal failure).

Further possible complications of acute overdose include intracerebral haemorrhage (secondary to a sudden increase in blood pressure), muscle rigidity with rhabdomyolysis, disseminated intravascular coagulopathy, adult respiratory distress syndrome, acute renal failure, hepatocellular necrosis and coma.[6,9]

Chronic abuse of ecstasy has recently been reported to cause a number of dysphoric reactions including flashbacks[10], anxiety, confusion, insomnia[1], a paranoid psychosis clinically indistinguishable from

schizophrenia[11], panic attacks[12], recurrent jaundice[13] and acute hepatitis.[7,14] Most of these effects are thought to be reversible after a prolonged drug-free state.

Treatment of ecstasy overdose – Since amphetamine overdose can affect multiple systems medical assessment should include monitoring of haemodynamic parameters, renal and clotting function, rectal temperature, psychological and neurological status. Management should be active and immediate. In patients who present within four hours of ingestion, gastric lavage should be followed by administration of activated charcoal. Further therapy depends on which symptoms predominate.

Anxiety, agitation and hyperactivity should generally be controlled by the use of repeated small doses of intravenous diazepam. Chlorpromazine has been suggested for treatment of severe agitation not controlled by diazepam, but it produces undesirable side effects and has been shown to enhance toxicity of some amphetamines.[15,16,17] Haloperidol was proposed to be safer and more effective than chlorpromazine[18] and has been used successfully in MDMA overdose.[19] However, due to their potential for enhanced toxicity, we do not recommend use of either of these two agents. Seizures should be treated with airway management, ventilatory support and intravenous diazepam. Convulsions refractory to diazepam may be controlled with phenytoin.

Tachycardia and hypertension should be treated with beta blockers (eg.atenolol) and alpha-blockers (eg. Phentolamine) respectively. Labetalol, a combined alpha- and beta-blocker, may be even more suitable.

Vigorous fluid replacement is necessary to correct volume depletion and to facilitate thermoregulation by sweating.[20] Mild fever should be treated with cool compresses and sponging. Rectal temperatures exceeding 39°C should be treated more aggressively with hypothermic blankets and ice baths as well as administration of dantrolene. Dantrolene infusions were shown to rapidly correct hyperpyrexia and the hpermetabolic state seen in MDMA overdose.[21] If dantrolene is ineffective in controlling pyrexia, the patient should be paralysed and mechanically ventilated.

Since amphetamines are weak bases urinary acidification increases the excretion of unmetabolised drug and causes a decrease in plasma half-life. The efficacy of this on clinical outcome, however, remains controversial since urinary acidification is contra-indicated in the presence of rhabdomyolysis and myoglobinaemia.[22] This is due to the potential for renal failure from myoglobin precipitation in the tubules. Maintaining a high urine output will help prevent acute renal failure secondary to the myogloinaemia produced by rhabdomyolysis.[22]

Reference

1 Greer G., Strassman R.J. Information on “Ecstasy” Am J Psychiatry 1985; 142 (11): 1391.

2 Shafer J. MDMA: Psychedelic drug faces regulation. *Psychol Today* 1985; 19(5): 68-9.

3 Henry J.A. Ecstasy and he dance of death. *BMJ* 1992; 305: 5.

4 Linden M.D., Smolinske S.C., Jones S.D. Hallucinogenic Amphetamines (Pharmacology Section) POISINDEX Information System, Micromedex, Ricaurte G., Ryan G., Strauss L., et al.; Hallucinogenic amphetamine selectively destroys brain serotonin nerve terminals. *Science* 1985; 229: 986-8.

6 Buchanan J.F., Brown C.R. Designer Drugs: A problem in Clinical Toxicology Medical *Toxicology* 1988; 3: 1-17.

7 Dowling G.P., Mc Donagh E.T., Bost R.O. Eve and Ecstasy: A Report of Five Deaths Associated with the Use of MDEA and MDMA. *JAMA* 1987; 257(12): 1615-7.

8 Henry J.A., Jeffries K.J., Dawling S. Toxicity and deaths from 3,4 methylenedioxymetamphetamine. *Lancet* 1992; 340: 384-7.

9 Simpson D.L., Rumack B.H. Methylenedioxyamphetamine: clinical description of overdose, death and review of pharmacology. *Arch Intern-Med* 1981; 141: 1507-9.

10 Creighton F.J., Black D.L., Hyde C.E. “Ecstasy:” Psychosis and Flashbacks *Br J Psyc* 1991; 159: 713-5.

11 Mc Guire P., Fahy T. Chronic paranoid psychosis after abuse of MDMA (“ecstasy”). *BMJ* 1991; 302: 697.

12 Whitaker-Azmitia P.M., Aronson T.A. “Ecstasy” (MDMA) – induced panic. *Am J Psychiatry* 1989; 146(1): 119

13 Gorard D.A., Davis S.E., Clark M.L. Misuse of Ecstasy (letter). *BMJ* 1992; 305: 309.

14 Shearman J.D., Chapman R.W.G., Satsangi J., Ryley N.G. Misuse of Ecstasy (letter). *BMJ* 1992; 305; 309.

15 Grinspoon L., Harvard University Press, Cambridge, Massachusetts.

16 Snyder S.H., Richelson E., Weingartner H. et al. Psychotropic methoxyamphetamines: structure and activity n man In: Amphetamines and Related Compounds; Proceedings of the Mario Negri Institute for Pharmacological Research E. Costa and S. Garattini (eds), Raven Press, 1970: 905-927.

17 Solursch L.P., Clement W.R. Hallucinogenic drug abuse – manifestations and management. *Can Med Assoc J* 1968; 98: 7-10.

18 Davis W.M., Logston D.G., Hickenbottom J.P. Antagonism of acute amphetamine intoxication by haloperidol and propanolol Toxicol Appl. *Pharmacol* 1974; 29: 397-403.

19 Hayner G.N., Mc Kinney H. MDMA. The dark side of ecstasy J Psychoactive. *Drugs* 1986; 18: 341-7.

20 Woods J.D., Henry J.A. Hyperpyrexia induced by 3,4-methylenedioxyamphetamine ("Eve"). *The Lancet* 1992; 340; 305.

21 Singarajah C., Lavies N.G. An overdose of Ecstasy: A role for dantrolene. *Anaesthesia* 1992; 47: 686-7.

22 Ellenhorn M.J. and Barceloux D.G. Amphetamines; Elimination Enhancement In: Medical Toxicology - Diagnosis and Treatment of Human Poisoning Elsevier Science Publishing Press 1988 : 638.

Correspondence: Ms Marie Cregg, Poisons Information Centre, Beaumont Hospital, Beaumont Rd, Dublin 9.