Peer reviewed article

Acute medical problems due to Ecstasy use

Case-series of emergency department visits

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Summary

Study aim: To describe the clinical characteristics of Ecstasy (3,4-Methylenedioxymethamphetamine, MDMA) toxicity.

Methods: Retrospective case-study of 52 self-reported Ecstasy intoxications presenting to our Emergency Department (ED) between January 2001 and December 2003.

Results: Most patients ingested Ecstasy together with other substances, including alcohol (51.9%) or other illicit drugs (71.1%). Medical problems leading to ED presentation were collapse or loss of consciousness (36.5%), palpitations (19.2%), dizziness or weakness (15.4%), and anxiety (13.5%). When other drugs were used in combination with Ecstasy the clinical presentation significantly changed. Panic reactions were observed in 4 of 13 patients with cocaine co-use (30.7%), compared to 3 of 39 patients without cocaine use (7.7%). Deep coma was found in 11 of 16 patients with co-use of gamma-hydroxybutyrate (GHB) or opiates (68.8%) but in none of the 36 patients who took Ecstasy without these drugs. Most patients were monitored in the ED. Six patients (11.5%) were transferred to an intensive care unit. Medical complications were severe in five patients and included cardiac arrest, hyperthermia, rhabdomyolysis, disseminated intravascular coagulation, renal insufficiency and liver failure, seizures, and one fatal outcome.

Conclusions: The clinical picture of Ecstasy related problems is complicated by multiple drug ingestion. Co-use of cocaine induces panic reactions. Co-use of GHB or opiates results in depressed levels of consciousness.

Key words: drug abuse; intoxication; ecstasy; 3,4-methylenedioxymethamphetamine; MDMA

Introduction

Ecstasy is a widely used recreational drug mainly containing the psychoactive substance 3,4-Methylenedioxymethamphetamine (MDMA). More than two hundred published case reports have described severe medical complications associated with the use of Ecstasy [1]. Mainly reported acute medical problems include hyperthermia-related syndromes [2], hepatotoxicity [2], hyponatraemia [3], and psychiatric complications [4]. Published case reports are probably more severe than cases that are not reported. Reports from poison control centres [5, 6] suggest that most acute adverse events involving Ecstasy are modest in severity. Investigations using pure MDMA in healthy volunteers in a controlled setting report symptoms of sympathomimetic activation but no serious medical complications [7]. Emergency departments (ED) could provide information about the relative frequency of the various adverse events due to Ecstasy use. In contrast to the large number of single case reports there are only two larger consecutive case series of Ecstasy-related problems presenting to an ED [8, 9]. Williams and colleagues analysed 48 cases of self-reported Ecstasy intoxication presenting to an ED in London, UK [8]. More recently, Sanjurjo et al. published data from 135 cases of self-reported Ecstasy including other amphetamine poisoning in Barcelona, Spain [9]. Both reports provide information on Ecstasy-related problems as encountered by emergency physicians and illustrate that the clinical picture is often complicated by multiple drug ingestion. In fact, most Ecstasy users consume other illicit drugs in addition to Ecstasy [9–11]. The present study aimed at describing the relative frequency of medical problems associated with self-reported Ecstasy use presenting to our ED. In addition, we wanted to analyse the frequency and kind of combined drug use and its effect on presenting symptoms. Based on data from interviews of Ecstasy users [12], we hypothesised that the conjunct use of other illicit drugs would lead to more serious adverse effects.

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Methods

The study was approved by the local ethics committee. A retrospective case-study design was used. We searched our hospital patient database for all consultations related to acute Ecstasy or MDMA use seen in our ED or ICU between January 2001 and December 2003. Only cases with acute Ecstasy intoxication were included. A case of Ecstasy intoxication was defined as any patient with acute medical problems resulting from self-reported Ecstasy use during the last 48 hours. Laboratory confirmation of MDMA use was available in 15 of 52 patients. In all other cases the history of Ecstasy ingestion was confirmed by the patients or by friends. We recorded demographic variables including age, sex, and hour and day of the ED visit; clinical variables including heart rate, diastolic and systolic blood pressure, Glasgow Coma Scale (GCS) score, body temperature, and laboratory tests. Hyperthermia was defined as a core body temperature above 38 ºC, hypothermia was defined as a core body temperature below 35 ºC. We recorded any co-ingestion of alcohol or other drugs, as noted in the history of the records by the emergency physician or as evidenced by the results of a blood ethanol test or a urine toxicology screen. Data were recorded on a standardised form for analysis.

Results

We recorded 52 episodes of intoxication with Ecstasy between January 2001 and December 2003. The annual number of intoxications was 17 cases in 2001, 22 cases in 2002, and 13 cases in 2003. Patient characteristics are shown in table 1. Data on previous drug use were available from 31 patients. As documented in the chart, at least twenty-seven patients (87.1%) had a prior history of illicit substance use including Ecstasy in at least 15 patients (48.4%). At least 18 (34.6%) were regular tobacco smokers. Most patients used illicit drugs at weekends at least once per month. Multiple drug consumption prior to the actual ED admission was common (table 1). Forty-seven patients (90.4%) currently used other drugs in combination with Ecstasy, 30 of which (57.7%) used more than one other drug in addition to Ecstasy. The most common additional substances were alcohol, cocaine, Gamma-hydroxybutyrate (GHB), cannabis, and other amphetamines. Data on the amount of Ecstasy tablets used were available in 26 cases. Sixteen patients (61.5%) used half or one tablet. 47 of all 52 patients (90.4%) had intentionally ingested Ecstasy. In 5 cases (9.6%) Ecstasy tablets were taken accidentally, ie tablets were mixed into a drink or mistaken for a medication. The median time from drug intake to presentation to the ED was six hours (range 1–48 hours). 29 patients (55.8%) were brought by an ambulance. Of all 52 patients, 20 (38.5%) lived in the city area of Zurich, 21 (40.4%) lived in Switzerland (not in Zurich), and 11 (21.1%) lived abroad. Twelve visits (23.1%) occurred during one of the three street parades taking place during the study period. The street parade is a large yearly dance and party event, attracting close to one million young people from all Europe. 6 of the 12 street parade cases lived abroad. Complaints and clinical findings in patients with Ecstasy intoxication are shown in table 2. The most frequent medical problems were unspecific and were related to sympathetic activation. Main complaints included palpitations, dizziness or weakness, and anxiety. The most frequent clinical findings were tachycardia, wide pupils, loss of consciousness, and hypothermia. Combined drug use significantly changed the clinical picture of the intoxication. Marked anxiety was observed in 4 of 13 patients with cocaine co-use (30.8%) compared to 3 of 39 patients with Ecstasy use without cocaine (7.7%). Deep coma (GCS = 3) was found in 9 of 13 patients with co-use of GHB (69.2%) compared to 2 of 39 patients who took Ecstasy without GHB (5.1%). Similarly, deep coma occurred in 3 of 4 patients with co-use of opiates (75%) compared to 8 of 48 patients who used Ecstasy without opiates (16.6%). All 11 patients who presented with deep coma (GCS = 3) had either used GHB or opiates in combination with Ecstasy, while deep coma was observed in none of the patients with Ecstasy use without co-use of these drugs. Hypothermia occurred in 5 of 13 patients with GHB co-use (38.5%) as compared to 2 of 39 patients with Ecstasy use without GHB co-use (5.1%). Similarly, hypothermia was found in 3 of 4 patients with opiate co-use (75%) compared to 7 of 48 patients without opiate use (14.6%). Finally, small pupils were registered in 2 of 4 patients with opiate co-use (50%) compared to one in 48 patients without opiate use (2.1%). Co-use of ethanol or of other amphetamines did not significantly affect the clinical picture of Ecstasy toxicity in the present study. Medical complications were severe in five patients (9.6%) including cardiac arrest in three patients, hyperthermia in two, rhabdomyolysis in two, disseminated intravascular coagulation (DIC) in two (including the fatal case and the one case with severe liver failure), renal insufficiency and liver failure in one, seizures in one and fatal outcome in one patient. Most of these complications occurred in four patients with combined drug use. However, in one patient with cardiac arrest, renal and severe liver failure and DIC, MDMA was the only drug confirmed by blood and urine analytic tests. Criteria for urgent liver transplantation were fulfilled in this patient but liver function recovered before a donor organ became available. Laboratory findings and data on the management of patients with Ecstasy toxicity are shown in table 2. Alcohol blood testing was performed in 17 of the 52 patients (32.7%) and 6 of these tests were pos-

Table 1.
Patient characteristics

Location of study	**Zurich**		**London**	**Barcelona**
Reference	**present study**		**[8]**	**[9]**
Study periode	**(2001–2003)**		**(1995–1996)**	**(2000–2002)**
Number of included patients	**N = 52**		**N = 48**	**N = 135**
	N	**%**	**%**	**%**
Male	41	78.8	66.6	68.1
Mean age [range]	26 [16–44]		23 [16–30]	24 [16–47]
16–20	17	32.7	NR	NR
21–30	19	36.5	NR	NR
31–44	16	30.8	NR	NR
Time of presentation				
Night arrival (20:00-8:00)	30	57.7	93.8	71
Week-end arrival (Friday 17:00 – Monday 8:00)	39	75	66.7	74.1
Place of drug use				
Night club or rave party	35	67.3	56.1	NR
At home	4	7.7	4.2	NR
Unspecified public place	3	5.8	2.1	NR
NR	10	19.2	37.5	NR
Place of living				
City area	20	38.5	NR	NR
Countryside (not city)	21	40.4	NR	NR
Abroad	11	21.1	NR	NR
Amount of consumed Ecstasy tablets				
0.5–2	22/26	84.6	80	NR
>2	4/26	15.4	20	NR
Concomitant current drug use				
Ecstasy alone (mono-intoxication)	5	9.6	33.3	NR
Ecstasy and only ethanol	10	19.2	1.7	NR
Ecstasy and other illicit drugs without ethanol	19	36.5	31.3	NR
Ecstasy and ethanol and other illicit drugs	18	34.6	18.8	NR
Ecstasy and more than one other drug (poly-intoxication)	30	57.7	NR	64.2
Coingestion of ethanol	28	53.8	35.4	51.9
Coingestion of other illicit drugs	37	71.7	50	NR
Cocaine	13	25	4	24.4
Gamma-hydroxybutyrate	13	25	4	15.6
Other amphetamine	10	19.2	25	*
Cannabis	10	19.2	10.4	6.7
Opiates	4	7.7	NR	1.5
Benzodiazepine	3	5.8	NR	1.5
LSD	2	3.8	6.3	NR
Ketamine	2	3.8	NR	8.9
Benzylpiperaziline	1	1.9	NR	NR

* The Study includes cases with Ecstasy and/or other amphetamine intoxication.
NR = not reported

itive (35.3% of those tested). The mean ethanol blood value was 35 mmol/l (range 5.8–56.8). Urine toxicology screens were available in only 15 of all 52 patients (28.8%). Management of Ecstasy intoxication was non-specific and consisted of cardiac monitoring in the ED during a mean time of 5.5 hours (range 1–16 h), intravenous fluid administration in 36 patients (71.1%) and sedation with benzodiazepines in 13 patients (25%). Five patients were intubated (9.6%) and six were transferred to an ICU (11.5%).

Table 2.

Clinical features of patients with Ecstasy intoxication

Place of study	Zurich		London	Barcelona
Reference	present study N = 52		[8] N = 48	[9] N = 135
	N	%	%	%
Vital signs/Clinical findings				
Tachycardia (HR >100/min)	28	53.8	66.7	25.2
Bradycardia (HR <60/min)	9	17.3	NR	2.2
Hypertension (SBP >160 mm Hg)	8	15.4	12.5	6.7
Hypotension (SBP <80 mm Hg)	2	3.8	NR	0.7
Hyperthermia (>38 °C)	2	3.8	18.8	0.7
Hypothermia (<35 °C)	6	11.5	NR	NR
Hyperventilation/Tachypnea (>20 breaths/min)	7	13.5	20.8	14.1
Collapse or loss of consciousness	19	36.5	22.9	8.8
GCS <3	11	21.1	NR	NR
GCS <8	17	32.7	NR	NR
GCS <12	20	38.5	NR	8.8
Wide pupils	22	42.3	37.5	NR
Symptoms				
Agitation	15	28.8	20.8	27.4
Confusion/Delir	7	13.5	4.2	10.4
Tremor	6	11.5	2.1	11.1
Myoclonus	5	9.6	NR	9.6
Seizures	3	5.8	4.2	6.7
Complaints				
Palpitations	10	19.2	20.8	18.5
Dizziness/Weakness/Feeling unwell	8	15.4	31.3	6.2
Anxiety/Panic	7	13.5	22.9	53.3
Nausea or vomiting	5	9.6	22.9	0.7
Dyspnea	4	7.7	8.3	NR
Chest pain	4	7.7	8.3	0.7
Thirst	1	1.9	6.3	NR
Headache	1	1.9	12.5	NR
Severe medical complications				
Severe rhabdomyolysis	3	5.7	0	0.7
Cardiopulmonary Arrest	3	5.7	0	1.5
Disseminated intravascular coagulation	2	3.8	0	0.7
Liver failure	1	1.9	0	0.7
Renal failure	1	1.9	0	0
Death	1	1.9	0	1.5
Laboratory findings				
Leucocytosis (>10 × 10^3/mm^3)	24	46.1	NR	NR
Creatine kinase (>300 U/l)	17	32.7	NR	16
Elevated creatinine (>105 mmol/l)	8	15.4	NR	NR
Hyponatremia (<135 mmol/l)	0	0	NR	NR
Management				
Monitoring in ED (mean, range)	5.5 h, 1–16 h		9 h, 1–12 h	4.6 h, 0.3–39 h
ECG/cardiac monitoring	51	98.1	85.4	39.3
Intravenous/oral fluids	37	71.1	31.3	NR
Medication given	22	42.3	12.5	NR
Benzodiazepines given	13	25	4.2	NR
Intubation/Resucitation	5	9.6	2.1	2.2
Admission to ICU	6	11.5	0	0.7
Admission to hospital ward	1	1.9	14.6	2.2
Admission to psychiatric service	2	3.8	0	2.2

HR = heart rate, SBP = Systolic blood pressure, GCS = Glasgow Coma Scale score, ED = Emergency Department, ICU = Intensive Care Unit, NR = not reported

Discussion

Patients presenting with Ecstasy-related medical problems were typically male, presented during the night and on weekends. The clinical features of patients with Ecstasy intoxication are shown in table 2 [8, 9]. Consistent with other reports, Ecstasy was frequently taken in combination with other drugs mainly ethanol, cocaine, GHB, other amphetamines, or cannabis (table 1) [8–11].

The clinical picture of Ecstasy toxicity was significantly influenced by some of the drugs typically ingested in addition to Ecstasy. Deep coma, defined as a GCS score of three, was exclusively associated with combined intoxications of Ecstasy with GHB or opiates and did not occur in Ecstasy users who co-abused different drugs. Recreational use of GHB is gaining popularity and leads to an increasing number of ED admissions due to non-reactive coma [13]. This trend is evidenced by GHB co-use in only four percent of the patients in 1996 in London [8] versus 25 percent GHB co-use in our patients, which explains the high number of patients with loss of consciousness or deep coma in our study sample. Verheyden et al. [12] reported that cocaine co-users scored higher on negative psychological effects including paranoia, anxiety and confusion than those who used Ecstasy alone. Confirming this finding we observed that cocaine co-users exhibited significantly more anxiety and panic reactions compared to Ecstasy users without cocaine use. In the present retrospective case series, we observed no changes in the picture of Ecstasy-intoxication associated with combined alcohol consumption. Co-use of ethanol with MDMA has previously been shown to increase plasma levels of MDMA in a controlled study in humans. Moreover, the MDMA-ethanol combination induced longer lasting euphoria compared to MDMA or ethanol alone [14]. Importantly, MDMA has also been shown to reverse subjective sedation induced by alcohol but did not reverse ethanol-induced psychomotor impairments. Thus, the combined use of MDMA and alcohol causes dissociation between subjective and objective sedation.

The true incidence of Ecstasy-related medical problems is not known. The estimation is that 10,000 Ecstasy exposures lead to one ED visit. The total number of ED visits associated with Ecstasy use is much lower than that due to the use of opiates, cocaine or methamphetamine [1, 15]. Severe medical complications due to Ecstasy consumption are relatively rare. The London ED study [8] did not report any severe medical problems requiring intensive care treatment or any fatal cases in their 48 patients. However, the authors did not mention whether severe cases were directly transferred to ICU services. The Barcelona ED study [9] reported three cases with severe intoxication including two fatalities in a total of 135 patients who used Ecstasy or other amphetamines. In the present series, the number of severe complications was five out of 52 intoxication cases including one fatality. Six patients (11.5%) were transferred to an ICU.

Two main patterns of Ecstasy-related fatalities are found in the many published single case reports: hyperthermia leading to multi-organ failure and hyponatraemia leading to brain oedema. The heat-shock-like pattern is associated with excessive physical activity, high ambient temperature (crowded parties), and inadequate fluid replacement [2]. MDMA itself produces only a slight increase in body temperature, possibly due to its serotonergic properties [16]. Hyponatraemia after MDMA use has been observed after excessive intake of water during physical activity. In addition, MDMA has been shown to induce a syndrome of inappropriate secretion of antidiuretic hormone (SIADH) [17]. While near-fatal hyperthermia was observed in several patients in the three case series discussed here, there was no single case of documented hyponatraemia or brain oedema [18]. MDMA-induced hyponatemia and brain oedema appear to be severe but rather rare events.

The present study is clearly limited by its retrospective design and the lack of laboratory tests confirming the presence of MDMA in most patients with self-reported Ecstasy consumption. Nevertheless, we can provide data on the relative frequency of the medical problems due to self-reported Ecstasy use and report about the clinical reality in an urban ED. The percentage of life-threatening clinical features in the present study is considerable and contrasts with reports from controlled studies where pure MDMA was used in prescreened healthy volunteers [7]. The problems observed in the present cohort of mixed street drug users cannot be attributed to the use of MDMA alone. Many additional factors need to be accounted for such as purity of the drugs used, the various combinations of drugs ingested, premorbid conditions, and ambient factors such as prolonged dancing at rave events in cases of hyperthermia-associated complications. In conclusion, the clinical picture is variable and complicated by multiple drug ingestion. Co-use of cocaine frequently induces anxiety. Co-use of GHB and opiates results in hypothermia and markedly depressed levels of consciousness.

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