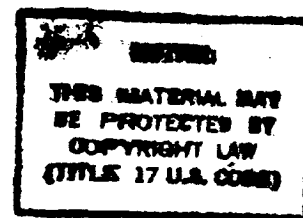


CASE REPORT

Joseph Crifasi, M.A., M.T. and Christopher Long, Ph.D.



Traffic Fatality Related to the Use of Methylenedioxymethamphetamine

REFERENCE: Crifasi J, Long C. Traffic fatality related to the use of methylenedioxymethamphetamine. *J Forensic Sci* 1996; 41(6):1082-1084.

ABSTRACT: A recent traffic fatality has been attributed to the use of the drug methylenedioxymethamphetamine (MDMA). The deceased was a 29-year-old white male with no known history of drug abuse. Toxicological analysis detected MDMA and metabolite methylenedioxyamphetamine (MDA) in the blood, urine, and vitreous humor specimens submitted for analysis. The concentrations of MDMA in clotted blood, sodium fluoride-potassium oxalate anticoagulated blood, vitreous humor, and urine were 2.32 mg/L, 2.14 mg/L, 1.11 mg/L, and 118.8 mg/L, respectively. The concentrations of the metabolite MDA were less than 0.25 mg/L in blood and vitreous, and 3.86 mg/L in the urine.

KEYWORDS: forensic science, forensic toxicology, toxicology, MDMA, methylenedioxymethamphetamine, MDA, methylenedioxyamphetamine

MDMA or 3,4-Methylenedioxymethamphetamine (Ecstasy, Adam, XTC) is a ring substituted derivative of methamphetamine that has been evaluated as an adjunct to psychotherapy (1-3). MDA or 3,4-methylenedioxyamphetamine is a psychotropic amphetamine first synthesized in 1914 (4). Metabolic demethylation of MDMA produces MDA, which is also pharmacologically active. MDMA and related drugs were added to schedule I of the Controlled Substance Classification in July 1985 (5).

These drugs have been referred to as designer drugs being analogs of the amphetamines. The effects of MDMA have been described as a "tranquil psychedelic experience" and nicknamed the "love drug." Most reports have concentrated on the complications of use, including hyperthermia, sweating, cardiac arrhythmias/arrest/tachycardia, and seizures (6-11).

We describe here the death of a 29-year-old male following traumatic injury while operating a motor vehicle under the influence of MDMA. Unlike other cases cited in recent reports (12,13), it is uncomplicated by the presence of other drugs that could contribute to this traffic fatality.

Case History

The deceased was a 29-year-old white male, the driver and lone occupant of a vehicle that suddenly veered off the interstate. From a witness and evidence at the scene, his vehicle suddenly left the roadway, straddled the guard rail, and then rolled down a rocky embankment, ejecting the deceased. This event occurred at approximately 6:30 am on a six lane divided highway with a 55-mph speed limit. The road surface was concrete, and it was dry at the time of the accident. Paramedics responding to the accident were unable to detect any vital signs and the deceased was pronounced dead at the scene.

Postmortem Findings

The examination was performed by the deputy medical examiner. The examination consisted of external examination and the collection of heart blood, urine, and vitreous for toxicological analyses. The immediate cause of death was determined to be due to multiple head and chest trauma and the manner of death reported to be an accident.

Toxicological Analyses

Toxicological analyses were conducted on blood, urine, and vitreous using a combination of enzyme multiplied immunoassay (EMIT) for the drugs of abuse, thin-layer chromatography (Toxi-lab), headspace-capillary gas chromatography for alcohol analyses and gas chromatography-mass spectrometry (GCMS) for confirmation and quantitation.

MDMA and MDA Analyses

Methylenedioxymethamphetamine (MDMA) and methylenedioxyamphetamine (MDA) were measured by GCMS using an internal standard method of analysis.

Drug stock solutions of MDMA and MDA were purchased from both Radian Corp. and Sigma Chemical Co. in 1-mg/mL solutions in methanol and stored at -20°C until use. Radian stock solutions were used in preparation of working standard solutions. Working standards were prepared in an appropriate drug free matrix to give concentrations from 0.25 to 2.0 mg/L for blood, urine, and vitreous.

¹Toxicology specialist and Director of forensic toxicology, respectively, St. Louis University, Medical School, Berkeley, MO 63136.

Received for publication 12 Jan. 1996; revised manuscript received 26 Feb. 1996 and 18 March 1996; accepted for publication 5 April 1996.

The case specimens were diluted to a level required to fall within the calibration curve range. The clotted blood was blended for a uniform solution. Drug stock solutions purchased from Sigma Chemical Co. were used in the preparation of positive control samples in the appropriate matrix for analysis. Drug free urine, plasma, and deionized water were used as negative control samples.

Deuterated drug stock internal standards, d5-MDMA, and d5-MDA were purchased from Radian Corp. in 100-mcg/mL solutions in methanol and stored at -20°C until use. Appropriate dilutions were made in deionized water to prepare the working internal standard solutions for each drug at a concentration of 5 mcg/mL.

A liquid-liquid extraction combining 1 mL of sample, 50 mL NH_4OH to pH the sample (pH 10 to 12), deuterated internal standards, and 5-mL n-butyl chloride was used to isolate the drugs from the biological samples. Organic extracts were derivatized with 50-mL pentfluoropropionic anhydride (PFPA). The derivatives were analyzed using a selected ion monitoring (SIM) on a 5970 Hewlett Packard MSD. Three ions were monitored for each drug (MDMA 204 162 339; MDA 162 77 325) and two ions for each of the deuterated internal standards (D5 MDMA 208 344; D5 MDA 167 330). The base ions were used for quantitation and the other two ions were used to determine acceptable ion ratios for identification of the drugs. Isomer identification was a chiral derivatization (14) of an extraction prepared in a similar fashion substituting 20-mL trifluoroacetyl propyl chloride (TPC) as the derivatization reagent.

Results and Discussion

MDMA and MDA concentrations in specimens submitted for analysis are shown in Tables 1 and 2. In addition to quantitative results, initial screening of urine indicated presumptive positive tests for amphetamines and cannabinoids by EMIT. Thin-layer chromatography reactions were consistent with MDMA. Positive screen results from urine were verified by GCMS. Alcohol/volatile screens were negative by headspace gas chromatography.

Delta-9-THC-carboxylic acid was confirmed in the urine at a concentration of 55 ng/mL, and was not considered as contributory to the impairment. No detectable levels of THC, 11-OH THC, or THC-COOH were identified in the blood.

In nine reported cases by Omtzigt (13) involving driving under the influence of MDMA, the average blood concentration was

0.18 ± 0.14 mg/L, this case report is 15 times greater. Bost (15) reports a fatal range 0.95 to 2.0 mg/L. Dowling (16) reported two fatalities, an asthmatic with 1.1 mg/L (anatomical cause of death) and an acute MDMA intoxication at 1.0 mg/L with a 0.04 g/% ethanol (MDMA intoxication as the cause of death). None of these cases reported which isomer was identified.

This individual having a significantly greater concentration than previous reports, was either impaired by or succumbed to the MDMA. The concentrations support an acute dosing in that the blood to vitreous concentration is 2:1 and that very little MDA was detected. Although the literature has not reported this observation, we have noted that the vitreous fluid lags behind the blood concentration until equilibration of tissues has occurred. The half life of MDMA has been reported at 7.6 h (17) that would further support an acute administration with very little MDA being detected. There was no significant difference between the clotted and sodium fluoride blood specimens.

The lack of history, with regard to drug use before or around the time of the accident, makes the data difficult to interpret. Whether death occurred prior to the accident as a direct result of drug action, or if a seizure occurred resulting in the accident is not clear. The L isomer, being in greater concentration than the D isomer, may not produce the same stimulation, analogous to the D/L activity of amphetamine. This lack of central nervous system excitatory effects may have caused an increase in self administration. The toxic concentration and subsequent overdose may have occurred accidentally in the self titration of the euphoric effects.

Our literature search failed to produce any reports in which a death or fatal traffic accident was linked solely to MDMA, or the relative concentration of the isomers, without underlying pathology or polypharmacy.

References

- (1) Dowling J. The psychological and physiological effects of MDMA on normal volunteers. *J Psychoact Drugs* 1986;18:335-40.
- (2) Greer G, Strassman R. Information on ecstasy. *Am J Psychiatry* 1985;142:1391.
- (3) Greer G, Tolbert R. Subjective reports on the effects of MDMA in a clinical setting. *J Psychoact Drugs* 1986;18:319-27.
- (4) Liester MB, Grob CS, Bravo GL, Walsh RN. Phenomenology and sequelae of 3,4-Methylenedioxymethamphetamine use. *J Nerv Ment Dis* 1992 June;180(6):345-52.
- (5) Lawn JC. *Federal Register* 1985 May 31;50(105):23118-20.
- (6) Peroutka SJ. Incidence of recreational use of 3,4-Methylenedioxymethamphetamine (MDMA, "ecstasy") on an undergraduate campus. *N Eng J Med* 1987 Dec;317(24):1542.
- (7) Simpson DL, Rumack BH. Methylenedioxymethamphetamine. *Arch Int Med* 1981 Oct;141:1507-9.
- (8) Sreaton GR. Hyperpyrexia and rhabdomyolysis after MDMA (ecstasy) abuse. *Lancet* 1992;339:677-8.
- (9) Rittoo DB, Rittoo D. Complications of "ecstasy" misuse. *Lancet* 1992;340(8816):725-6.
- (10) Ellis SJ. Complications of "ecstasy" misuse. *Lancet* 1992;340(8816):726.
- (11) Larner AJ. Complications of "ecstasy" misuse. *Lancet* 1992;340(8816):726.
- (12) Henry JA, Jeffreys KJ, Dawling S. Toxicity and deaths from 3,4-methylenedioxymethamphetamine. *Lancet* 1992;340(8816):384.
- (13) Omtzigt JG, Vermaase CJ, Zweipfening GM. Deaths associated with amphetamine, 3,4-methylene-dioxymethamphetamine (MDMA), 3,4-methylenedioxymethamphetamine (MDEA) or 3,4-methylenedioxymethamphetamine (MDA) Abuse. Presented at Society of Forensic Toxicology Tampa 1994.
- (14) Manius G, Tscheme R. Gas-liquid chromatograph separation of some optically-active amines by diastereomer formation. *J Chromatogr Sci* 1979 June;17:322-6.

TABLE 1—MDMA and MDA concentrations in postmortem specimens.

Specimen	MDMA	MDA
Blood (clotted)	2.32 mg/L	<0.25 mg/L
Blood (NaF)	2.14 mg/L	<0.25 mg/L
Vitreous	1.11 mg/L	<0.25 mg/L
Urine	118.8 mg/L	3.86 mg/L

TABLE 2—Isomer identification.

Specimen	MDMA		MDA	
	D	L	D	L
Urine	39%	61%	34%	66%

- (15) Bost RO. 3,4-Methylenedioxymethamphetamine (MDMA) and other amphetamine derivatives. *J Forensic Sci* 1988;33(2):576-87.
- (16) Dowling GP, McDonough ET, Bost RO. Eve and ecstasy: a report of five deaths associated with use of MDEA and MDMA. *JAMA* 1987;257(12):1615-7.
- (17) Baselt RC, Cravey RH. Disposition of toxic drugs and chemicals in man. 4th Ed. Chicago: Year Book Medical, 1995;508.
- (18) Gilman AG, Rall TW, Nies AS, Taylor P. The pharmacological basis of therapeutics. 8th Ed. New York, Pergamon Press, 1990;211.

Address requests for reprints or additional information to
 Christopher Long, Ph.D.
 Director of Forensic Toxicology
 St. Louis University Medical School
 Department of Pathology
 Forensic Toxicology Laboratory
 George Gantner Building
 6039 Helen St.
 Berkeley, MO 63134