"ECSTASY" IN THE A.M. AND P.M. - MDMA CONCENTRATIONS IN FATALITIES FOLLOWING HOSPITAL ADMISSION

Dr S. P. Elliott, Regional Laboratory for Toxicology, City Hospital, Birmingham, U.K.

Aim

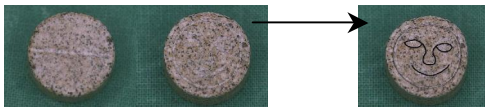
The aim of this study was to evaluate the concentrations of MDMA found in ante-mortem plasma and post-mortem blood in fatalities admitted to hospital following "Ecstasy" ingestion.

Introduction

3,4-Methylenedioxymethamphetamine (**MDMA**) is a common component of "Ecstasy" tablets (Figure 1), ingested by the user to achieve a subjective euphoric state with additional empathic effects. "Ecstasy" use has been reported in social settings such as parties and nightclubs for over 15 years.

MDMA can exhibit various symptoms including; visual hallucinations, confusion, agitation, sweating, coma and hypotension. Other common toxic symptoms include hyponatraemia (usually due to excessive water intake) and/or hyperpyrexia; leading to secondary features such as cerebral oedema, seizures, organ damage and ultimately death. It is also thought that MDMA can precipitate cardiotoxicity in individuals with an existing heart condition.

Partly due to variation in MDMA content in tablets, the quantity ingested and any resultant idiosyncratic toxic effects, concentrations of MDMA vary in both non-fatal and fatal cases. Typical concentrations following "recreational" use are less than 0.4 mg/L. In overdosage, concentrations greater than 2 mg/L may be achieved. Early observations in post-mortem specimens have suggested that MDMA is not necessarily prone to redistribution after death. Such data is mainly based on comparison of concentrations between anatomical sites and have not involved comparison of ante-mortem and post-mortem concentrations. This poster presents both ante-mortem and post-mortem concentrations including data from serial collection times and varying anatomical sites, respectively.



Back Front

Highlighted "smiley face" logo on Front

Figure 1. "Ecstasy" tablet seized/analysed during hospital admission. Contents found to be paracetamol, MDA, ketamine and amphetamine.

Analytical Methods

MDMA and MDA quantitative analysis was performed using high performance liquid chromatography with diode-array UV detection (HPLC-DAD). 500 µL of internals standard (5 mg/L norfenfluramine or 2 mg/L cinchonine (in 0.2M Na_2CO_3) was added to 500 µL of sample and extracted with 5 mL of 1-chlorobutane and back extracted into 100 µL of 0.05M H_2SO_4. Chromatography was based on a Waters 5 micron OD/CN column using 10% acetonitrile-buffer mobile phase. 210 nm was used as the detection wavelength. A linear calibration range of 0.1 to 5 mg/L (MDMA) and 0.05 to 2.5 mg/L (MDA) was produced using blank (pre-screened) equine plasma. Inter-analytical precision was determined using internal quality control standards (0.2 mg/L and 2 mg/L MDMA and 0.1 mg/L and 1 mg/L MDA). Mean concentrations of 0.20 mg/L and 1.96 mg/L (MDMA) and 0.11 mg/L and 1.04 mg/L (MDA) were calculated (n=10). Limit of detection was 0.01 mg/L.

Case Results

MDMA and (where possible) MDA concentrations were measured in 5 instances of fatal poisoning following hospital admission (**Tables** below).

CASE 1: 31 year old male admitted to hospital following suspected injection of crushed amphetamine and "Ecstasy" tablets. Developed malignant hyperpyrexia and later died. Amphetamine (0.183 mg/L AM and 0.342 mg/L PM) and ethanol were also detected.

Sample (and site)	MDMA conc^n (mg/L)	MDA conc^n (mg/L)	Conc^n ratio (MDMA)	Conc^n ratio (MDA)	Collection time in relation to death (+/- days or hours and mins)
AM Serum	1.22	NA		NA	- 45 minutes
PM Blood (brachial)	2.37	NA	PM:AM 1.9	NA	+ 2 days

CASE 2: 30 year old male recovered from a river after a night out drinking. Admitted to hospital but later died. Chlordiazepoxide and ethanol were also detected.

Sample (and site)	MDMA conc^n (mg/L)	MDA conc^n (mg/L)	Conc^n ratio (MDMA)	Conc^n ratio (MDA)	Collection time in relation to death (+/- days or hours and mins)
AM Serum	0.55	NA		NA	- 20 hours 15 minutes
AM Serum	0.58	NA		NA	- 19 hours 0 minutes
AM Plasma	0.47	NA		NA	- 16 hours 30 minutes
AM Plasma	0.36	NA		NA	- 14 hours 15 minutes
AM Plasma	0.36	NA		NA	- 12 hours 15 minutes
AM Plasma	0.31	NA		NA	- 9 hours 15 minutes
PM Blood (trunk)	0.47	NA	PM:AM* 1.5	NA	+ 3 days
PM Blood (left arm)	0.52	NA	PM:AM* 1.7	NA	+ 3 days

* PM:AM ratio based on ante-mortem concentration nearest to death; NA = Not analysed

CASE 3: 26 year old male found collapsed in the street after having taken several "Ecstasy" tablets. Admitted to hospital but later died after suffering hyperpyrexia. A trace amount of paracetamol was also detected but no ethanol.

Sample (and site)	MDMA conc^n (mg/L)	MDA conc^n (mg/L)	Conc^n ratio (MDMA)	Conc^n ratio (MDA)	Collection time in relation to death (+/- days or hours and mins)
AM Blood	2.04	0.06			- 1 hour 10 minutes
PM Blood (femoral)	2.25	0.09	PM:AM 1.1	PM:AM 1.5	+ 2 days
PM Blood (jugular)	2.99	0.14	PM:AM 1.5	PM:AM 2.3	+2 days

CASE 4: 22 year old female admitted to hospital with hyperthermia following ingestion of approximately 12 "Ecstasy" tablets. Cocaine metabolite and ethanol were also detected.

Sample (and site)	MDMA conc^n (mg/L)	MDA conc^n (mg/L)	Conc^n ratio (MDMA)	Conc^n ratio (MDA)	Collection time in relation to death (+/- days or hours and mins)
AM Serum	4.33	0.10			- 1 day
PM Blood (left femoral)	7.25	0.21	PM:AM 1.7	PM:AM 2.1	+ 2 days
PM Blood (right femoral)	6.19	0.19	PM:AM 1.4	PM:AM 1.9	+2 days
PM Blood (heart)	28.39	1.33	PM:AM 6.6	PM:AM 13.3	+2 days
PM Vitreous Humour	11.93	0.39	PM:AM 2.8	PM:AM 3.9	+2 days

CASE 5: 63 year old male found collapsed at home having allegedly ingested 4 "Ecstasy" tablets. He was taken to hospital but later died following a cardiac arrest. Cannabinoids, cocaine metabolite and ethanol were also detected.

Sample (and site)	MDMA conc^n (mg/L)	MDA conc^n (mg/L)	Conc^n ratio (MDMA)	Conc^n ratio (MDA)	Collection time in relation to death (+/- days or hours and mins)
AM Serum	1.08	0.03			- 2 days
AM Serum	0.76	0.02			- 1 day
AM Serum	0.44	<0.01			0 day
PM Blood (femoral)	1.14	0.02	PM:AM 2.6	PM:AM* >2.0	+ 2 days

* PM:AM ratio based on ante-mortem concentration nearest to death

Overall Results

- **Reduction with time of MDMA and MDA plasma concentrations during survival period.**
- **Post-mortem (PM) blood MDMA and MDA concentrations higher than ante-mortem (AM) concentrations in all 5 cases (PM:AM ratio typically between 1 to 2).**
- **Significant difference between anatomical sites (heart greater than femoral) in Case 3 for both MDMA and MDA.**

Note: Difference between PM and AM concentrations may be influenced in part by possible blood-plasma matrix differences.

Conclusions

- **There is an apparent rise in MDMA and MDA concentrations after death, regardless of post-mortem collection site. However, the subsequent increase in concentration may vary depending on the anatomical site, indicating possible redistribution.**
- **Data indicate PM blood concentrations may not accurately relate to concentration either at the time of, or prior to death. Therefore, calculations based on this assumption (e.g. dosage) should not be made.**

References

- R. de La Torre et al, "Non-linear pharmacokinetics of MDMA ("Ecstasy") in humans" *Brit. J. Clin. Pharm.* 49: p104-109 (2000)
- H. Kalant, "The pharmacology and toxicology of "Ecstasy" (MDMA) and related drugs" *Canadian Medical Association Journal*. 165(7): p917-928 (2001)
- J.A. Henry et al, "Toxicity and deaths from 3,4-methylenedioxymethamphetamine ("Ecstasy")" *Lancet*. 340: p384-387 (1992)
- D. Yew, "MDMA Toxicity" *eMedicine Journal*. 2(7) (2001) http://www.emedicine.com
- R. C. Baselt, "MDMA" in *Disposition of toxic drugs and chemicals in man (Sixth Edition)* (2002)
- C. R. Brown et al, "Severe adverse reaction to MDMA" *Vet. Hum. Tox.* 28: p490 (1986)