

# Relationship between Drug Levels and Manners of Death in Methamphetamine- Related Casualties: A Retrospective Study

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## ABSTRACT

Methamphetamine (MAP), an illicit, stimulant drug, has resulted in serious social problems in Taiwan and other parts of the world. A pilot study was designed to determine whether toxicological profiles of decedents' body fluids can be used to implicate the status of mood at the moment of death. High blood/urine ratios can be associated with acute MAP use, a short period of time after MAP intake and a manic emotional status. In comparison, a low blood/urine ratio can be associated with chronic MAP use, a longer period of time after MAP intake and a depressive emotional status. Our retrospective review of 18,973 fatalities collected from Institute of Forensic Medicine in Taiwan from 1991 to 2007, 215 cases which had MAP levels both in blood and urine that were greater than 0.02 mg/L and with positive impressions of the causes and manners of death. Distinct patterns of MAP levels were distinguished to be associated with manner or pattern of death.

Higher MAP concentrations were found in blood than in urine when death occurred shortly after an overdose of MAP that was linked either to accidental overdose (2.98 ± 0.52 mg/L blood, 16.96 ± 2.55 mg/L urine and 21.01 ± 4.45 urine/blood ratio; n=81) or to intentional suicide (13.33 ± 5.09 mg/L blood, 24.39 ± 5.93 mg/L urine and 7.33 ± 4.32 urine/blood ratio; n=7). Lower MAP blood levels and urine/blood ratios were found in cases of deaths by accidents (0.25 ± 0.04 mg/L blood, 4.72 ± 0.92 mg/L urine and 30.44 ± 6.40 urine/blood ratio; n=45) and suicides that not related to high MAP dose (0.37 ± 0.06 mg/L blood, 6.95 ± 1.79 mg/L urine and 37.29 ± 10.04 urine/blood ratio; n=20), those making a highly suspect of influence of MAP mediated through depression and psychotic behaviors. Much higher MAP urine/blood ratios and lower MAP blood levels were found among casualties of natural (0.25 ± 0.05 mg/L blood, 15.06 ± 5.65 mg/L urine and 102.49 ± 55.99 urine/blood ratio; n=15) or homicidal causes (1.28 ± 0.20 mg/L blood, 13.43 ± 1.98 mg/L urine and 16.89 ± 2.86 urine/blood ratio; n=47), suggesting that were relatively unaffected by the lower blood level of MAP. Chronic MAP abusers appear to provoke violent behaviors resulting in the homicidal fatalities, and relationship to amphetamine (AMP)-like psychosis is postulated.

These results suggest that the toxicological profile of MAP concentrations in blood and urine can play a crucial role and are related better to patterns of death than manner of death. The findings may enable one better utilization of the toxicological profiles in future judgment of forensic parameters including the cause and manner of death in MAP related fatalities.

## INTRODUCTION

MAP is the most prevalent illicit drug in Taiwan. In contrast to D-amphetamine, MAP has a longer half-life and causes greater mapping of the central nervous system (CNS) by accumulation of MAP in the brain, corresponding to the greater effects of MAP. Furthermore, growing numbers of MAP abusers are experiencing the significant increasing in the half-life and MAP-induced toxicities. MAP psychosis in humans is believed to be a homologous phenomenon to behavioral sensitization of animals, which is the most hazardous injury next to the pathological lesions directly caused by MAP. In general, determination of the cause of death and manner of death are based on extensive resources including scene investigation, psychological status, social orientation and physical capability. To comprehend the toxicological parameters of MAP-related fatalities, body fluids could be used to estimate the cause of death, time of death, mental and emotional status, as well as the manner of death.

The levels of MAP in blood and urine and the blood/urine concentration ratio are possible criteria to strengthen the medicolegal investigation so as to interpret the time of intake, time of death, mental status of stimulant, depression or delirium. A retrospective study of toxicological results of decedents' body fluid with identified mental status at the moment of death may yield a pattern which is useful for further understanding of MAP toxicity and fatalities. Therefore, a pilot study through a retrospective view of MAP-related fatalities, with unequivocal impressions of the causes and manners of deaths, collected from the Forensic Medicine Center (Taipei, Taiwan) was conducted to understand the relationship of the toxicologic profiles of blood and urine MAP levels, and their ratio, in conjunction with the cause and manner of death. Subclassification of manners of death into patterns of death is probed by statistical evaluation so as to comprehend better the toxicological profiles. The distinct patterns in the causes and manners of death may implicate different statuses of decedents under the influence of MAP.

A pilot study was designed to determine whether toxicological profiles of decedents' body fluids can be used to implicate the status of mood at the moment of death. The ratio of blood/urine can be implicated with the status and mood of MAP abuser.

## MATERIALS AND METHODS

This retrospective study was designed to study the relationship of manner and cause of death with toxicological profiles of MAP. Out of the total of 18,973 forensic cases that included autopsy, medicolegal death investigation procedure and toxicologic screening at the Forensic Medicine Center of the Public Prosecutor's Office for Taiwan High Court from 1991 to 2007, 215 MAP-related cases were selected by the criteria: (A) MAP levels measured quantitatively in both blood and urine, with MAP blood/urine ratio > 0.02 mg/L in blood or urine, (B) unequivocal impression of manner of death, (C) scene investigation and/or evidence at the scene to make a determination of the manner and cause of death during the forensic investigation, which included background history and scene investigation, and (D) a complete medicolegal autopsy with pathological and toxicological studies following standard procedures.

### Manners and Patterns of Death among MAP-related Fatalities

MAP-related fatalities had been routinely categorized during the forensic investigation according to four manners of death: accidental, suicidal, homicidal and natural causes of death, with no cases of unknown or uncertain cause among the group. For the purpose of this study, it is important to determine in which cases MAP is the lethal agent. Thus, both accidental and suicidal deaths were subdivided according to the identified direct responsibility of MAP for the responsibility of other causes for death and indirect effect of MAP. As with manners of death, patterns of death also included the categories of homicidal and natural deaths, yielding a total of six "patterns of death".

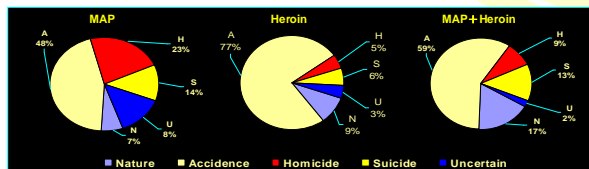
### Toxicological Studies and Statistical Evaluation

Toxicological studies of postmortem body fluids included screening by TDx analyzer, REMED, Tox Lab and TDx (Abbott, USA), confirmation by gas chromatography (GC) and quantitative confirmation by gas chromatography/mass spectrometry (GC/MS) following well-established laboratory guidelines. A Hewlett-Packard (HP) 5890A gas chromatograph with splitless injection, 5970A mass selective detector (MSD) was used. The GC was equipped with an HP-1 fused silica capillary column 25 m x 0.2 mm i.d./0.33 μm film thickness. The mass spectrometer was operated in the selected ion monitoring (SIM) mode. MAP levels were monitored at m/z 204, 160 and 118. Quantity was measured by multiple-point calibration using the ion ratio of each internal standard compared to the same ion ratio in the extracted standard.

MAP concentrations are presented as mean ± standard error mean (SEM). Toxicological profiles of MAP-related fatalities were tested to challenge the category of their manners and patterns of death. Student's t-test and one-way ANOVA were used to evaluate the significance of manners and patterns of death.



Package of MAP



Manners of Death of Drug Abuse-Related Fatalities Collected from IFM during 1997-1999

## RESULTS

Table 1. Distributions between manner of death and MAP-related cases during 1991-2007

Manner of death	All cases 1991-2007 (%)	MAP-related * (%)
Natural	5,820 (30.7)	15 (7.0)
Accidental	6,323 (33.3)	126 (58.6)
Homicidal	3,387 (17.9)	47 (21.9)
Suicidal	2,168 (11.4)	27 (12.5)
Undetermined	1,275 (6.7)	-
Total	18,973	215

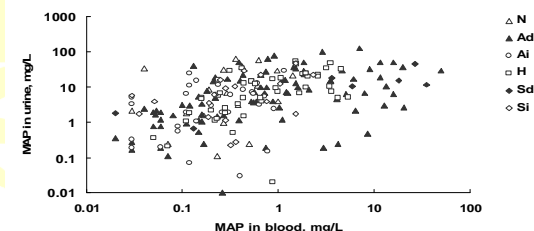
\* MAP levels both of blood and urine ≥ 0.02 mg/L

Table 2. The epidemiological analysis of MAP-related fatalities in Taiwan (1991-2007)

Year	Case No.	MAP related	%
1991	236	3	1.3%
1992	347	30	8.6%
1993	500	49	9.8%
1994	630	24	3.8%
1995	845	32	3.8%
1996	914	69	7.5%
1997	930	43	4.6%
1998	1145	37	3.2%
1999	1115	39	3.5%
2000	1189	48	4.0%
2001	1374	27	2.0%
2002	1470	26	1.8%
2003	1444	33	2.3%
2004	1579	58	3.7%
2005	1841	63	3.4%
2006	1816	36	2.0%
2007	1661	44	2.6%
Total	18973	661	3.5%

Table 3. The MAP Concentrations of Blood and Urine of MAP-related Cases Classified to Six Groups Dependent on Their Pattern of Death

Manner of Death (Symbol)	n	Data range, mean ± SEM		
		Blood (mg/L)	Urine (mg/L)	Urine / Blood
Natural cause (N)	15	0.03-0.63	0.11-63.68	0.48-865.00
		0.25 ± 0.05	15.06 ± 5.65	102.49 ± 55.99
Accident death by MAP overdose (Ad)	81	0.03-20.70	0.11-128.66	0.06-300.17
		2.98 ± 0.52	16.96 ± 2.55	21.01 ± 4.45
Accident death unrelated drug lethality (Ai)	45	0.02-1.15	0.03-29.44	0.08-204.00
		0.25 ± 0.04	4.72 ± 0.92	30.44 ± 6.40
Homicide (H)	47	0.05-5.34	0.02-54.22	0.03-95.09
		1.28 ± 0.20	13.43 ± 1.98	16.89 ± 2.86
Suicidal death by MAP overdose (Sd)	7	1.51-35.20	10.68-48.49	0.33-32.20
		13.33 ± 5.09	24.39 ± 5.93	7.33 ± 4.32
Suicidal death unrelated drug lethality (Si)	20	0.02-1.51	0.22-29.86	0.69-188.53
		0.37 ± 0.08	6.95 ± 1.79	37.29 ± 10.04
Total	215	0.02-35.20	0.02-128.66	0.03-865.00
		1.94 ± 0.30	12.80 ± 1.21	28.84 ± 4.71



## CONCLUSION

- (1) The MAP blood/urine ratio is useful to determine the pattern of death, to estimate the time of death and suggest the mental status at the time of death.
- (2) Low urine/blood MAP with a relatively high MAP level in blood favors MAP-attributable accidental (Ad) and suicidal (Sd) causes of death.
- (3) High MAP ratio (urine/blood) supports the natural cause (N), accidental (Ai) and suicidal (Si) causes of death.
- (4) High and low urine/blood ratios suggests chronic and acute status, depressive and manic status, long and short period of time after MAP intake, respectively.
- (5) Chronic MAP abusers provoke violent behaviors leading to homicide, representing a high percentage of deaths.
- (6) These results suggest that the toxicological profile of MAP concentrations in blood and urine can play a crucial role and are related better to patterns of death than manner of death. These results of the toxicological profiles in future judgment of forensic parameters including the cause and manner of death in MAP related fatalities.