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Brief Communication

# Outcome of treatment in patients with methamphetamine poisoning in an Iranian tertiary care referral center

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## ABSTRACT

**Objective:** Methamphetamine is the second most widely abused drug worldwide. We performed a study on the treatment outcome of acute methamphetamine intoxication in a referral tertiary care University hospital in Iran.

**Methods:** In this hospital-based, retrospective study which was carried out from 2012 to 2013, medical records of all patients aged 18 to 65 years who were admitted with a reliable history and clinical diagnosis of acute methamphetamine intoxication were abstracted and analyzed. Patients' data included gender, age, type and route of poisoning, clinical manifestations, duration of hospitalization, and the treatment outcome. ANOVA, Chi-square, and binary logistic regression statistical tests were used for data analysis.

**Findings:** A total of 129 patients with a mean age of 30.70 ± 0.93 (mean ± standard error), including 111 (86%) males, had been fully evaluated. Most of the patients had intentional poisoning (93.7%). In 42.6% of patients, inhalation was the main route of exposure. Most of the patients had complete improvement without any complication (89.1%). Age (odds ratio [OR], 1.05; 95% confidence interval [95% CI] 1.006–1.099), suicide history (OR, 30.33; 95% CI 3.11–295.24), route of poisoning ([ingestion: OR, 0.21; 95% CI 0.05–0.87], [inhalation: OR, 0.19; 95% CI 0.04–0.78]), and pulmonary system manifestations (OR 1.84; 95% CI 1.15–2.93) were predictive in patients outcome ($P < 0.05$).

**Conclusion:** Methamphetamine poisoning was more common in males with intentional poisoning. Age, past history of suicide, route of poisoning, and pulmonary manifestations on admission could be considered as important predictive factors in patients' outcome.

**Keywords:** Methamphetamine; poisoning; treatment outcome

## INTRODUCTION

Methamphetamine is the most widely abused type of amphetamine, a class of stimulant drugs.[1] Amphetamine or methamphetamine use was documented in many countries. Uses have been more prevalent in East and South East Asia, North America, South Africa, New Zealand, Australia, and a number of European countries.[2] Methamphetamine has contributed to a substantial number of deaths in Australia.[3] Individuals with methamphetamine use disorders had a higher mortality risk than those with diagnoses related to cannabis, cocaine, or alcohol.[4]

In a study, which evaluated the global prevalence of amphetamine dependence and the burden of disease attributable to these disorders, there were an estimated 24.1 million psychostimulant dependent people in 2010. There were significant differences between amphetamines in the geographic distribution

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of crude disability-adjusted life year (DALY). Over half of amphetamine dependence, DALYs were in Asian regions (52%).[5] In Alabama, cocaine and methamphetamine among fetuses/neonates were three- and five-fold greater than the general population.[6] Also, at least 84% of deaths were violent or drug-related (12% suicides) in Sweden population.[7] The data, presented for the Dresden region, Saxony, Germany, demonstrate the escalation of MA-related crime and fatalities between 2005 and 2011.[8]

Methamphetamine has neurobiological effects on the nervous system; some of which are transitory and some longer lasting. Signs of toxicity include hot, flushed or very sweaty skin, headache, chest pain, changes in consciousness and mental status, tremor, spasm, agitation, difficulty breathing, seizures, and psychosis.[9] Most cases of methamphetamine toxicity can be managed supportively. In the case of a severe overdose, immediate supportive care, including airway control, oxygenation and ventilation support, and appropriate monitoring, is required.[10]

Methamphetamine abuse and also poisoning seems to be increasingly common in Iran,[11] especially in our tertiary care poisoning referral center in the central part of Iran.[12] The aim of this study was to depict a better clinical and toxicoepidemiological picture of methamphetamine poisoning in the central part of Iran and the factors, which are related to the outcome of therapy in these patients.

## METHODS

This hospital-based, retrospective study was carried out from April 2012 to April 2013 in the department of clinical toxicology of Noor and Ali Asghar (PBUH) University hospital (affiliated with the Isfahan University of Medical Sciences), which is the referral medical center for poisonings in the central part of Iran and is facilitated, staffed, and designed for the management of poisoned patients, in which approximately 600 poisoned patients are admitted monthly.

The study protocol was approved by the Institutional Board of Human Studies at the Isfahan University of Medical Sciences. In addition, all of the patients' personal details were not recorded or coded. We used the hospital poisoning registry to retrieve information on the incidence and management of methamphetamine overdoses using the 10$^{th}$ revision of the International Statistical Classification of Diseases and Related Health Problems, which is a medical classification published by the World Health Organization.[13] Medical records of all patients aged 18 to 65 years who were admitted with a positive and reliable history of acute methamphetamine poisoning and drug overdose was diagnosed clinically by an attending medical toxicologist[14] and confirmed by laboratory methods, were abstracted and analyzed. Collected information included patients' gender, age, type of poisoning (accidental or intentional), route of poisoning (oral, inhalation, intravenous, intramuscular, subcutaneous, and mixed), clinical manifestations at the time of admission, duration of hospitalization, and clinical outcome (survived with or without complication and death). Data abstractor was a last-year pharmacy student (PP) who was trained for correct data abstraction of medical records' details and supervised by a medical toxicologist (NEM). For reducing the abstraction errors to the possible minimum, in each session of data gathering only five medical records were screened and if eligible fully abstracted.[15] Data abstraction reliability was tested before the study. At least 20% of the abstracted records were re-abstracted by a qualified physician, and the consistency of the results was evaluated by calculating Cohen's kappa for each item of the abstracting form.[16,17]

Since we have analyzed all the eligible patients who were admitted within the aforementioned time range, we have not calculated sample size and for the same reason have not used a sampling method.[18] According to our previous study, more than 75% of the methamphetamine poisoned patients are directly referred to our poisoning patients' emergency room, and this may reflect an acceptable picture of methamphetamine poisoning in Isfahan city.[19]

The outcome of therapy was documented as survived without any complication (including coma, mechanical ventilation, serious arrhythmia, refractory hypotention or hypertensive crisis, and altered mental status), or survived with complication or death.

Missing data of medical records was completed via direct contact with the corresponding patient and in case of conflicting data, documentation of a senior physician was recorded where appropriate.[20]

Descriptive analysis of data was done on all baseline characteristics of the study patients. For continuous and quantitative variables, mean and standard deviation was calculated, and histograms were plotted to assess the distribution of these variables. In the case of categorical variables, frequencies were reported and tested. Mean values of continuous quantitative variables were compared between the two groups of outcomes using the independent *t*-test. For categorical variables that had cell counts less than five, the Fisher's exact test was used. Predictive factors for clinical outcome of treatment were evaluated by the binary logistic regression analysis, and results were reported

as odds ratios (ORs) with confidence intervals (CIs). All *P* values were based on two-sided tests and significance was set at $P < 0.05$. Data processing was performed using Statistical Package for the Social Sciences software (SPSS Inc., Chicago, IL, USA) version 15.

## RESULTS

During the study period (1-year), 129 eligible patients (86% male) were presented to our medical center with the mean age of 30.70 ± 0.93 (mean ± standard error). About 18.6% had a previous history of psychiatric disorders and 10.1% had a previous history of suicidal attempt. Most of the patients had intentional poisoning/overdose (93.7%). Inhalation was the main route of exposure (42.6%). Forty cases used only methamphetamine and the others (89 cases) ingested or inhaled other drugs with methamphetamine. Six patients had skin lesions and 25 (19.37%) patients had pulmonary manifestations. The most frequent presented cardiovascular sign was tachycardia in 23 patients (17.82%). Most of the patients survived without any complication (89.1%).

Time elapsed from overdose to the hospital admission was averagely 11.9 ± 1.0 h. The mean length of hospital stay was 18.86 ± 2.2 h. One hundred and fifteen patients finally survived and 14 patients were dead or survived with complications. The results comparing the different variables based on outcome has been shown in Table 1.

Age (OR, 1.05; 95% CI 1.006–1.099), suicide history (OR, 30.33; 95% CI 3.11–295.24), route of poisoning ([ingestion: OR, 0.21; 95% CI 0.05–0.87] [inhalation: OR, 0.19; 95% CI 0.04–0.78]), and pulmonary system manifestations (OR 1.84; 95% CI 1.15–2.93) were predictive in patients outcome ($P < 0.05$).

Coma, agitation, hypotension, tachycardia, bradycardia, and pulmonary manifestations were more prevalent in patients who died or survived with complications [Table 2]. Creatinine phosphokinase was high only in two patients (6100 and 2061 U/L). There were no significant statistical differences in routine laboratory tests performed on admission between the two groups ($P > 0.05$).

To find the predictive variables in patients' outcome, the backward step binary regression was used. Age, previous suicide history, route of poisoning, and pulmonary system manifestations had predictive values in the outcome of therapy for these patients [Table 3].

**Table 1: Patient's history and clinical details and the outcome of treatment in patients with methamphetamine poisoning**

| Variables | Outcome | | *P* |
|---|---|---|---|
| | Survived without complication | Complications or death | |
| Age (years) | 30.01±0.90 | 37.14±3.97 | 0.01* |
| Gender | | | |
| Male | 98 (85.2) | 13 (92.9) | 0.69** |
| Female | 17 (14.8) | 1 (7.1) | |
| Drugs | | | |
| Methamphetamine | 36 (31.3) | 4 (28.6) | 0.59** |
| Alcohol | 1 (0.9) | 0 (0) | |
| Hashish | 5 (4.3) | 0 (0) | |
| Opioids | 58 (50.5) | 7 (50) | |
| Benzodiazepines | 6 (5.2) | 0 (0) | |
| Antidepressants | 7 (6.1) | 2 (14.3) | |
| Analgesics | 2 (1.7) | 1 (7.1) | |
| Route of exposure | | | |
| Inhalation | 51 (44.3) | 4 (28.6) | 0.07** |
| Oral | 46 (40) | 4 (28.6) | |
| Injection | 3 (2.6) | 0 (0) | |
| Mixed | 15 (13) | 6 (42.9) | |
| Type of exposure | | | |
| Suicide | 36 (31.3) | 6 (42.9) | 0.64** |
| Accidental | 8 (7) | 0 (0) | |
| Abuse | 71 (61.7) | 8 (57.1) | |
| History of psychiatric disease | | | |
| Yes | 19 (16.5) | 5 (35.7) | 0.13** |
| No | 96 (83.5) | 9 (64.3) | |
| History of suicide | | | |
| Yes | 6 (5.2) | 7 (50) | <0.001** |
| No | 83 (72.2) | 6 (42.9) | |
| Unknown | 26 (22.6) | 1 (7.1) | |
| History of addiction | | | |
| Yes | 98 (85.2) | 14 (100) | <0.001** |
| No | 17 (14.8) | 0 (0) | |
| Time from usage to admission (h) | 11.77±1.12 | 13±2.24 | 0.71* |

Data are presented as mean±SE or *n* (%), where appropriate. *Independent *t*-test, **Fisher exact test. SE=Standard error

## DISCUSSION

Methamphetamine use varies geographically, but overall, amphetamine-type stimulants, which include methamphetamine, are the fastest rising drug of abuse worldwide.[21] Since methamphetamine poisoning has become more prevalent in our toxicological emergencies referral center in recent years,[12] the main purpose of this study was to evaluate the predictive values of different related factors on the outcome of treatment in methamphetamine poisoning.

In our study, most of the cases were young men which are consistent with many similar studies.[22-24] In 42.6% of our patients, inhalation was the main route of exposure. Routes of administration that produce rapid onset of the drug effects (i.e., smoking and injection) are likely to lead to more medical and psychiatric effects.[25]

**Table 2: Clinical manifestation of the study patients with methamphetamine poisoning and the outcome of treatment**

| Variables | Outcome | | *P* |
|---|---|---|---|
| | Survived without complication | Complications or death | |
| Gastrointestinal decontamination | | | |
| Yes | 33 (28.7) | 4 (28.6) | 0.90* |
| No | 82 (71.3) | 10 (71.4) | |
| GCS | 14.07±0.16 | 13.21±0.74 | 0.28** |
| Level of consciousness | | | |
| Alert | 28 (24.3) | 2 (14.3) | 0.058* |
| Lethargic | 49 (42.6) | 3 (21.4) | |
| Stupor | 4 (3.5) | 2 (14.3) | |
| Coma | 1 (0.9) | 2 (14.3) | |
| Agitation | 33 (28.6) | 5 (35.7) | |
| CVS | | | |
| Without CVS toxicity | 90 (78.3) | 7 (50) | 0.03* |
| Tachycardia | 19 (16.5) | 4 (28.6) | |
| Bradycardia | 3 (2.6) | 1 (7.1) | |
| Chest pain | 1 (0.9) | 0 (0) | |
| Arrhythmia | 1 (0.9) | 0 (0) | |
| Hypotension | 1 (0.9) | 2 (14.3) | |
| Gastrointestinal manifestations | | | |
| No | 94 (81.7) | 12 (93.2) | 0.10* |
| Yes | 21 (18.2) | 2 (6.8) | |
| Skin manifestations | | | |
| No | 113 (98.3) | 10 (76.9) | 0.002* |
| Yes | 2 (1.7) | 4 (24.1) | |
| Pulmonary manifestations | | | |
| No | 97 (84.3) | 7 (50) | 0.001* |
| Yes | 18 (15.7) | 7 (50) | |
| Pupil size | | | |
| Normal size | 50 (43.5) | 4 (28.6) | 0.4* |
| Miosis | 31 (27) | 6 (42.9) | |
| Mydriasis | 34 (29.6) | 4 (28.6) | |
| Respiratory rate (/min) | 17.52±0.26 | 18.21±1.45 | 0.44** |
| Heart rate (/min) | 88.13±1.96 | 91.07±3.39 | 0.61** |
| Systolic blood pressure (mmHg) | 130.25±9.7 | 119.4±4.69 | 0.69** |
| Diastolic blood pressure (mmHg) | 75.73±1.15 | 71.07±2.78 | 0.18** |
| Temperature (°C) | 36.66±0.1 | 37.06±0.19 | 0.22** |
| Length of hospital stay (h) | 16.99±1.76 | 34.21±14.6 | 0.26** |

Data are presented as mean±SE or *n* (%), where appropriate. *Fisher exact test, **Independent *t*-test. SE=Standard error, GCS=Glasgow Coma Scale, CVS=Cardiovascular system

Forty cases used only methamphetamine and the others (89 cases) ingested other drugs with methamphetamine. Although due to the methodological limitations of the present study, we could not find the difference between patients' survival or death regarding the co-ingestion of other drugs; co-ingestants increased the risk of morbidity and mortality.[25]

**Table 3: Predictive factors of the outcome of treatment in patients with methamphetamine poisoning**

| Variables | *P* | OR (95% CI) |
|---|---|---|
| Age | 0.027 | 1.05 (1.006-1.099) |
| Suicide history | 0.003 | 30.33 (3.11-295.24) |
| Route of poisoning | | |
| Ingestion | 0.032 | 0.21 (0.05-0.87) |
| Inhalation | 0.22 | 0.19 (0.04-0.78) |
| Pulmonary system manifestations | 0.01 | 1.84 (1.15-2.93) |

OR=Odds ratio, CI=Confidence interval

Previous history of psychiatric disorder (35.7%) and suicide (50%) was observed in patients with the worse outcome. Depression has been reported commonly among methamphetamine users and symptoms of depression may persist for weeks, months, or in some cases even several years after stopping methamphetamine use.[26] Most of our patients had a history of addiction. Chronic use of methamphetamine can produce significant neurological damage as well as damage to cardiovascular, pulmonary, and other organ systems. Chronic exposure to methamphetamine may cause personality changes, psychotic syndrome, and ulcers of the lips and tongue.[27]

Coma, agitation, hypotension, tachycardia, and pulmonary manifestations were more frequent in patients with the worse outcome as compared to patients survived without any complications. All clinical manifestations were compatible with methamphetamine poisoning, which has been reported in previous studies.[25] Methamphetamine hydrochloride poisoning may ultimately result in collapse, shock, systemic acidosis (accumulation of acid in the body), coma, and convulsions.[28]

We could not find any significant difference in laboratory tests data between the two groups with respect to the outcome. However, hypokalemia due to the direct sympathomimetic effects of methamphetamine, and hyperkalemia related to hyperthermia, rhabdomyolysis, or renal failure after methamphetamine poisoning has been reported previously.[29] Also, hypernatremia from dehydration and hyponatremia have been reported in methamphetamine overdose.[25]

## CONCLUSION

Methamphetamine poisoning was more common in males with intentional poisoning. Age, past history of suicide, route of poisoning, and pulmonary

manifestations on admission may be considered as important predictive factors in the outcome of treatment in these patients.

## AUTHORS' CONTRIBUTION

NEM and AMS contributed in designing and conducting the study. PP, HP, and AJ collected the data, and NEM did the data analysis. AMS rechecked the statistical analysis and prepared the manuscript. All authors have assisted in the preparation of the manuscript and have read and approved the content of the manuscript and are accountable for all aspects of the work.

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### Conflicts of interest

There are no conflicts of interest.

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