

ORIGINAL RESEARCH

Predictive Factors of Mortality in Acute Amphetamine Type Stimulants Poisoning; a Review of 226 Cases

Mitra Rahimi¹, Somaieh Lookzadeh¹, Roxana Sadeghi², Kambiz Soltaninejad³, Shahin Shadnia^{1*}, Abdolkarim Pajoumand¹, Hossein Hassanian-Moghaddam¹, Nasim Zamani¹, Masoud Latifi-Pour¹

1. Toxicology Research Center, Excellence Center of Clinical Toxicology, Department of Clinical Toxicology, Loghman Hakim Hospital, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

2. Cardiology Department, Loghman Hakim Hospital, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

3. Department of Forensic Toxicology, Legal Medicine Research Center, Legal Medicine Organization, Tehran, Iran.

Received: August 2017; Accepted: October 2017; Published online: 10 January 2018

Abstract: **Introduction:** Amphetamine type stimulants (ATS) such as amphetamine and methamphetamine (MA) are one of the most important causes of poisoning in the world. In this study we aimed to define the predictive factors of mortality in acute ATS poisoning patients. **Methods:** This is a retrospective cross-sectional study on all cases with acute ATS poisoning who were referred to a referral center for poisoning, Tehran, Iran, from April 2011 to March 2014. Using patients' medical records, demographic data, route of exposure, type and amount of ATS, the cause of poisoning, clinical presentations, and electrocardiogram (ECG) and laboratory findings, as well as patient's outcomes were collected and analyzed regarding the independent predictive factors of mortality. **Results:** 226 cases with the mean age of 32.9 ± 10.9 years were studied (77% male). MA was the most abused ATS (97.4%) and the most frequent route of exposure was oral (55.3%). The mortality rate was 5.4%. There was a significant association between agitation ($p = 0.002$), seizure ($p = 0.001$), loss of consciousness ($p < 0.001$), creatine phosphokinase level ($p = 0.002$), serum pH ($p = 0.002$), serum HCO₃ ($p = 0.02$), and PCO₂ ($p = 0.01$) with mortality. However, serum HCO₃ [OR=1.27 (95% CI: 1.07-1.50); p value=0.005], PCO₂ [OR=0.89 (95% CI: 0.84-0.96); p value=0.002], and loss of consciousness [OR=0.019 (95% CI: 0.003-0.106); p value=0.000] were the only independent predictive factors of mortality. **Conclusion:** PCO₂ ≥ 51 mmHg, serum bicarbonate ≤ 22.6 mEq/L, and loss of consciousness on admission could be considered as prognostic factors of mortality in acute ATS poisoning cases presenting to emergency department.

Keywords: Amphetamines; patient outcome; prognostic factors; poisoning; substance abuse

© Copyright (2018) Shahid Beheshti University of Medical Sciences

Cite this article as: Rahimi M, Lookzadeh S, Sadeghi R, Soltaninejad K, Shadnia Sh, A Pajoumand, Hassanian-Moghaddam H, Zamani N, Latifi-Pour M. Predictive Factors of Mortality in Acute Amphetamine Type Stimulants Poisoning; a Review of 226 Cases. *Emergency*. 2018; 6(1): e1.

1. Introduction

Amphetamine type stimulants (ATS) refer to a class of substances whose main derivatives are amphetamine and methamphetamine (MA). Also, a range of other substances such as ephedrine, pseudoephedrine, methylphenidate, methcathinone, and 3,4- methylenedioxymethamphetamine (MDMA) are included in this group

(1, 2).

The production and abuse of ATS have increased worldwide. However, the pattern of abuse of each type of ATS is different throughout the world based on social, cultural and geographic parameters (1). For example, amphetamine abuse tends to be more common than MA in Europe, except in Czech Republic, Slovakia, Estonia, and Latvia. Amphetamine is used therapeutically and illicitly in the United Kingdom (3). MA, which is the second most popular illicit drug with an annual global prevalence estimated at 0.4% (3), is more dominant in the east, southeast Asia and Oceania (4).

ATS abuse is a serious health, social and economic problem all over the world. Previous reports have determined the sig-

* **Corresponding Author:** Shahin Shadnia; Department of Clinical Toxicology, Loghman Hakim Hospital Poison Center, Kamali Street, South Karegar Avenue, Tehran, Iran. Tel/Fax: +98-21-55424041, Cell Phone: +98-912-1947601 Email: shahin1380@yahoo.com



nificant correlation between ATS abuse (mostly MA) via injection and risk of the transmission of blood-borne viruses (3). Dependency and addiction are other mental and clinical health problems among ATS abusers. Dependence and chronic usage are associated with MA psychosis and other related psychosomatic and clinical adverse consequences (3). Another health problem in ATS abusers is acute poisoning, which is considered as a major problem in emergency settings (5, 6). The common features of ATS poisoning include agitation, dilated pupils, tachycardia, hypertension, and tachypnea. Other clinical findings include tremor, dyspnea, chest pain, hyperpyrexia and cardiac, hepatic and/or renal failure. Coma or seizures occur less frequently (7). Although there are reports about acute ATS poisoning (8-11), to the best of our knowledge there are limited data about prognostic factors of mortality in acute ATS poisoning cases (12, 13). Therefore, the aim of the present study was to define the predictive factors of mortality in acute ATS poisoning patients.

2. Methods

2.1. Study design and setting

This is a retrospective cross-sectional study. All cases of pure acute ATS poisoning, who were referred to the Toxicology Center of Loghman Hakim Hospital, Tehran, Iran, since April 2011 to March 2014, were studied. This educational hospital serves as a referral center for poisoning patients of Iranian capital, Tehran. The study was approved by Ethical Committee of Shahid Beheshti University of Medical Sciences (Grant No.: M-384). The authors adhered to the principles of Helsinki declaration. The patients' data were kept confidential.

2.2. Participants

All cases of pure acute ATS poisoning who were admitted during the mentioned period were enrolled to the study using census sampling. The patients with co-ingestion or those discharged against medical advice were excluded.

2.3. Data gathering

Using a self-made checklist, demographic data (sex, age), route of exposure, type and amount of ATS, the cause of poisoning, history of addiction, clinical presentations, laboratory findings, electrocardiography (ECG) finding, duration of hospitalization, and outcomes (mortality, disposition, and complications during admission) were collected by a trained physician for all participants according to the patients' medical records. We used ICD10 classification for extracting patients' medical records from the hospital's archive. Diagnosis of acute ATS poisoning was done based on the history given by the patients or their relatives, physical examination and

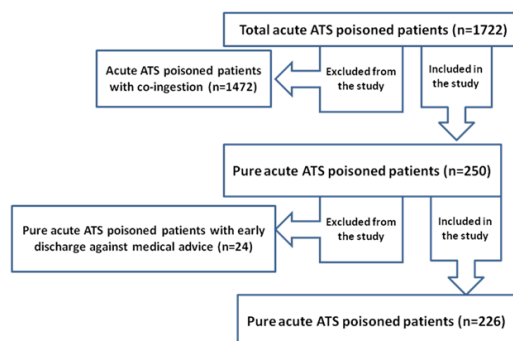


diagram 1: Flow diagram of patient selection. ATS: Amphetamine Type Stimulants

laboratory confirmation.

2.4. Statistical Analysis

We used the social package for statistical analysis (SPSS) software version 16. The data were expressed as mean \pm SD for continuous or discrete variables and as frequency and percentage for categorical variables. Chi-square test was used for statistical analysis of qualitative variables. The normal distribution of quantitative variables was tested by Kolmogorov – Smirnov test. The statistical comparison was done with Mann–Whitney U -test for nonparametric variables and independent student t-test for parametric variables. Logistic regression was used for evaluating the predictive factors of mortality. The best cut off points was determined by calculating the area under the receiver operating characteristics (ROC) curve. P values of 0.05 or less were considered to be statistically significant and data were presented with 95% confidence interval (CI).

3. Results

3.1. Baseline characteristics

1722 ATS intoxicated patients' files were evaluated, out of which, 226 (13%) cases with acute ATS poisoning were included (Diagram 1). The mean age of the patients was 32.9 ± 10.9 (14 - 77) years (77% male). Baseline characteristics, clinical presentations, and laboratory results, as well as ECG findings are summarized in table 1 and 2.

The most common type of ATS used was MA (97.4%) and the most frequent route of exposure was oral (55.3%). Abuse was the most common cause of poisoning (66.8%) and the mean ATS dose was 1.64 ± 1.59 grams. The mean time from exposure to admission was 5.9 ± 9.6 hours. History of addiction was positive in 123 (54%) cases with 5.3 ± 3.8 years mean duration of addiction.

Table 1: Comparing the baseline characteristics of acute amphetamine type stimulants (ATS) intoxicated patients who survived and those who died

| Parameter | Total (n=226) | Survived (n=214) | Died (n=12) | P value |
|-------------------------------------|--------------------|-------------------|-------------------|---------|
| Sex | | | | |
| Male | 174 (77) | 165 (77.1) | 9 (75) | 0.6 |
| Female | 52 (23) | 49 (22.9) | 3 (25) | |
| Type of ATS | | | | |
| Methamphetamine | 220 (97.4) | 208 (97.2) | 12 (100) | 0.9 |
| MDMA | 1 (0.4) | 1 (0.5) | 0 | |
| Methylphenidate | 5 (2.2) | 5 (2.3) | 0 | |
| Route of exposure | | | | |
| Oral | 125 (55.3) | 116 (54.2) | 9 (75) | 0.7 |
| Inhalation | 93 (41.2) | 90 (42) | 3 (25) | |
| Injection | 4 (1.8) | 4 (1.9) | 0 | |
| Oral and Inhalation | 3 (1.3) | 3 (1.4) | 0 | |
| Oral and Injection | 1 (0.4) | 1 (0.5) | 0 | |
| Cause of poisoning | | | | |
| Abuse | 151 (66.8) | 146 (68.2) | 5 (41.7) | 0.7 |
| Suicide | 54 (23.9) | 47 (22) | 7 (58.3) | |
| Accidental | 2 (0.9) | 2 (0.9) | 0 | |
| Body packer | 15 (6.6) | 15 (7) | 0 | |
| Body stuffer | 4 (1.8) | 4 (1.9) | 0 | |
| ATS dose (gram) | 1.64±1.59 (0.5-13) | 1.7±1.6 (0.5-13) | 1.1±0.3 (1-1.5) | 0.8 |
| Exposure to admission (hour) | 5.9±9.6 (0.5-72) | 6±9.8 (0.5-72) | 4.4±3.1 (1-10) | 0.9 |
| Duration of addiction (year) | 5.3±3.8 (1-20) | 5.3±3.9 (1-20) | 5.5±3.1 (3-10) | 0.9 |
| Age (year) | 32.9±10.9 (14-77) | 32.6±10.7 (14-77) | 38.1±13.6 (19-55) | 0.2 |

Data were presented as mean ± standard deviation (minimum-maximum) or frequency (%).
MDMA: 3,4-Methylenedioxymethamphetamine.

3.2. Outcomes

19 (8.4%) cases were admitted to Medical Toxicology Intensive Care Unit (ICU) and others (207, 91.6% of cases) were admitted to general ward. In most of the cases (61.6%), the duration of hospitalization was ≤ 24 hours. Intubation was indicated in 24 (10.6%) cases. The mortality rate was 5.4% (12/226). 2 cases of acute respiratory distress syndrome (0.9%), 2 ventilator associated pneumonia (0.9%), 2 rhabdomyolysis (0.9%), and 1 case of deep vein thrombosis (0.4%) were the complications detected in 7 (3.1%) patients (All of them were male).

3.3. Predictive factors of mortality

Table 1 and 2 compare the baseline characteristics, clinical presentations, laboratory results, and ECG findings of acute ATS poisoning among survived and non-survived cases. Based on univariate analysis, there were significant associations between agitation (p = 0.002), seizure (p = 0.001), loss of consciousness on admission (p < 0.001), creatine phosphokinase level (p = 0.002), serum pH (p = 0.002), serum HCO₃ (p = 0.02), and PCO₂ (p = 0.01) with mortality. However, the results of multivariate regression analysis showed serum HCO₃ [OR=1.27 (95% CI: 1.07-1.50);

p value=0.005], PCO₂ [OR=0.89 (95% CI: 0.84-0.96); p value=0.002], and loss of consciousness on admission [OR=0.019 (95% CI: 0.003-0.106); p value=0.000] as the independent predictive factors of mortality in acute ATS poisoning.

Based on the area under the ROC curve (AUC) the best cut off points of PCO₂ and serum HCO₃ for prediction of mortality were ≥ 51 mmHg [AUC = 0.61 (95% CI: 0.401-0.822)] and ≤ 22.6 mEq/L [AUC = 0.704 (95% CI: 0.525-0.882)], respectively (figure 1).

Screening performance characteristics of PCO₂ ≥ 51 mmHg and HCO₃ ≤ 22.6 mEq/L in prediction of acute ATS intoxicated mortality are summarized in table 3.

4. Discussion

ATS are potent psychostimulants that are abused all over the world (4). ATS poisoning has recently emerged as a crucial health problem in clinical and forensic settings (8, 14, 15). Therefore, the emergency department staff should be aware of the clinical presentations, paraclinical findings and prognostic factors of acute ATS poisoning. In this study, the most common cause of poisoning was abuse and majority of cases, had oral exposure. In the previous study done in the same



Table 2: Comparing the vital signs, clinical presentations, laboratory results, and electrocardiogram (ECG) findings among acute amphetamine type stimulants (ATS) intoxicated patients who survived and those who died

| Parameter | Total (n=226) | Survived (n=214) | Died (n=12) | P value |
|--------------------------------|--------------------------|-------------------------|----------------------------|---------|
| Vital signs | | | | |
| SBP (mmHg) | 125.5±23.6 (80-230) | 126±22.7 (80-230) | 115.8±36.3 (80-180) | 0.1 |
| DBP (mmHg) | 78.5±13.9 (40-150) | 78.9±13.7 (50-150) | 70±16.5 (40-100) | 0.054 |
| Pulse rate (/minute) | 99.2±19 (52-168) | 99.2±18.5 (52-168) | 99.8±27.1 (66-160) | 0.6 |
| Clinical presentations | | | | |
| Agitation | 172 (76.11) | 168 (78.50) | 4 (33.33) | 0.002 |
| Confusion | 66 (29.20) | 65 (30.37) | 1 (8.33) | 0.09 |
| Judgment disorder | 48 (21.24) | 48 (22.43) | 0 | 0.053 |
| Seizure | 16 (7.08) | 11 (5.14) | 5 (41.67) | 0.001 |
| LOC | 16 (7.08) | 9 (4.21) | 7 (58.33) | 0.000 |
| Hallucination | 14 (6.19) | 13 (6.0) | 1(8.3) | 0.6 |
| Diaphoresis | 12 (5.31) | 12 (5.31) | 0 | 0.5 |
| Flushing | 7 (3.1) | 7 (3.1) | 0 | 0.7 |
| Abdominal pain | 5 (2.21) | 5 (2.21) | 0 | 0.8 |
| Blurred vision | 2 (0.88) | 2 (0.88) | 0 | 0.9 |
| Laboratory findings | | | | |
| Sodium (mEq/L) | 140.1±5.0 (124-188) | 140.1±5.0 (124-188) | 140.1±5.1 (130-148) | 1 |
| Potassium (mEq/L) | 4.1±0.5 (3-7.7) | 4.1±0.5 (3.1-7.7) | 4.2±0.9 (3-5.9) | 0.5 |
| CPK (U/L) | 1067.9±2981.9 (28-30000) | 813.2±1952.4 (28-17253) | 7309.1±10263.3 (103-30000) | 0.002 |
| LDH (U/L) | 909.1±841.3 (42-6033) | 885.7±854.6 (42-6033) | 1225±635.2 (563-2043) | 0.1 |
| Serum pH | 7.36±0.09 (6.90-7.90) | 7.36±0.09 (6.90-7.90) | 7.27±0.15 (6.90-7.40) | 0.002 |
| PCO ₂ (mmHg) | 43.9±9.8 (13-78) | 43.6±9.2 (13-74) | 51.2±16.5 (32-78) | 0.01 |
| Serum HCO ₃ (mEq/L) | 24.3±4.9 (8.7-56) | 24.5±4.9 (8.7-56) | 21.2±4.5 (15.8-28.4) | 0.02 |
| ECG findings | | | | |
| Normal sinus | 104 (46) | 97 (45.3) | 7 (58.3) | |
| Sinus tachycardia | 103 (45.6) | 100 (46.7) | 3 (25.0) | |
| Sinus bradycardia | 8 (3.5) | 7 (3.2) | 1 (8.3) | |
| T inversion | 10 (4.4) | 9 (4.2) | 1 (8.3) | 0.3 |
| QRS widening | 7 (3.0) | 6 (2.8) | 1 (8.3) | |
| ST change | 4 (1.7) | 3 (1.4) | 1 (8.3) | |
| Ventricular Dysrhythmia | 3 (1.3) | 2 (0.9) | 1 (8.3) | |
| Hospitalization (hour) | | | | |
| ≤24 | 139 (61.6) | 132 (61.7) | 7 (58.3) | 0.07 |
| >24 | 87 (38.4) | 82 (38.3) | 5 (41.7) | |

Data were presented as mean ± standard deviation (minimum-maximum) or frequency (%). SBP: Systolic blood pressure, LOC: Loss of consciousness, DBP: Diastolic blood pressure, CPK: Creatine Phosphokinase, LDH: Lactate dehydrogenase; ECG: Electrocardiogram.

Table 3: Screening performance Characteristics of PCO₂ ≥ 51 mmHg and serum HCO₃ ≤ 22.6 mEq/L in predicting the risk of mortality in acute amphetamine Type Stimulants (ATS) intoxicated patients

| Character | PCO ₂ (95% CI) | HCO ₃ (95% CI) |
|----------------------------------|---------------------------|---------------------------|
| Sensitivity | 50.00 (22.28 – 77.71) | 66.66 (35.43 – 88.72) |
| Specificity | 78.97 (72.77 – 84.10) | 72.89 (66.33 – 78.62) |
| Positive Predictive Value | 11.76 (04.87 – 24.55) | 12.12 (05.74 – 23.03) |
| Negative Predictive Value | 96.57 (92.34 – 98.59) | 97.50 (93.31 – 99.19) |
| Positive Likelihood Ratio | 0.13 (0.06 – 0.28) | 0.13 (0.07 – 0.26) |
| Negative Likelihood Ratio | 0.03 (0.01 – 0.07) | 0.02 (0.01 – 0.06) |

hospital, although the main cause of poisoning was abuse, the common route of exposure was inhalation (12). In our study, most of the patients were young men, which is in concordance with the results of previous studies (6, 12, 13). Most of our patients had a positive history of addiction. This result

is in line with previous studies (6, 12). MA was the most frequent type of ATS used by our patients. The result is the same as previous studies in Iran (12, 16), however, the studies in European countries showed amphetamine and MDMA as the most frequent type of ATS



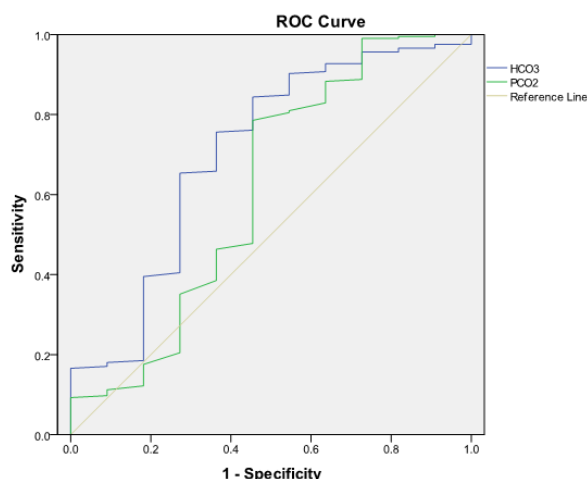


Figure 1: Receiver operating characteristic (ROC) curve for PCO₂ and serum HCO₃ in predicting the risk of mortality in acute amphetamine Type Stimulants (ATS) intoxicated patients.

among intoxicated cases (10, 17). This difference could be due to demographic variables such as marital status and level of education (18). Previous studies introduced curiosity in trying different things and looking for pleasure as the most important reasons for MA abuse in Iran (18, 19). Other factors are lower effectiveness of previous drugs, popularity and low price of new drugs, and emulation of others (18, 20, 21). Khodabandeh et al. reported MA abuse among methadone maintenance participants. The most common reasons were the good sensation, getting high, to enhance their sexual performance, and in some instances as self-medication for depression (22, 23). Agitation, confusion and judgment disorder were the most common clinical manifestations, which are the same as the result of a previous study in Australia (6). In another study in Iran, loss of consciousness was the most common clinical finding, which could be due to co-ingestion with opioids and other drugs (12).

Most of the patients had abnormal ECG, and sinus tachycardia was the major finding, which has been reported previously (12, 24).

The mortality rate was 5.4%, which was lower than previous studies (12, 13). This may be related to the delayed admission of the patients to the hospital in the previous studies (12).

In our study, lower serum HCO₃, higher PCO₂ and low level of consciousness on admission were considered as predicting factors of mortality in ATS poisoning cases. In the previous study performed in this center, age, history of suicide, route of poisoning and pulmonary manifestations on admission were considered as predictive factors of patient's outcome (12), which is not supported by the results of our study. According to our results, PCO₂ ≥ 51 mmHg and serum HCO₃ ≤ 22.6 mEq/L can predict the poisoned patients' mortal-

ity rate with specificity (78.97% and 72.89%, respectively) and sensitivity (50.00% and 66.66%, respectively). However, based on the AUC measures, serum HCO₃ can better discriminate between those who die and those who survive. We did not find a study that had evaluated the relationship between these laboratory findings and prediction of mortality.

5. Limitation

We evaluated the patients' records retrospectively, which could be considered as a limitation of our study.

6. Conclusion

This study showed that high PCO₂, low serum bicarbonate and loss of consciousness on admission, could be associated with higher rate of mortality of acute ATS intoxicated cases.

7. Appendix

7.1. Acknowledgements

This article is the part of Dr. Somayeh Lookzadeh's thesis, who was an Internal Medicine Resident at the time of the study. The authors wish to thank the nurses of Loghman Hakim Hospital Poisoning Center; especially Mrs. S. Bana-Jafari, the head nurse of MTICU, Mrs. M. Rezvani and Mrs. B. Barari the staff of MTICU. The authors would like to convey their full appreciation to Toxicology Research Center for their financial support.

7.2. Authors' contribution

All authors made a substantial contribution to analysis and writing of the paper draft and met the four criteria for authorship recommended by the International Committee of Medical Journal Editors.

7.3. Funding/Support

This study was supported by a grant from Toxicology Research Center, Shahid Beheshti University of Medical Sciences. Grant number: M-384.

7.4. Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

References

1. World Health Organization. Amphetamine-type stimulants. Available 1 August 2017. [Available from: www.who.int/substance_abuse/facts/ATS/en/].
2. Kumar MS, Kumar S. Amphetamine type stimulants (ATS) use in India- An exploratory study. United Nations



- Office on Drugs and Crime (UNODC); New Delhi, India, 2015.
3. United Nations Office on Drugs and Crime (UNODC), World Drug Report, Vienna, 2015.
 4. United Nations Office on Drugs and Crime (UNODC), The Challenge of Synthetic Drugs in East and South-East Asia and Oceania, Vienna, May 2015.
 5. Alam Mehrjerdi Z, Noroozi A. Methamphetamine intoxication in emergency departments of hospitals in iran: implications for treatment. *Iran J Med Sci.* 2013;38(4):347-8.
 6. Bunting PJ, Fulde GW, Forster SL. Comparison of crystalline methamphetamine ("ice") users and other patients with toxicology-related problems presenting to a hospital emergency department. *Med J Australia.* 2007;187(10):564-6.
 7. Cruickshank CC, Dyer KR. A review of the clinical pharmacology of methamphetamine. *Addiction.* 2009;104(7):1085-99.
 8. Yazdani MR TN, Masoumi GR, Gheshlaghi F, Dana-Siadat Z, Setareh M, et al. Demographic factors, duration and costs of hospitalization, and causes of death in patients intoxicated with opioids and amphetamines. *International Journal of Medical Toxicology and Forensic Medicine.* 2014;4(4):122-9.
 9. Hassanian-Moghaddam H, Zamani N, Rahimi M, Shadnia S, Pajoumand A, Sarjami S. Acute Adult and Adolescent Poisoning in Tehran, Iran; the Epidemiologic Trend between 2006 and 2011. *Arch Iran Med.* 2014;17(8):534-8.
 10. Le Roux G BC, Lelievre B, Bretaudeau Deguigne M, Turcant A, Harry P, et al. Recreational phenethylamine poisonings reported to a French poison control center. *Drug Alcohol Depend* 2015;154:46-53.
 11. Jones AW HA. Amphetamine abuse in Sweden: subject demographics, changes in blood concentrations over time, and the types of co-ingested substances. *J Clin Psychopharmacol.* 2013;33(2):48-52.
 12. Paydar P, Sabzghabaee AM, Paydar H, Eizadi-Mood N, Joumaa A. Outcome of treatment in patients with methamphetamine poisoning in an Iranian tertiary care referral center. *J Res Pharm Pract.* 2015;4(3):167-72.
 13. Lan KC, Lin YF, Yu FC, Lin CS, Chu PL. Clinical manifestations and prognostic features of acute methamphetamine intoxication. *J Formos Med Assoc.* 1998;97(8):528-33.
 14. Schifano F, Corkery J, Naidoo V, Oyefeso A, Ghodse H. Overview of Amphetamine-Type Stimulant Mortality Data - UK, 1997-2007. *Neuropsychobiology.* 2010;61(3):122-30.
 15. Arendt M, Munk-Jorgensen P, Sher L, Jensen SOW. Mortality among individuals with cannabis, cocaine, amphetamine, MDMA, and opioid use disorders: A nationwide follow-up study of Danish substance users in treatment. *Drug Alcohol Depen.* 2011;114(2-3):134-9.
 16. Behnoush B, Taghadosinejad F, Arefi M, Shahabi M, Jamalain M, Kazemifar AM. Prevalence and complications of drug-induced seizures in Baharloo hospital, Tehran, Iran. *Iran J Toxicol.* 2012;6(16):588-93.
 17. Dines AM, Wood DM, Yates C, Heyerdahl F, Hovda KE, Giraudon I, et al. Acute recreational drug and new psychoactive substance toxicity in Europe: 12 months data collection from the European Drug Emergencies Network (Euro-DEN). *Clin Toxicol (Phila).* 2015;53(9):893-900.
 18. Barati M, Ahmadpanah M, Soltanian AR. Prevalence and factors associated with methamphetamine use among adult substance abusers. *J Res Health Sci.* 2014;14(3):221-6.
 19. Shams Alizadeh N, Moghadam M, Mohsenpour B, Rostami Gooran N. Prevalence of substance abuse in medical students of Kurdistan University. *Scientific J Kurdistan Uni Med Sci.* 2008;13(2):18-28.
 20. Farhadinasab A, Allahverdipour H, Bashirian S, Mahjoub H. Lifetime Pattern of Substance Abuse, Parental Support, Religiosity, and Locus of Control in Adolescent and Young Male Users. *Iran J Public Health.* 2008;37(4):88-95.
 21. Doaghoyan D, Habibzadeh Maleki A. Factors influencing the changing patterns of drug use among young people, from light drug to heavy drug. *J Disciplinary Knowledge.* 2011;13(1):105-33.
 22. Khodabandeh F, Kahani S, Shadnia S, Abdollahi M. Comparison of the Efficacy of Methadone Maintenance Therapy vs. Narcotics Anonymous in the Treatment of Opioid Addiction: A 2-Year Survey. *Int J Pharmacol.* 2012;8:445-9.
 23. Shariatirad S, Maarefvand M, Ekhtiari H. Methamphetamine use and methadone maintenance treatment: an emerging problem in the drug addiction treatment network in Iran. *Int J Drug Policy.* 2013;24(6):e115-6.
 24. Smets G, Bronselaer K, De Munnynck K, De Feyter K, Van de Voorde W, Sabbe M. Amphetamine toxicity in the emergency department. *Eur J Emerg Med.* 2005;12(4):193-7.