

Demographic Factors, Duration and Costs of Hospitalization, and Causes of Death in Patients Intoxicated with Opioids and Amphetamines

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ABSTRACT

Background: Intoxications are medical emergencies and among the significant causes of morbidity and mortality worldwide. In recent years, prevalence of intoxication with opioids and stimulants, such as amphetamines, is increasing particularly among young people. In this study, we investigated demographic factors, duration of hospitalization, costs of hospitalization, and cause of death in patients intoxicated with amphetamines and opioids.

Materials and Methods: This study was a prospective descriptive-analytic study. Sampling method was census, and Subjects were patients intoxicated with amphetamines and opioids, alone or combined, who referred to toxicology ward of Ali-Asghar hospital in Isfahan, from October 2009 to April 2010.

Results: During 6 months, among 2325 subjects, 419 patients used opioids, 98 patients used amphetamines, and 25 patients used both of them. The mean age of patients in the three groups was not significantly different. Most patients were male in all groups. The most common route of intoxication was orally in opioid group and inhalation in amphetamine group. The most common cause of intoxication was intentional attempt. Vital signs at admission were normal in three groups, but the average of heart rate, body temperature, respiratory rate and blood pressure, was slightly higher in the amphetamine group than the opioid group. Duration and cost of hospitalization were not significantly different between groups. Four patients were died totally and the outcome was not significantly different between groups. The mean age and duration of hospitalization were significantly higher in died compared to living patients.

Conclusion: Opioids and amphetamines accounted for high percentages of intoxication, especially in young single men with self-employed job. Therefore, control and prevention

of opioids and amphetamines consumption are important ways to reduce this kind of intoxication in this group.

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► *Implication for health policy/practice/research/medical education:* Patients Intoxicated with Opioids and Amphetamines

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1. Introduction:

Intoxications are medical emergencies and among the most common causes of morbidity and mortality worldwide. Annual incidence rate of intoxication in the United States is about 5 million (1). Because intoxications are among the most significant and treatable causes of emergencies, prevention and timely treatment of intoxications can considerably decline the rate of mortality worldwide (2). Mortality rate, due to consumption of opioids and amphetamines are different in various countries. In different studies in Washington and Norway in 2009, mortality rate due to consumption of opioids were 1668 persons, accounted for 6.4 deaths per 100,000 populations and 1.9%, respectively (3, 4). Furthermore, several studies indicated that these intoxications and subsequent mortality rates are rising. A study in the United States in 2011, showed that the incidence rate of intoxication, including opioids, has been increased more than three times during 1999-2006 (5). In the United States over these years, mortality and morbidity rates due to intoxications have been increased about two times more than previous years (3). The last study relating to intoxications in Isfahan, central of Iran, indicated that consumption of opioids was

the leading cause of mortality and morbidity in 2000 patients, and the second cause of death in the toxicology ward in the Ali-Asghar hospital during 1998-2001 (2).

Clinical manifestations of intoxications with opioids include; loss of consciousness (from lethargy to coma), changes in pupil diameter (mostly pin point miosis), respiratory depression and cyanosis. Pulmonary edema is also a common and serious complication of opioids overdose and has never been seen with treatment doses. Intoxication with opioids can occur accidentally due to substance abuse, or intentionally for suicidal or homicidal purposes (6).

In recent years, consumption and intoxication are rising with stimulants, including amphetamines, particularly among young people. A study in Tehran, capital of Iran, showed that consumption prevalence of amphetamines was 7.2% in the age group of 15 to 35 years, in 2008 (7). Clinical manifestations of amphetamines overdose include the increased body temperature, hallucination, convulsion, irritability, and even death (8). Obviously, demographic factors, duration and cost of hospitalization in intoxicated patients are vary widely in different geographical areas due to differences in medical capacities (1); therefore, specific information about each area is required for proper preventive and therapeutic planning in the field of toxicology.

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There are not any data regarding amphetamine intoxication and new data regarding opioid intoxication in Isfahan province, central Iran. Considering that understanding the updated data would be useful in planning more effective programs for controlling intoxications and their related morbidity and mortality. The aim of this study was to determine demographic factors, clinical manifestations, duration and cost of

2. Materials and Methods:

This study was a prospective descriptive–analytic study which approved by the Ethics Committee of the Isfahan University of Medical Sciences. The study conducted from October 2009 to April 2010 in the toxicology ward of the Ali-Asghar hospital, the referral center of toxicology in Isfahan.

All patients intoxicated with

Table 1: Frequency distribution of demographic factors, routes and causes of intoxications

Group	Variable	Opioids	Amphetamines	Combined	p value
	Age*	30.67±13.51	28.3±7.75	27.82 ±8.36	0.25
	Sex** < 0.02				
	Male	233 (77.2)	80 (87)	11 (100)	
	Female	69 (22.8)	12 (13)	0 (0)	
	Marital Status**				< 0.04
	Single	148 (49)	60 (65.2)	6 (54.5)	
	Married	149 (49.3)	29 (31.5)	5 (45.5)	
	Divorced or Widow	5 (1.7)	3 (3.3)	0 (0)	
	Job**				0.053
	Employee	11 (3.6)	3 (3.3)	0 (0)	
	Self- employed	124 (41.1)	51 (55.4)	10 (90.9)	
	Student	10 (3.3)	5 (5.4)	0 (0)	
	Unemployed	39 (12.9)	9 (9.8)	1 (9.1)	
	Military	1 (0.3)	0 (0)	0 (0)	
	Other	117 (38.7)	24 (26.1)	0 (0)	
	Route of intoxication**				0.00
	Oral	225 (74.5)	18 (19.8)	2 (18.2)	
	Inhalational	37 (12.3)	39 (42.9)	2 (18.2)	
	Injection	23 (7.6)	27 (29.7)	1 (9.1)	
	Combinations	17 (5.6)	7 (7.7)	6 (54.5)	
	Cause of intoxication**				0.057
	Accidental	22 (7.3)	1 (1.1)	0 (0)	
	Intentional	280 (92.7)	91 (98.9)	11 (100)	

*: Standard deviation ± mean **: number (percent)

Table 2: Frequency distribution of outcome in the study subjects

Group	Outcome	Opioids number (percent)	Amphetamines number (percent)	Combined number (percent)	p value
	Recovery without complication	276 (4.91)	87 (94.6)	11 (100)	
	Recovery with complication	22 (7.3)	5 (5.4)	0 (0)	0.62
	Death	4 (1.3)	0 (0)	0 (0)	

hospitalization, outcome, and cause of death in patients intoxicated with amphetamines and opioids in Isfahan, the second largest province of Iran.

amphetamines and opioids, alone or combined were enrolled by the census method. Diagnosis of intoxication was made by taking history of the patients or

their relatives, physical examination, and laboratory confirmation. Each patient who discharged voluntarily from the ward was excluded from the study.

Patients were divided into three groups: intoxicated with opioids alone, intoxicated with amphetamines alone, and intoxicated with both of them concurrently. For each patient, a checklist was recorded, included vital signs, gender, age, marital status, occupation, type of drug used, cause of intoxication (accidental or intentional), route of intoxication (oral, inhalational, intravenous, intramuscular, subcutaneous or combined), usage of other medications, duration and cost of hospitalization, outcome (recovery, morbidity or mortality), and cause of death. Data were collected from patients' records in the toxicology ward and archived in the forensic medicine unit.

Data were analyzed using SPSS, version 16, ANOVA, chi-square, and Pearson correlation tests. P-values of less than 0.05 were considered as significant.

3. Results:

During the 6 months, 2325 intoxicated patients were referred to the toxicology ward, from which 542 (23.3%) patients

both were 419 (77.3%) patients, 98 (18%) patients, and 25 patients (4.7%) respectively.

Demographic data, routes and causes of intoxication in the study subjects are shown in table 1.

Mean age of the three groups were not significantly different. Frequency of men was more than women in three groups and frequency of men in the combine group was more than two other groups. In all groups, the most frequent occupation was self-employed job and less frequent was related to the military. In all groups, the most frequent cause of consumption was intentional attempt.

Patients had three types of outcome after therapeutic modalities: recovery without complication, recovery with short term or long term complications including liver failure, renal failure, endocarditis, aspiration pneumonia, and finally death. Frequency distributions of outcome in the three groups are shown in table 2.

Mean of duration and cost of hospitalization in the three groups are shown in table 3. As shown, these factors were not different significantly between three groups.

Vital signs at the time of admission

Table 3: Mean of duration and cost of hospitalization in the study subjects

Group	Opioids SD± mean	Amphetamines SD± mean	Combined SD± mean	p value
Mean of duration of hospitalization*	21.05±1.70	16.47±1.90	15.18±4.57	0.31
Mean of cost of hospitalization**	60.25±5.57	51.95±5.68	36.35±6.90	0.53

*: hours **: US dollars

Table 4: Mean of vital signs at admission in the study subjects

Group	Opioids SD± mean	Amphetamines SD± mean	Combined SD± mean	p value
Heart rate*	85.58±0.95	87±1.71	90.54±5.93	0.51
Respiratory rate*	16.52±4.93	18.48±4.54	15.36±3.95	0.00
Body temperature**	36.95±0.01	36.97±0.02	36.87±0.07	0.18
Systolic BP***	110.51±13.41	120.59±17.31	113.63±19.63	0.00
Diastolic BP***	70.90±8.75	75.00±12.02	72.72±7.530.00	

*: number per minute **: degree of Celsius ***: mmHg

had been taken opioids, amphetamines or both. They were enrolled in this study. Among enrolled, Numbers of patients who consumption of opioids, amphetamines, or

according to the agent used are shown in table 4. As shown, respiratory rate and systolic and diastolic blood pressure were different significantly between three

Table 5: Frequency distribution of use of other drugs (except opioids and amphetamines) in the study subjects

Group \ Other drugs	Opioids number (percent)	Amphetamines number (percent)	Combined number (percent)	p value
Positive history	78 (25.8)	20 (21.7)	3 (27.3)	0.71
Negative history	224 (74.2)	72 (78.3)	8 (72.7)	0.71

groups, but not in heart rate and body temperature.

Frequency distributions of use of other drugs (except opioids and amphetamines) in patients are shown in table 5.

Overall, mortality rate in the three groups was 4 in 405 patients; thus, 98.77% of patients were survived. Mean age of expired cases was 44.75 ± 10.55 . All 4 expired cases belonged to opioid group and among them 3 cases were male and one case was female. Mean duration of hospitalization in these cases was 88.57 hours. Causes of death were: 1) pulmonary edema in two cases, 2) degeneration in liver cells and atelectasis in lungs in one case, and 3) degeneration in liver and kidney cells in one case. Intervals among intoxication to death in aforementioned four expired cases were 2.25 and 11.30 hours in the first two cases, 12:50 hours in the third case, and 363 hours in the fourth case, respectively.

4. Discussion:

Considering that, opioids especially methadone are more readily available, higher rates of intoxication with opioids compared to two other groups is reasonable. This is compatible with other studies. In a study conducted in Kerman, southeastern of Iran, highest proportion of intoxication was related to opioids (9). In another study conducted in 2009 in Gilan, northern of Iran, use of opioids was about two folds than amphetamines (10). A study in the United States showed that, mortality rates due to opioids had the highest increase among other causes of death due to intoxications (11). In a study that conducted in South Africa, reported that, the highest proportion (28%) among opioid intoxications was related to methadone (12) and in another study in

Australia showed that, 6.1% of people above 14 years old have experienced opioids or amphetamines at least once; marijuana was reported as the most abused substance (13).

In all three groups, drug abusers were young people. This may be explained by the fact that young people often use these agents for entertainment and they may be triggered to use high doses in friendly meetings and therefore intoxications may occur. But in older ages, these agents are often used to relieve pain, not entertainment, thus lower doses are used and therefore intoxications occur less frequently. Study in the United States indicated that, the most dangerous time for intoxications with opioids and amphetamines is middle age (5). Study in Iran, showed that intoxications with these agents were seen most often in the age group of 12 to 39 years (9). Another study in 2010 in the United States revealed an inverse association between age and opioid intoxication (14).

In all three groups, proportion of men was more than women. This can be due to more liberal and social relations and more readily access to illegal drugs in men. In a study in Tehran, amphetamine usage in men was more than women also in another study. The proportion of men and women were 64.3% and 35.7% respectively (15, 10). A study in Virginia around drug induced intoxications, including opioids and amphetamines, the proportion of men and women were 63% and 37% respectively (16). In our study, frequency distribution of gender had significant difference among three groups; so that the proportion of men in the amphetamine and combined groups was more than the opioid group. This may be explained by the fact that amphetamines are newer drugs and

more introduced to people in friendly meetings; as well as, men are more liberal and participate, so more frequently in friendly meetings, are more fearless to experience new drugs compared to women; therefore, amphetamines are more likely used by men.

There was no significant difference between single or married cases in the opioid group, but singles accounted for most cases in the amphetamine and combined groups; perhaps because singles participate more frequently in friendly meetings and are more vulnerable to introduction and encouragement for consumption of these agents. In most studies, similar to our study, proportion of singles was more than married and divorced persons, which can be due to lack of commitment to family and also the expense of most of income for such entertainments in the single persons. In the study conducted in Gilan, proportion of singles, married and divorced cases were 89.4%, 9.6%, 1%, respectively (10).

In all three groups, the most frequent occupation was self-employed job. This can be due to the diversity of self-employed job and inclusion of many people to those in Iran, as well as, higher incomes in some of these jobs. But in the study in Kerman, the most common jobs, in descending order of frequency, were housewife, student, worker, employee and self-employed job (9). However, the Kerman study had been conducted in 2005 and this process is obviously changing over time.

The most frequent route of intoxication in opioid group was orally, due to the higher proportion of methadone usage in this group that has taken as a pill or liquid. The most frequent route in amphetamine and combine groups were inhalational and combinations of routs respectively. However, in a 2005 study in Iran, the most frequent route of intoxication of opioids was inhalational (9).

In all three groups, the most frequent cause of consumption was intentional attempt. A 2-years study conducted in Loghman

hospital of Tehran in 1998-99, revealed that 95% of intoxications had been occurred by intentional attempt (17).

The mean of heart rate and body temperature at admission was within normal limits in all three groups, but heart rate and body temperature in the amphetamine and combined groups were slightly higher than the opioid group that was correlated with previous studies (8).

Respiratory rate, systolic and diastolic blood pressures were significantly different among three groups, but all were within normal limits. Respiratory rate and blood pressure in the amphetamine and combined groups were slightly higher than the opioid group. As mentioned in other studies, amphetamine scan increases the respiratory rate and blood pressure (8).

Frequency distribution of consumption of other drugs (except opioids and amphetamines) were determined and compared in the study subjects, and were not significantly different among three groups. In A 2004 study in Tehran, 72% of intoxications were mono-drug and 28% were multi-drug (17). Low proportion of using other drugs can be explained by the fact that most people with suicidal motivation use multiple drugs to achieve their purpose; but most opioids and amphetamines users consume these agents for entertainment or healing pain and not to suicide, thus they do not use other medications with them.

Frequency distribution of outcome was not significantly different among three groups, correlated with other studies in the world. In a similar study in Norway in 2009, this rate had been reported 1.9% (4). Mortality rates due to drug intoxications were in different countries. So that, according to a 2006 study in the United States, mortality rates due to drug intoxications in the USA varied from 1.6/100,000 in Iowa to 12.4/100,000 in New Mexico (18).

The mean age at death of patients was higher than recovered (with or without complications) cases; that can be due to underlying and chronic diseases and consumption of additional drugs, as well

as the lower body capability to tolerate the effects of abused drugs in older adults. The mean age of patients who had complications was 37.48 ± 13.49 , which was correlated with previous studies in Isfahan (20). A study in the USA also revealed that the most mortality rate has been in the age group of 40 to 49 years (21).

The mean of duration and cost of hospitalization were not significantly different among three groups. No study has been done around duration and cost of hospitalization in patients intoxicated with opioids and amphetamines in recent years in Iran.

Cause of death was pulmonary edema in two cases. As mentioned in the articles and references, pulmonary edema is a common and serious complication of opioids overdose and never seen after therapeutic doses (6).

In conclusion, opioids and amphetamines, especially former, accounted for high percentages of intoxications. Intoxication with these agents was seen more frequently in young single men with self-employed job. Therefore, control and prevention of access to opioids and amphetamines are the important ways to reduce this kind of intoxication in these persons. Extensive community education should be implemented to increase popular awareness of danger of these agents. Furthermore, because methadone consumption led more frequently to intoxication than other drugs, access to methadone in drugstores should be restricted to physicians' prescriptions.

References

1. Mowry JB, Spyker DA, Cantilena LR Jr. 2012 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 30th Annual Report. *Clin Toxicol (Phila)*. 2013;51:94-9.
2. Sharafi E. Study of Fatal Poisonings in the Ali Asghar Hospital, Isfahan [MD Thesis]. Isfahan: Isfahan University of Medical Sciences; 2003.

3. Coolen P, Best S, Lima A, Sabel J, Paulozz L. Overdose deaths involving prescription opioids among Medicaid enrollees - Washington, 2004-2007. *MMWR Morb Mortal Wkly Rep*. 2009;58(42):1171-5.
4. Clausen T, Waal H, Thoresen M, Gossop M. Mortality among opiate users: opioid maintenance therapy, age and causes of death. *Addiction*. 2009;104(8):1356-62.
5. Webster LR, Cochella S, Dasgupta N, Fakata KL, Fine PG, Fishman SM, et al. An analysis of the root causes for opioid-related overdose deaths in the United States. *Pain Med*. 2011;12(Suppl. 2):S26-S35.
6. Montazeri K, Khalili Gh, Saghaei M, Eizadi N, Heidari M. *General Principles of Care in Toxicology and Emergency Medicine*. Isfahan: Isfahan University of Medical Sciences Publications; 2003. p. 261-89.
7. Hamdih M, Matlabi N, Asheri H. Study of prevalence of stimulant drugs, alcohol and amphetamine use in adolescents and young people, aged 15-35 years old in Tehran. *Journal of the Faculty of Medicine, Shahid Beheshti University of Medical Sciences*. 2008;32(4):315-9.
8. Montoya ID, McCann DJ. Drugs of abuse: management of intoxication and antidotes. *EXS*. 2010;100:519-41.
9. Ziaaddini H, Ziaaddini MR. The Household Survey of Drug Abuse in Kerman, Iran. *Journal of Applied Sciences*. 2005;5(2):3802.
10. Zarrabi H, Najafi K, Kafi M, Shirazi M. Substance use among students of Guilan University of Medical Sciences in Iran in 2005-2006. *Acta Medica Iranica*. 2009;47(6):473-8.
11. Enteen L, Bauer J, McLean R, Wheeler E, Hurliaux E, Kral AH. Overdose prevention and naloxone prescription for opioid users in San Francisco. *J Urban Health*. 2010;87(6):931-41.
12. Peltzer K, Ramlagan S, Johnson BD, Phaswana-Mafuya N. Illicit drug use and treatment in South Africa: a review. *Subst Use Misuse*. 2010;45(13):2221-43.
13. Degenhardt L, Day C, Conroy E, Gilmour S. Examining links between cocaine use and street based sex work in New South Wales, Australia. *J Sex Res*. 2006;43(2):107-14.

14. Edlund MJ, Martin BC, Fan MY, Devries A, Braden JB, Sullivan MD. Risks for opioid abuse and dependence among recipients of chronic opioid therapy: results from the TROUP study. *Drug Alcohol Depend.* 2010;112(1-2):90-8.
15. Barooni S, hrdad R, bari E. A survey of Ecstasy use among people aged 15-25 years-old in five areas of Tehran. *Tehran University Medical Journal.* 2008;65(11):49-54.
16. Wunsch MJ, Nakamoto K, Behonick G, Massello W. Opioid deaths in rural Virginia: a description of the high prevalence of accidental fatalities involving prescribed medications. *Am J Addict.* 2009;18(1):5-14.
17. Najjari F, Afshar M. Reports of Fatal Poisoning which Referred to Forensics. Tehran: Legal Medicine Organization. 2004; p. 309-18.
18. Paulozzi LJ, Ryan GW. Opioid analgesics and rates of fatal drug poisoning in the United States. *Am J Prev. Med.* 2006;3(6):506-11.
19. Scott G, Thomas SD, Pollack HA, Ray B. Observed patterns of illicit opiate overdose deaths in Chicago, 1999-2003. *J Urban Health.* 2007;84(2):292-306.
20. Khorvash F, FasihiDastjerdi M, Zarefar S, IzadiM, onaidiJafari N. Infectious complications and mortality due to norgesic in comparison with other injecting narcotics. *Journal of Military Medicine.* 2006;8(2):149-54.
21. Bohnert AS, Fudalej S, Ilgen MA. Increasing poisoning mortality rates in the United States, 1999-2006. *Public Health Rep.* 2010;125(4):542-7.

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