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ORIGINAL ARTICLE

A Clinico-Epidemiological Study on Poisonings due to Cardiovascular Drugs in Ahvaz, Iran

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Abstract

Background: Overdoses with cardiovascular drugs are related with significant morbidity and mortality. Beta-adrenergic blockers, calcium-channel blockers (CCBs), thiazide, digoxin and angiotensin converting enzyme (ACE) inhibitors represent five of the most important classes of cardiovascular drugs. Overdoses with cardiovascular drugs are typically caused by exploratory ingestion by children or intentional ingestion by suicidal adults. As no study has been performed about poisoning with this kind of drug in Khuzestan, this study aimed to investigate the frequency of cardiovascular drug poisoning and its clinical features in patients presenting in Razi Hospital of Ahvaz from 2005 to 2009.
Methods: A retrospective review of medical records of patients poisoned with cardiovascular who were treated at Clinical Toxicology Department was executed. A total of 70 poisoning cases referred to Razi Hospital were identified. These unselected cases included intentional, accidental, criminal and occupational circumstances. Beta-blocker poisoning, digital poisoning, calcium-channel blockers poisoning, ACE inhibitor poisoning, thiazide poisoning and poisoning with other cardiovascular drugs were evaluated on the basis of recorded data. Poisoning with one or several agents, time of admission, type of poisoned agents, sex, age, therapeutic intervention and mortality were investigated.
Results: This study revealed that most of the people poisoned with cardiovascular drugs were females, single people and urban population. Most of the patients were 15-25 years old. Most poisoning was with beta blocker and calcium channel blockers. Their first symptom was headache and most of them needed ICU admission. Most of the patient ECGs were normal. There were 2 cases of death.
Conclusion: This study revealed that continuous health care and the administration of the exact dose of drugs in the appropriate time and also developing of the toxicology centers seem necessary.

Keywords: Cardiovascular Drugs; Iran; Mortality; Poisoning

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INTRODUCTION

Overdoses with cardiovascular drugs are related with significant morbidity and mortality (1). Beta-adrenergic blockers, calcium-channel blockers (CCBs), thiazide, digoxin and angiotensin converting enzyme (ACE) inhibitors represent five of the most important classes of cardiovascular drugs. Overdoses with cardiovascular drugs are typically caused by exploratory ingestion by children or intentional ingestion by suicidal adults. Other reasons for intoxications include medication errors (e.g., double dosing) or adverse effects. Interactions with drugs that affect cardiac conduction, inotropy, or metabolism via the cytochrome P450 enzymes may also produce toxicity (2, 3). The CCB and β-blocker drugs most frequently implicated in fatalities are verapamil and propranolol. Newer agents in both classes have better safety profiles. Any drug may be injurious if the dose is large enough. Determining an exact toxic dose for a given individual is difficult because of the variability in patient-specific factors such as age, genetics, health status, and other recently ingested substances (1, 4, 5).

Poisoning may induce failure in multiple organs and lead to death. Helpful managements and supplementation of failing organs are regularly well-organized. In contrast, the helpfulness of cardiopulmonary bypass in drug-induced shock remains a problem to discuss. There is a requirement for extra aggressive treatment in patients not responding to conventional treatments. The development of new antidotes is limited. In contrast, experimental studies support the hypothesis that cardiopulmonary bypass is life-saving (6). High-dose insulin treatment has occurred as an actual treatment for severe beta-blocker and calcium channel-blocker poisoning (7). Epidemiological studies in toxicology frequently expressed that the pattern of poisonings divides to pharmaceuticals, alcohols, illegal drugs, etc. Specific studies divide pharmaceuticals to dissimilar classes such as

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sedativehypnotic, cardiovascular, anticonvulsant, etc. However, the greatest epidemiological studies do not pay attention to the drugs involved within a specific class. In numerous countries, calcium channel blockers (CCBs) and beta blockers are the most common cardiovascular drugs involved in acute poisonings. The severe problems in overdose with these drugs are well known and labeled in several publications (6, 8, 9). Despite the rising trend of drug abuse in our country, the increasing poisoning statistics in this area have not been adequately studied. This study aimed to investigate the frequency of clinical symptoms due to the toxicity of cardiovascular drugs in patients referred to Razi Hospital Ahvaz (2005-2009).

METHODS

A retrospective review of medical records of patients poisoned with cardiovascular drugs who were treated at Clinical Toxicology Department of Razi Hospital in Ahwaz, Iran during 2005 to 2009 was executed. A total of 70 poisoning cases referred to Razi Hospital in Ahvaz (2005-2009) were identified. These unselected cases included intentional, accidental, criminal and occupational circumstances. Beta-blocker poisoning, digital poisoning, calcium-channel blockers poisoning, ACE inhibitor poisoning, thiazide poisoning and poisoning with other cardiovascular drugs were evaluated on the basis of recorded data. Poisoning with one or several agents, time of admission, type of poisoned agents, sex, age, therapeutic intervention and mortality were investigated. In order to analyze the data and describe the variables descriptive statistics including frequency tables, graphs and numerical measures were used. Then, in order to determine the relationship between qualitative and quantitative variables, t-test and chi-square (x2) were used and significance level of 0.05 was considered. Analysis was performed using SPSS software.

RESULTS

In this study, all the patients poisoned with cardiovascular drugs during 2005-2009 were 70 cases. This retrospective study indicated that the majority of hospitalized poisonings (68.6%) occurred in women. In this study, 44 (62.9%) patients were single and 26 (37.1%) patients were married. 15 (21.4%) patients lived in rural areas and 55 (78.6%) lived in urban areas. 41 (58.6%) patients were aged 15 to 25 years, 22 (31.4%) 25 to 45 years and 7 (10%) of them were above 45 years old. The study showed that 43 (61.4%) cases were taken to hospital less than 6 hours after ingestion, 26 (37.1%) cases between 6 to 24 hours and one (1.5%) over 24 hours. According to the research, 45.7% (32 patients) had beta-blocker poisoning, 10% (7) had digital poisoning, 10% (7) had calcium-channel blockers poisoning, 7.1% (5 patients) had ACE inhibitor poisoning, 4.3% (3) had thiazide poisoning and 22.9% (16 patients) had poisoning with other cardiovascular drugs. In evaluation of the first symptom, the first sign included 22.9% (16) headache, 21.4 % (15) loss of consciousness, 18.6 % (13 patients) nausea and vomiting, 14.3 % (10 patients) seizures and 22.9 % (16) of the cases were presented with other symptoms. According to the survey, 68.6% (48 people) of the patients needed to stay in the ICU and 31.4% (22 people) did not. In this study, 87.1% (61 people) of the patients needed antidote consumption and 12.9% (9 people) did not require the use of antidote. Moreover, the mortality rate due to poisoning was 2.9%. This study showed that in less than 24 hours 10% (7) were admitted to hospital, 62.9% (44) between 24-72 hours, and 27.1% (19) more than 72 hours. The survey showed that 81.4% (57 cases) were poisoning synced and 18.6% (13) did not sync with other medicines. EKG changes have been shown as the following: 27.1% (19 patients) bradycardia, 10% (7) changes in ST, 1.4% (1 person) changes in PR and 61.4% (43) were normal.

On the relationship between age and sex in patients with cardiovascular drugs poisoning: there was a significant relationship between these two variables (P value: 0.03)**.** 48 patients were women (28 patients between 15-25 years, 15 people between 25-45 years and 5 patients were more than 45 years). 22 cases were male (13 patients between 15-25 years, 7 between 25-45 years, and 2 patients were over 45 years). In examining the relationship between age and mortality: between the ages of 15-25 years, two deaths occurred but in patients that aged 15-25 years and more than 45 years there were no deaths. There was no statistically significant relationship between these two variables (P value: 1.45).

On the relationship between age and the type of drug: 32 cases used beta blocker (19 cases were between 15-25 years, 10 patients were between 25-45 years old and 3 cases were more than 45 years). 7 cases used digital (4 cases were between 15-25 years and 3 patients were between 25-45 years old). 7 cases used calcium-channel blockers (5 cases were between 15-25 years and 2 patients were between 25-45 years old). 5 cases used ACE (3 cases were between 15-25 years, 1 patient was between 25-45 years old and 1 case was more than 45 years). 3 cases used thiazide (2 cases were between 25-45 years and 1 case was more than 45 years). 16 cases used other cardiovascular drugs (10 cases were between 15-25 years, 4 patients were between 25-45 years old and 2 cases were more than 45 years). There was no statistically significant relationship between these two variables (P value: 7.5) (Figure 1).

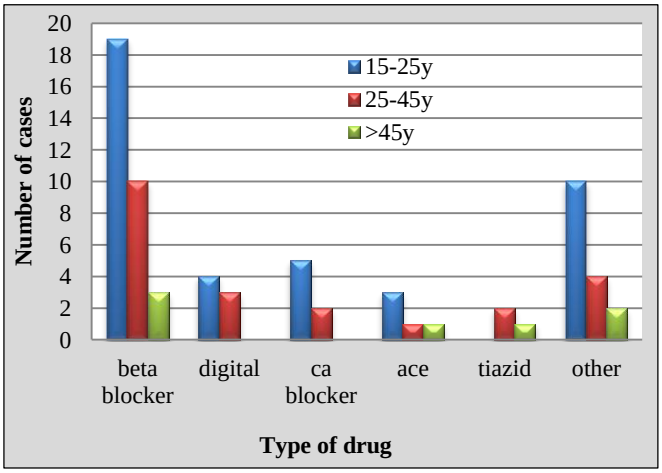

Figure 1. Age and the type of drug in patients with cardiovascular drugs poisoning

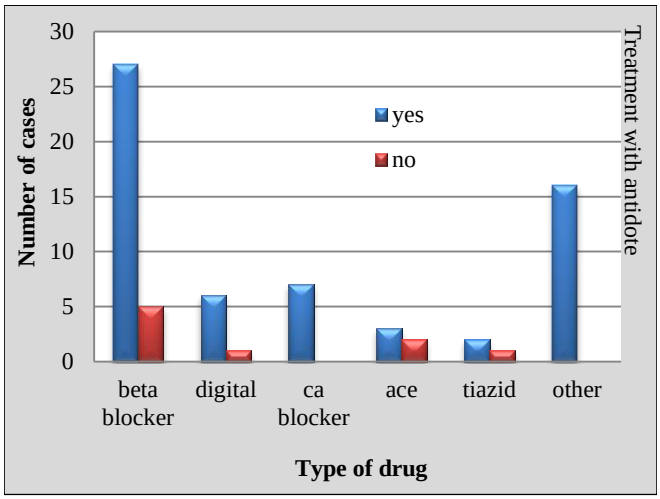

Figure 2. Type of drug and antidote in patients with cardiovascular drugs poisoning

Of the total, 61 (87.1%) patients had not received any antidote, whereas 9 (12.9%) had. There was no statistically significant relationship between these two variables (P value: 8.0) (Figure 2). There was no statistically significant relationship between mortality and time of admission (P value: 4.66). Of the 70 patients admitted, 7 (10%) were monitored for less than 24 hours, 44 (62.9%) for 24-72 hours, and 19 (27.1%) for >72 hours. The proportion of the patients with prolonged hospitalizations (longer than 2 days) was 90% (n=63). Factors influencing the mean duration of hospitalization and prolonged hospital stay were evaluated and there was no statistically significant relationship between these variables. The mean length of hospital stay was longer for beta-blocker poisoning (P value: 0.06) and those who had been admitted 6 hours after poisoning (P value: 4.01).

DISCUSSION

In spite of a rise in admission of cardiovascular drug cases and their poisoning, there are not enough studies about that. Since health planning in each region needs statistics and no study has been carried out about poisoning with this kind of drug in Khuzestan, this study aimed to investigate the frequency of cardiovascular drug poisoning and its clinical features in patients presenting in Razi Hospital of Ahvaz. This study revealed that most of the people poisoned with cardiovascular drugs were 15-25 years old. The total frequency of hospital treated poisoning in rural area of Ahvaz is lower than that of urban population. However, the difference may relate to the decreased referral of rural cases with minimal or no symptoms. Suicidal self-poisoning with beta blocker and calcium channel blockers was more common in single females as reported in other areas. Their first symptom was headache and most of them needed ICU admission. Most of the patient ECGs were normal.

Additionally, Reith DM et al. using different clinical data collected prospectively on a relational database of subjects presenting in hospital with self-poisoning, coroner's data and prescription data have demonstrated that in comparison with the toxicity of beta blockers in overdose and to identify clinical features predictive of serious toxicity main outcome measures were death, seizure, cardiovascular collapse, hypoglycemia, coma and respiratory depression. All patients who developed toxicity did so within six hours of ingestion. The use of ipecac was temporally associated with cardiorespiratory arrest in one patient. Propranolol was the only beta blocker associated with seizure. Of those who ingested more than 2 g of propranolol, two thirds had a seizure. There was a significant association between QRS duration of > 100 ms and risk of seizures. Propranolol was over represented in beta blocker poisoning when prescription data were also examined. Propranolol was the only beta blocker associated with death. Propranolol was taken by a younger age group. Propranolol should be avoided in patients at risk of self-poisoning. Propranolol poisonings should be observed closely for the first six hours after ingestion. Syrup of ipecac should not be used to decontaminate the gastrointestinal tract after beta blocker overdose (10).

Furthermore, in order to characterize beta blocker-related deaths, historical and laboratory data were used to determine those fatalities which resulted primarily from beta blocker intoxication. Love JN et al. results using beta blocker-related exposure data and fatality case abstracts reported to the American Association of Poison Control Centers Toxic Exposure Surveillance System during the 11-year period 1985 to 1995 strongly demonstrate that of 52,156 reported beta blocker exposures, 164 were fatal. In 38 cases, beta blockers were implicated as the primary cause of death. Propranolol was responsible for the greatest number of exposures (44%) and implicated as the cause of death in a disproportionately high percentage of fatalities (71%). Patients were generally young women; 63% were female and 92% were less than 50 years old.

The dysrhythmias, most often noted in fatal cases, were bradycardia and asystole. Cardiopulmonary arrest did not develop until patients were in the care of health care personnel in 59% of cases. Although glucagon was initiated more than any other intervention in fatal intoxications (83%), optimal dosing and maintenance infusions have been underutilized. The predominance of fatalities associated with propranolol compared to other beta blockers reflects both its greater frequency of use over the time period studied and its greater toxicity. Since 59% of the patients developed cardiac arrest after reaching health care personnel, further study should focus on identifying medical intervention that can reduce mortality in this group (11).

Evaluating the pattern of poisoning by cardiovascular drugs during one year in a major industrial city in Russia, Yekaterinburg showed that the most common drugs causing hypotension and cardiac arrhythmias were clonidine, CCBs, drotaverine and the veterinary drug veratrine. Drotaverine, clonidine and CCBs were the most common drugs causing death (12).

Van Asselt DZ et al. in their study that was set up to, on the one hand, find the prevalence and associated mortality of digoxin toxicity in patients admitted to two geriatric wards in London and, on the other hand, study the relationship between

serum digoxin level and age, serum urea, serum potassium and serum calcium in geriatric patients with digoxin toxicity suggest that over a period of three years 1438 patients (aged 75-93) were admitted of whom 452 (31%) were on digoxin (13).

In summary, this study revealed that continuous health care and the administration of the exact dose of drugs in the appropriate time and development of toxicology centers seem necessary.

LIMITATIONS

The diagnosis in the present study was mostly based on patients' history and clinical examination. Because of the short observation time and lack of follow-up on patients who were not transported to a hospital, the evaluation of complications from the pre-hospital phase was limited.

CONCLUSION

It is obvious that Poisonings due to Cardiovascular Drugs is still an important health problem. By public education about probable risks of use, we can reduce the incidence of poisoning by these drugs.

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Conflict and interest: None to be declared.

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