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Evaluation of demographic features of acute drug poisoning with Benzodiazepines; a cross – sectional study

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ABSTRACT

Background: Poisoning is one of the important social problems in developing countries, and acute poisoning due to suicide by drug overdose or toxins is one of the most common cases of poisoning that requires emergency care. This study was aimed to determine the demographics of benzodiazepines poisoned patients in one of the referral centers for poisoning in Iran.

Materials and Methods: This cross-sectional study was conducted on patients who referred to the poisoning emergency ward of Loghman Hakim Hospital from April 2015 to March 2016. Among 10624 patients who referred to the hospital at the study period, 2543 of them were poisoned by benzodiazepines. A total of 263 patients were selected randomly and were assessed for age, gender and the type of the benzodiazepine. The data were analyzed by version 15 of SPSS software.

Results: Among 263 patients, 127 were males (48.2%) and 136 were females (51.7%). The mean age of patients was 31 years old with a range of 13 – 80 years old. In addition, most patients were in the age of between 18 to 35 years (n = 152). In this study, 91 patients (34.6%) were single-drug poisoned with benzodiazepines and 172 cases (65.4%) were poisoned by multi-drug regimens including benzodiazepines. Between different types of benzodiazepines, the most common type was Alprazolam and the least common benzodiazepine was Oxazepam. Almost 96% of patients (n = 252) were treated successfully and 8 patients (3%) got discharged with self-consent. Furthermore, the mortality rate was approximately 1% (n = 3).

Conclusion: Benzodiazepines poisoning is common in younger patients; thus, close attentions are needed for the prescription of these drugs in young patients. Considering easy access to benzodiazepines in the community, periodic visits to psychiatrists may be useful for the reduction of benzodiazepine poisoning.

INTRODUCTION

Poisoning is one of the most important medical emergencies that is responsible for a wide range of problems, from sickness to death [1-4]. Poisonings are responsible for 15 – 20 % of referrals to the emergency rooms which 99% of poisoned cases eventually lead to death in the developing countries [5]. This complication affects all the age groups, but the groups of 15-40 years old are the most affected [6, 7]. Currently, due to the accessibility of drugs and the intentional use of high dosages to suicide, the rate of the drug-induced poisoning has increased [8-11].

Drugs and chemical intoxication is one of the most common causes of poisoning, with around 25,000 cases annually in Tehran, Iran with a mortality rate of 1% [12]. Analgesics, sedatives, common cold and cough drugs in addition to the benzodiazepines are the most common drugs in the drug poisoned patients [13]. Benzodiazepines are sedative-hypnotic agents and Alprazolam, Clonazepam, Lorazepam, Oxazepam and Chlordiazep-

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oxide are some of the famous drugs among benzodiazepines [14]. Benzodiazepines are among the most abundant prescribed medicines in the world, especially in developing countries [15, 16]. Due to their good efficacy, low side effects and high therapeutic index, they are used extensively in anxiety and sleep disorders [17-20]. Benzodiazepines have a great rate of poisoning, which include 2,543 reported cases among 10624 drug poisoning cases recorded in poisoning emergency ward at Loghman Hakim Hospital in Tehran in 2005 whether they were single or multi-drug poisoning including benzodiazepines [21]. In addition, recent studies have shown that benzodiazepine usage and poisoning rate increases with age and is more prevalent among women [22-25].

Regarding the outbreak of poisoning with benzodiazepines, the aim of this study was to determine the prevalence of benzodiazepine poisoning and its related factors at Loghman Hakim Hospital between 2015 and 2016.

MATERIALS and METHODS

Study design

This cross-sectional study was conducted to investigate the demographic characteristics of benzodiazepine poisoning in patients referred to the poisoning emergency center of Loghman Hakim Hospital in Tehran, Iran from April 2015 to March 2016. Considering the prevalence of benzodiazepine poisoning that was based on the data derived from the department of poisoning emergency in Loghman Hakim Hospital in 2013, with a p value of 0.05 and standard deviation of 0.5 and Z score of 90%, using the sample size formula, 263 patients were selected for the study. Sampling was performed randomly from files recorded in the hospital archives. It should be noted that before the questionnaire was prepared, several records were randomly studied and information were extracted from patients' records. Then the questionnaire was designed and edited with the help of this review. Therefore, fortunately, all the files that were selected in a random manner for this study were eligible for inclusion in the study, and since the retrospective study was done through records filed in the archives, no items have been excluded from the study.

Data collection

The data were collected using a questionnaire designed by researchers and through recorded data in hospital archives. Demographic information including age and sex, patterns of drug consumption, time of use, dosage form and dosage of drug(s) consumed, patient history, procedures done by the health services and the patient's status during discharge were considered.

Statistical analysis

The data were entered into the SPSS software for the final analysis. The results were reported as numerical data including the number and the percent of variables.

Ethical consideration

After approval of the subject for the study and its final registration, a permission was obtained from the research committee of the faculty of medicine and the Ethics committee as well and was done in coordination with the deputy chief of the hospital and the chief of the Department of poisoning for starting the study. Considering that this study was a retrospective study and the extraction of information was done by case study, it was strictly prohibited to mention any of the patients' first name, surname or any other data that led to the disclosure of patient information.

RESULTS

In the present study, 263 cases were investigated, including patients poisoned with benzodiazepines single or multi-drug poisoning from April 2015 to March 2016.

Among 263 cases; 136 (51.72%) females and 127 (48.28%) males; the highest prevalence was in the age group of 18-35 years with a frequency of 152 patients (57.8%) and the lowest prevalence was in the age group of 80-60 years with an incidence of 3 patients (1.14%) (Table 1). Also, the minimum age among patients was 13 and the maximum age was 80 years old.

Between the single-drug or multi-drug poisoning cases, 91 cas-

Table-1. Demographic factors in patients poisoned with benzodiazepines.

Type of benzodiazepine		Alprazolam	Diazepam	Lorazepam	Clonazepam	Oxazepam	Chlordiazepoxide
Sex	male	57	33	18	43	20	11
	female	51	35	17	36	5	12
age category	13-18	12	7	1	6	1	6
	18-35	56	35	27	45	4	10
	35-60	29	25	6	27	2	7
	60-80	1	1	1	1	0	0
Drug consumption (number)	minimum	2	2	3	1	10	5
	maximum	100	120	200	160	40	120

es (34.6%) were due to single-drug poisoning with benzodiazepines (one or more types of benzodiazepines) and 172 cases (65.4%) were due to multi-drug poisoning (benzodiazepine poisoning along with other drugs).

In multi-drug poisoning, benzodiazepines were taken mostly with NSAIDs, with 13.7% of patients with multi-drug poisoning taking NSAIDs in addition to benzodiazepines. After NSAIDs, antihypertensive drugs, tramadol, and opioids were in the forefront. Also, the lowest amount of multi-drug poisoning with benzodiazepines was accompanied by antibiotics, alcohol, organophosphorus and stimulants. Furthermore, in multi-drug poisoning, opioid abuse along with benzodiazepines is higher in male patients whereas the abuse of SSRIs with benzodiazepines is higher in female patients.

As shown in Table 1, the prevalence of benzodiazepine poisoning among male and female patients is not significantly different. In addition, evidently, the mean number of the Lorazepam pills consumed by patients who committed suicide was the most prevalent (32.7 tablets) and in the case of Alprazolam, it should be noted that although it is the most common benzodiazepine used in poisoned patients, but the average number of tablets consumed is 21.5.

Approximately 83% of the patients referred to the emergency department have been referred or brought to the emergency in less than 8 hours after the drug abuse; Approximately half of them (105 patients) are referred to the emergency in less than two hours after drug abuse, and the other half (113 patients) are referred to the emergency in between two and eight hours after drug abuse. Also, about 17% of patients are referred to the emergency in 8 hours after drug abuse. The majority of drug poisoning cases referred to the emergency in Loghman Hakim Hospital in 2015 were deliberate poisoning and only 6 (2.3%) out of 263 patients had an inadvertent poisoning. By being over the cases of inadvertent poisoning, the most cases were reported in patients over 36 years of age, 66% of whom were in the age group between 60-80 years.

Regarding to patients' history, 67.7% of patients had no history of previous poisoning, and this was their first referral to the poisoning emergency. 32.3% of patients have had a history of poisoning, but the frequency of the previous poisonings is unclear, and since this is not documented in patients' records, perusal is inconceivable.

Regarding to patient management, the regular treatment regimen for most cases of poisoning in the poisoning emergency department at Loghman Hakim Hospital is the administration of charcoal (50 cc) and Sorbitol (50 cc), which prevents further absorption of the abused drug. Therefore 188 out of 263 (71.5%) patients under study were initially treated with charcoal and Sorbitol.

The prognosis of the studied poisoned patients may be of the most value. Nearly 96% (252 patients) of the patients studied were recovered at the time of discharge and left the hospital in good general condition. 3% (8 patients) also left the hospital consensually before receiving complete treatment. Three patients (1/1%) died, that 2 of whom had taken benzodiazepines following Aluminum phosphide and one of whom had consumed opioids and high TCA dosage levels in addition to benzodiazepine and were referred to the emergency department in a long interval after poisoning.

DISCUSSION

In the present study, the most frequent age group was between (35-18) years-old (58%). The frequency of the patients' gender was almost the same. The most commonly used benzodiazepine was Alprazolam and subsequently Clonazepam, Diazepam, Lorazepam, Chlordiazepoxide, and Oxazepam respectively.

About 35% of the patients had single-drug poisoning and 65% had multi-drug poisoning with benzodiazepines and the most drug used accompanied by benzodiazepines were NSAIDs (13.7%), followed by antihypertensive drugs, tramadol, and opioids. Most likely, the cause of high rates of NSAIDs and antihypertensive consumption following benzodiazepines in multi-drug poisoning is that they are readily available and easily accessible. The consumption of opioids in males was slightly higher than females and SSRIs consumption was significantly higher in females than males. One reason that SSRIs are more commonly used in females is that they are likely to be more cautious about their physical and mental health and may tend to consume SSRIs for their mental disorders like depression.

In the study of the type of poisoning (intentional or inadvertent), nearly 98% of patients had intentional attempt and only 2% had an inadvertent poisoning. It is noteworthy that, although the age group of 60-80 years old is a very small percentage of the total patient population, but 66% of the cases in this group have inadvertent poisoning. Therefore, it may be concluded that at an older age, probably due to loss of memory and accuracy, misuse of another medicine instead of daily taken medicine is possible. However, it is necessary to note that the population of the 60-80 years' age group is small and judgment about this age group may be unfair and inaccurate. Furthermore, although patients in the 18-35 age group account for the highest proportion of patients in this study, none of these groups have been poisoned inadvertently and all of them are in the category of intentional poisoning.

The time interval of referral to the emergency room after poisoning is an important factor in determining their prognosis. In this study, 83% of the patients were referred to the poisoning emergency center within a time interval of less than 8 hours. The sooner the patients come after drug abuse, they have a better prognosis. Although it is likely that the most important factor in determining the prognosis of these patients is the type and amount of the abused drugs.

The most common treatment for poisoned patients was the administration of Charcoal and Sorbitol, prescribed in about 71% of the patients. Also, about 3% of the patients were in need of respiratory and intubation support. Clearly, treatment of all cases of poisoning is not Charcoal and Sorbitol, and even administration of Charcoal and Sorbitol is contraindicated in some cases; For example, in the case of tramadol poisoning, since seizure is one of the most common side effects of tramadol poisoning, administration of charcoal and sorbitol in these patients is inappropriate since the occurrence of seizure episodes is likely at the onset of Charcoal and Sorbitol action and loss of consciousness and also aspiration is possible. Therefore, gastric washing is the preferred treatment in this group of patients.

The latest result in this study was the prognosis of poisoned patients, of which 96% (252 patients) recovered and got discharged in good general conditions. 3% (8 patients) left the hospital consensually and 1.1% (3 people) died. It is interesting to note that in examining of cases belonging to deceased patients, it was found that all the 3 patients had multi-drug poisoning and in fact, no cases of single-drug poisoning with benzodiazepines had died.

In a descriptive cross-sectional study; done by Heidari et al; 280 cases of deliberate poisoning were recorded, of which 93.93% were females. Most cases of poisoning were reported at the age in between 11-30, with an average age of 23.98. In 66.1% of cases, poisoning occurred due to drug abuse, most of which were benzodiazepines [26]. In the present study, female patients also had a slightly higher proportion of poisoning. In addition, in both studied groups; adults and young age groups (18-35 years and 11-30 years old respectively) are the most common cases of poisoning. This matter requires special attention to this age group and designing programs to prevent such cases. It is concluded that Benzodiazepines are the most commonly used drugs in poisoning in both studies.

In a study conducted by Mohamadi et al., among the 3789 cases of poisoning, 69.5% were males and 30.5% were females. The majority of cases belonged to the age group of 21-30 years (37.3%). Most cases of intentional poisoning were due to drug poisoning, especially with benzodiazepines, and the most frequent cases of inadvertent poisoning were due to substance abuse [27]. As you can see, in this study, teenagers and young adults have the largest share in poisoning, and benzodiazepines are the most commonly used drugs. Therefor the results are similar to our study.

In another study, out of 723 cases of drug poisoning, 76% of cases were intentional poisoning, more than 31% of which were caused by benzodiazepines hence they also had the highest rates of poisoning in this study [28].

CONCLUSION

As a conclusion, intentional drug toxicity is the most common form of poisoning, and benzodiazepines are the most commonly abused drugs. Teenagers and young adults make the most cases of poisoning, which highlights the importance of special attention to this age group at risk.

Limitation of study

Due to the incompleteness of the information recorded in the data, it was impossible to design a thorough questionnaire. Information such as marital status, educational level, history of physical illnesses and current taken medications are not routinely recorded in most cases. So it was impossible to check them thoroughly. Additionally, in many cases, the amounts of consumed drugs were not accurately reported and, if they were, the number of medications and the dosage of drugs were not reported accurately. Therefore, in this study, as the data were collected, the number of medications consumed in each case was determined as the amount of the drug taken.

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CONFLICT of INTREST

There are no conflicts of interest.

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