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Investigating the Pattern of Benzodiazepine Poisoning in Gorgan, 2008-2014

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ABSTRACT

Background and objectives: Benzodiazepine poisoning is one of the most important and common medical emergencies worldwide. The purpose of this study was to evaluate the pattern of poisoning with benzodiazepines in Gorgan, Iran.

Methods: This cross-sectional and descriptive-analytical study was conducted on patients with acute benzodiazepine poisoning admitted to 5th Azar Hospital in Gorgan between 2008 and 2014. Data were collected from medical records of patients. Statistical analysis was performed using SPSS software (version 16).

Results: Benzodiazepine poisoning accounted for 37.2% of all drug poisoning cases. Of the 230 cases of benzodiazepine poisoning, 108 (50.7%) were female, and most cases (53.5%) belonged to the 20-29 years age group. Suicide attempt was the predominant (91.1%) type of benzodiazepine poisoning. Among the benzodiazepines, alprazolam (33.3%) and diazepam (30.5%) were the chief causes of drug poisoning. In addition, in 7.5% of the subjects, benzodiazepines were taken in combination with other drugs, especially tramadol (19.2%). Age, marital status, employment status, education level and place of residence were significantly associated with benzodiazepine poisoning ($P<0.001$).

Conclusion: Benzodiazepines, particularly alprazolam and diazepam, are responsible for more than one-third of all drug poisoning incidents in Gorgan. Self-poisoning with this group of drugs as an attempt to commit suicide is most prevalent among young individuals.

KEYWORDS: Suicide, Poisoning, Benzodiazepines, Gorgan, Iran

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INTRODUCTION

Benzodiazepines are one of the most commonly used sedative-hypnotics, which are widely used for treatment of anxiety, sleep disorders, alcohol withdrawal syndrome and epilepsy. These drugs entered the pharmaceutical market in the 1960s and are currently available in forms of tablet, ampoule, etc. (1, 2). Today, drug poisoning, particularly with benzodiazepines, is one of the most important health challenges worldwide. In some developed countries, including Norway, benzodiazepines are among the most important causes of drug poisoning. Studies in different parts of Iran including Tehran, Mashhad, Sari and Gilan Province have shown that benzodiazepines rank first among causes of drug poisoning (3-5).

Drug abuse is a principal aspect of benzodiazepine poisoning. Incidents of drug dependence and tolerance resulting from long-term use of benzodiazepines were first reported in the 1970s. In 2012, it was suggested that benzodiazepine withdrawal syndrome is more severe than the initial symptoms of the patient, and therefore, it is recommended not to use these drugs for treatment of easy-to-treat conditions. In spite of this recommendation and other limitations imposed in different countries, the trend of benzodiazepine misuse is increasing in many countries, including Iran (3-6). Numerous studies in Iran, Turkey and India has reported the significant association of benzodiazepines use and suicide attempts. In this regard, easy access, low prices and familiarity of people with these drugs can be considered as the chief factors involved in benzodiazepines frequent use (5-7). Therefore, considering the high frequency of benzodiazepines use in the community and the importance of this group of drugs in terms of abuse and suicide attempts (3, 7), the present study was conducted to investigate the pattern of benzodiazepines poisoning in Gorgan, North of Iran.

MATERIALS AND METHODS

This cross-sectional, descriptive-analytical study was done to determine the frequency, demographic characteristics and clinical symptoms of acute benzodiazepine poisoning patients admitted to the 5th Azar Hospital of Gorgan between 2008 and 2014. The subjects were selected based on their medical record, and outpatients and those with an incomplete medical record were excluded from the study. After obtaining ethical approval (code: 14791793061931) for the study, data of relevant variables were collected through a checklist within four months. The checklist consisted of 21 questions including six questions on demographic information and 15 questions on conditions and consequences of poisoning. The data were analyzed by Microsoft Excel and SPSS (version 16) using the chi-square test. A P-value of less than 0.05 was considered statistically significant.

RESULTS

Overall, 573 cases of drug poisoning had been admitted to the 5th Azar Hospital of Gorgan during 2008-2014. Among them, 213 cases (37.2%) admitted with benzodiazepines poisoning (37.2%). The mean age of these patients was 26.17 ± 15.52 years (range: 12-79 years). The majority of patients were single, employed females (age range of 20-29 years), living in urban areas (Table 1).

Table 1. Demographic information of the patients admitted with drug poisoning

Variable		Number	Percent	P-value
Gender	Male	105	49.3	P=0.63
	Female	108	50.7	
Age (years)	Less than 20	50	23.5	P<0.001
	20-29	114	53.5	
	30-59	46	21.6	

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	60 and above	3	1.4	
Marital status	Single	113	53.1	P<0.001
	Married	95	44.6	
	Widowed/divorced	5	2.3	
Employment status	Unemployed	57	26.8	P<0.001
	Employed	73	34.3	
	Housekeeper	53	24.9	
	Student	30	14.1	
Education level	Illiterate/primary school	18	8.5	P<0.001
	Middle school	49	23	
	High school	132	62	
	University degree	14	6.6	
Place of residence	Urban	169	79.3	P<0.001
	Rural	44	20.7	

As shown in table 2, most cases of poisoning occurred in the summer (28.6%) and at home (74.2%). In most cases, the drug was taken orally (99.1%) and as a suicidal attempt (91.1%). In 88 cases (41.3%), the subjects only used benzodiazepines, while the rest of the patients (58.7%) also taken other drugs including tramadol (24 cases), cardiac medications (23 cases) and antidepressants (22 cases). Moreover, the most commonly used drugs were alprazolam (33.3%), diazepam (30.5%) and clonazepam (26.8%) (Figure 1).

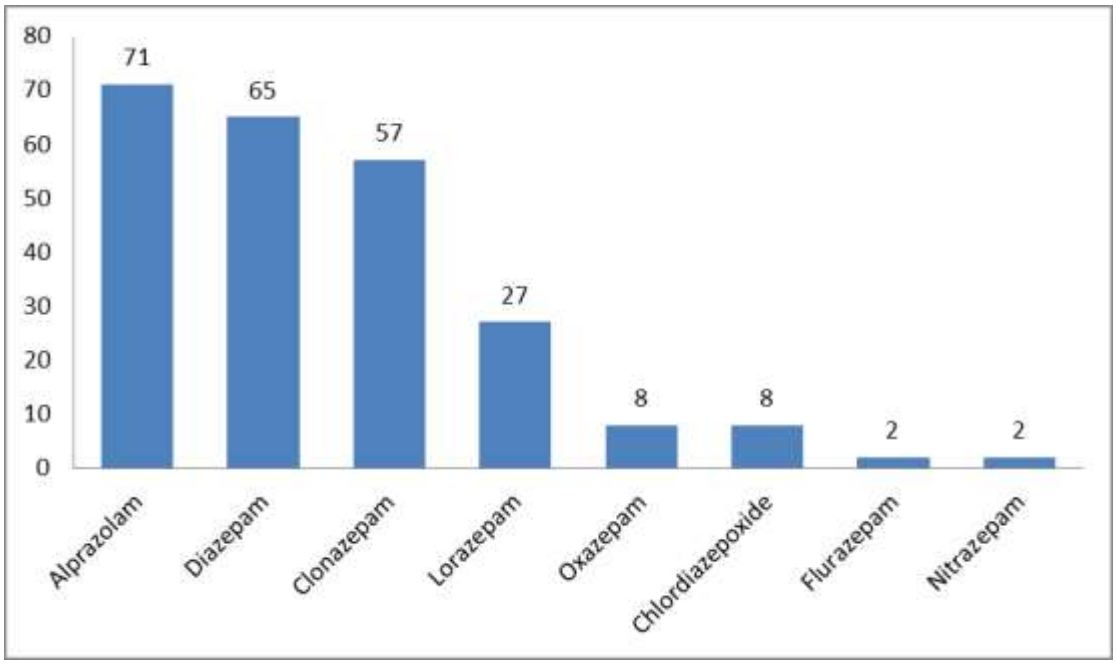

Figure 1. Frequency of benzodiazepine poisoning in the patients admitted to the 5th Azar Hospital

The hospital admission rates were highest in the afternoon and at night (67.6%). The clinical symptoms at time of admission included neurological symptoms (90.1%), gastrointestinal symptoms (19.7%) and psychological symptoms (8%). The majority of patients (44.1%) were hospitalized for 24 to 72 hours, and 21 cases had a Glasgow Coma Scale (GCS) score of 8 or less. In addition, 97 cases (45.5%) required hospitalization in the intensive care unit. Methods used for the treatment of patients

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included oral administration of activated charcoal-sorbitol suspension (162 cases), gastric lavage (135 cases) and antidote administration (25 cases). Eventually, 212 patients (99.5%) were treated and only one case (admitted because of benzodiazepines-antidepressants combination) died of respiratory complications (Table 2).

Table 2: Frequency of the variables related to drug poisoning among patients admitted to the 5th Azar Hospital

Variable		Frequency	Percent	P-value
Season	Spring	55	25.8	P=0.057
	Summer	61	28.6	
	Autumn	54	25.4	
	Winter	43	20.2	
Type of poisoning	Suicide	194	91.1	P<0.001
	Overdose	11	5.2	
	Misuse	8	3.8	
Administration route	Oral	211	99.1	P<0.001
	Injection	2	0.9	
Location of poisoning	Home	158	74.2	P<0.001
	Others	55	25.8	
Time of admission	6-12	31	14.6	P<0.001
	12-18	73	34.3	
	18-24	71	33.3	
	24-6	38	17.8	
Duration of hospitalization	Less than 24 hours	44	20.7	P<0.001
	24-72 hours	94	44.1	
	More than 72 hours	75	35.2	
Time from drug use to hospital admission	Less than an hour	17	8	P<0.001
	1-3 hours	87	40.8	
	More than 3 hours	91	42.7	
	Unknown	18	8.5	
GCS score	8 or less	21	9.9	P<0.001
	More than 8	192	90.1	
Hospitalization in the intensive care unit	No	97	45.5	P<0.001
	Yes	116	54.5	
Consequence of poisoning	Treated	212	99.5	P<0.001
	Death	1	0.5	

DISCUSSION

In the present study, benzodiazepines were the most common cause of drug poisoning. This result is similar to the findings of studies conducted in Tehran, Tabriz and Norway (3). In a study in Kentucky (USA), benzodiazepines were responsible for 30% of all drug poisoning incidents (8). Contrary to these findings, studies conducted in Turkey, Malaysia and Oman claimed that acetaminophen and antidepressants are the main cause of drug poisoning (3). The difference in the pattern of drug poisoning in different societies could be due to socioeconomic and cultural reasons (3, 5).

Similar to numerous previous studies, we found that benzodiazepine poisoning was more common in women. In this regard, some researchers claim that physical and emotional vulnerability as well as psychosocial stress, probably due to social and cultural limitations of some societies, contribute to this issue (3, 7). Therefore, it is necessary to limit access to these drugs without prescription. In a study in Khorasan (Iran), only 45% of the subjects who were taking benzodiazepines had a

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doctor's prescription, and 29% continued taking the medication without doctor's consultation. The remaining 26% started to take medication without prescription. Given the teratogenicity of benzodiazepines during pregnancy, the uncontrolled access of women of reproductive age to these compounds can also increase the burden of poisoning with these drugs (6).

In the present study, drug poisoning was more prevalent in single individuals and in summer. Considering that most poisonings were suicide attempts, marriage might be a protective factor against suicide. In this regard, Durkheim believed that married individuals are less likely to commit suicide. Durkheim also found that drug poisoning is more common in warm months of the year due to increased social relations between individuals and the subsequent increase in psychological pressure on those with poor communication skills (9). According to the World Health Organization, nearly 73% of male and 84% of female suicide attempts are due to drug overdoses (10). Other studies in Iran, India and Turkey also confirm that benzodiazepines are the most commonly used drugs for drug-induced suicide (7, 11).

The highest rate of benzodiazepine poisoning was among those with high school education, which is in line with results of a study in Mashhad (6). Our results are also somewhat consistent with the Kaplan's theory, which states that the higher the level of education in a society, the greater the odds of committing suicide (12).

In line with some other studies (13, 14), benzodiazepines poisoning was more prevalent in individuals aged 20 to 29 years, which is not surprising, since some studies has determined suicide as the third leading cause of death in people aged 21 to 30 years (15).

Among benzodiazepines, alprazolam was the most common cause of poisoning, followed by diazepam. In a study in Mashhad (Iran), diazepam and chlordiazepoxide were determined as the most common cause of drug poisoning (6). In a study in Macedonia, diazepam and bromazepam were the first and the second most frequent cause of drug poisoning, respectively (16). Social and cultural factors as well as the level of access to medications may have a determining role in the drug consumption patterns (17). In the present study, tramadol was mostly taken along with benzodiazepines. Previous studies have shown that taking benzodiazepines with a low dose of tramadol can increase the risk of drug poisoning (18, 19).

One of the limitations of this study was the retrospective design of the study and the inability to directly collect information from the subjects. The results of this study can provide a useful background for more detailed future studies and health planning and policy making. Furthermore, it is important to raise public awareness, especially in high-risk individuals, and develop preventive programs to limit access to these medications without prescription.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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