Analysis of Intoxication Deaths: Causes and Manners of Death

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Akhgari, *et al.*: Causes and Manners of Intoxication Deaths

The aim of the present study was to provide an overview of deaths caused by drug poisoning or intoxication with other substances in Qom province, Iran from 2008 to 2012. The data on poisoning deaths were collected from the autopsy reports and defined cause of death in death certificates. Death profiles and demographic characteristics were analysed. Intoxication death cases were recorded 388 subjects during the five year study period, of which 264 cases (68 %) were male. Results showed that the rate of intoxication deaths was 93 cases per one million populations in 2008, decreasing to 49 cases in 2010 and then increasing to 69 cases in 2012. Opium alkaloids caused the highest mortality rate in male and female cases. Tramadol and tricyclic antidepressants were the second cause of death in males and females, respectively. The majority of cases were in the age range of 21-30 years. Accidental poisoning with opioids was the most reported manner of death. Death cause analysis revealed that opioids contributed to death in the majority of cases. The findings of the present study highlight the importance of regulatory controls on clandestine illicit opioid production, distribution and abuse by heath care authorities.

Key words: Intoxication deaths, toxicity, opioid abuse, forensic toxicology

Drug poisoning related deaths are considered as deaths in which at least one drug or poison is detected in postmortem samples and attributed to death. Drug could be a causative agent and poisoning with that drug a contributory factor leading to death[1]. Type of drug used, health status, licit and illicit drug availability and geographic position are factors affecting the pattern of poisoning. Therefore, epidemiologic studies can help to define intoxication deaths and its pattern[2]. Various approaches and studies are available for estimating intoxication deaths.

United Nations Office on Drugs and Crime (UNODC) estimated that 264 million people (one out of twenty) aged 15-64 y had used one illicit drug in 2013. In this report it was indicated that 187/100 deaths were related to drug use[3]. According to the investigation of European Drug Markets Report in 2016, some countries that use protocols and practices of substitution treatment, face drug related deaths too[4]. Social Affairs Bureau damage of Ministry of Cooperative, Labour and Social Affairs of Iran reported changes in the pattern of drug abuse. There was a 28 % increase in the

seizure of clandestine methamphetamine laboratories from 2005 to 2013[5]. United Nations reported that Iran ranked fifth behind Mexico, United States, China and Thailand in methamphetamine seizure between 2010-2012[6,7]. Drug related deaths were investigated by American and European researchers[8,9]. Iranian Legal Medicine Organization documented that 551, 627, 599 and 747 cases of drug poisoning related deaths were investigated during 2010-2013[10].

There are informal reports that drug related deaths have surged in some provinces in Iran. Assessment and documenting drug related deaths is of crucial importance in every province in Iran. To accomplish this goal all assumed death poisoning cases in Qom province, Iran are subjected to forensic autopsy and forensic toxicology investigation to establish the

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manner and cause of death. The aim of the present analytical study was to assess intoxication deaths referred to Legal Medicine Organization, Qom province, Iran during a 5 y period. Yearly patterns of intoxication deaths, demographic characteristics (age, gender) and the correlation between drug use and death would be analysed.

MATERIALS AND METHODS

A retrospective analytical survey was conducted on drug poisoning related deaths referred to Legal Medicine Organization, Qom province, Iran from March 2008 to February 2012. Cases were considered when their underlying cause of death was intoxication with drugs or poisons. The protocol to undertake the present study has been approved by the Ethics Committee of Legal Medicine Organization, Qom, Iran. All information about human individuals was fully confidential and all private information including name, surname and burial permit was removed from datasheets. Natural deaths and deaths with causes other than poisoning were excluded from the study. Forensic toxicology and pathology results, autopsy findings, medical history or criminal records were all required and important factors to determine and confirm the cause of death. All of the overdose cases were investigated from forensic toxicology point of view. Moreover forensic pathology investigation of heart, liver and brain were performed for the determination the cause of death in combination with forensic toxicology analyses results. Census method was used for data collection. Necessary data were extracted from death certificates by trained staff under the supervision of forensic medicine specialist and toxicologist.

It should be noted that the below procedure was validated in the laboratory for the analysis of drugs and poisons in biological matrices obtained from intoxication cases. Biological samples of each suspicious case were analysed in a forensic toxicology laboratory.

Liquid-liquid extraction was carried out on urine, liver, stomach content and bile samples with chloroform and isopropanol (80:20). Extracts were reconstituted in minimum amount of methanol and analysed using thin layer chromatography as screening and the more specific high performance liquid chromatography and gas chromatography/mass spectrometry as confirmatory methods. Carboxyhemoglobin was analysed using spectrophotometry. For quantitative determination of ethanol and methanol in blood and vitreous humor samples, headspace gas chromatography equipped with a flame ionization detector was used. Cyanide was detected in samples using Prussian blue and voltammetry/polarography methods.

Data were analysed in SPSS software (version 13.0, SPSS Inc., Chicago, IL) using percentage for categorical variables and mean and standard deviation (SD) for continues variables. Before each analysis, test variables were checked for normality, so all data were evaluated by the Kolmogorov-Smirnov test to follow a posterior parametric or non-parametric statistical analysis. Chi-square test was used to analyse categorical variables. P values of <0.05 were considered statistically significant. Intoxication death rates were calculated by dividing the number of deaths due to intoxication by the population of Qom province, Iran in March 2008 to February 2012, and were presented per one million of population.

RESULTS AND DISCUSSION

In the present study all intoxication death cases in Qom province, Iran were investigated from 2008-2012. During the five year study period 4085 cases were referred to Legal Medicine Organization, Qom, Iran, from which 388 cases (8.7 %) were related to intoxication deaths. The majority of drug poisoning related deaths were attributed to opium abuse and its side effects (314 cases, 80.93 %). The incidence rate of intoxication deaths per one million of Qom population in 5 y study is shown in fig. 1. The incidence rate of intoxication deaths showed significant decline in the year 2010 in comparison to the year 2008 (p<0.05). This incidence rate rose significantly in 2011 and 2012 in comparison to 2010 (p<0.05). Tramadol, methadone, tricyclic antidepressants, lidocaine, pethidine and propranolol poisoning accounted for 6, 3, 7, 1, 1 and 1 cases, respectively in the 5 y study. It should be stated that in 2010, the cause of death of 3 cases was mixed poisoning with opium alkaloids, methadone and tramadol. Fig. 2 shows drugs and poisons categories that induced death. The most common cause of death was opium toxicity followed by tramadol and amitriptyline in male and female subjects, respectively. Carbon monoxide (CO) poisoning was the cause of death of 30 cases that is equal to 5.62 per one million of Qom population in the five year study. About 95 % of CO poisoning cases were attributed to the incomplete combustion of carbon fuels of heaters and car exhausts in inadequately ventilated places. Of the total drug poisoning related deaths, 68 % were males (n=264)
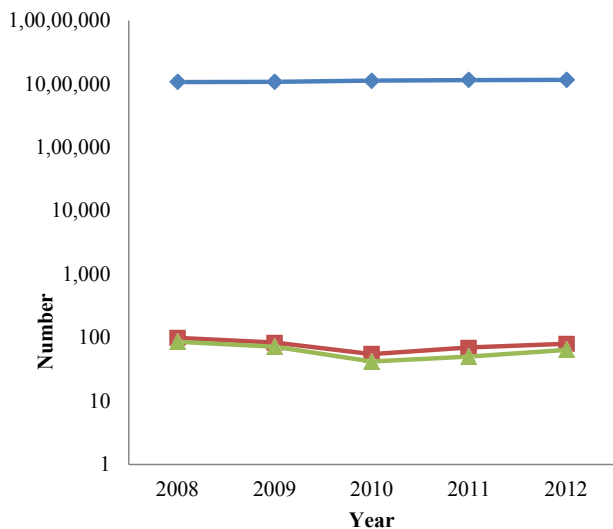
Fig. 1: Incidence of all intoxication and opioid poisoning-related deaths in Qom province
Incidence rate of all intoxication and opioid poisoning-related deaths in Qom province, Iran during 2008-2012. Yearly Qom province population (—◆—), number of intoxication deaths (—■—) and number of opioid poisoning deaths (—▲—)
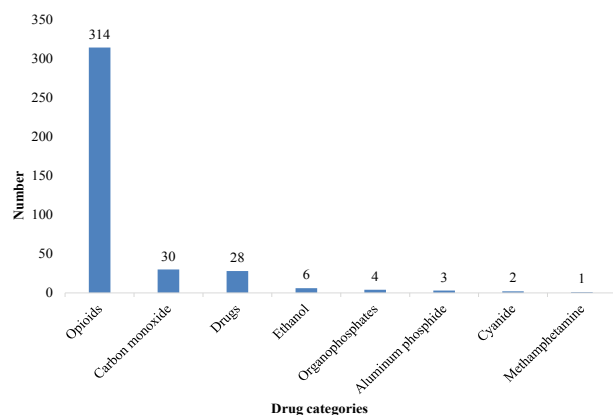

Fig. 2: Drugs and poisons categories that induced death
Drugs and poison categories of substances that induced death in Qom province, Iran during 2008-2012

and 32 % were females (n=124). Therefore males significantly outnumbered their female counterparts (p<0.05). A separate analysis examining intoxication deaths showed that intoxication deaths were most common in younger people (age range 21-30) compared to older population (OR= 2.321, CI= 2.38–4.36). The odds of intoxication deaths were significantly higher in male subjects in comparison to females (OR= 1.98, CI= 2.1–3.27).

Among six age groups, the maximum numbers of cases were observed in the 21-30 y age group (fig. 3). The number of young age group was significantly higher than other groups (p<0.05). The mean age±SD of cases was 25.64±10.38 y. When age plotted against gender, there was no significant difference between age of men

(26.5±12.1 y) and women (23.5±7.6 y). As it is shown in fig. 4, self-poisoning (suicide) with opium alkaloids was the common manner of death (64 %) followed by accidental poisoning (17 %). Oral route was the most common route of exposure to drugs and poisons (70.6 %) followed by inhalation (22.7 %) and injection (6.7 %). Fig. 5 shows the employment status of cases. Intoxication deaths were more prevalent in non-governmental employees (46 %). This was significant (p<0.05) in comparison to other groups. No significant difference was observed between single and married cases. However single cases had a significant lower suicide rate in comparison to married ones (p<0.05). The majority of deaths were referred from home (35 %) and then hospital (32 %). A large proportion of intoxication deaths were reported during summer season (35 %). In the present study 95 % of cases were illiterate, or educated up to primary school and high school.

The purpose of the present study was to analyse intoxication deaths in Qom province, Iran in a five year study period. The results indicated that the majority of deaths were ascribed to opioid poisoning. This is possibly due to several factors such as poly substance abuse, use of impure street level opium, mass production
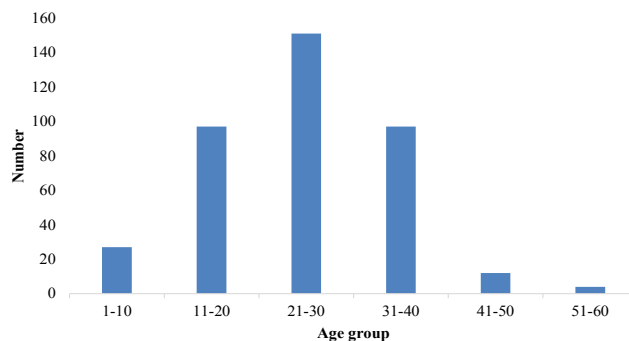
Fig. 3: Age groups of intoxication death cases
Age groups of intoxication death cases in Qom province, Iran during 2008-2012
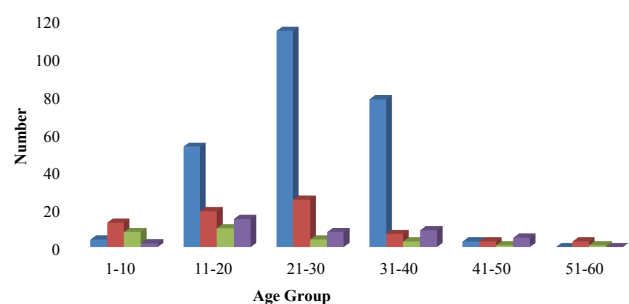
Fig. 4: Manner of intoxication deaths
Manner in which deaths by intoxication occurred in Qom province, Iran during 2008-2012. ■ Suicidal poisoning; ■ accidental poisoning; ■ medical; ■ undetermined
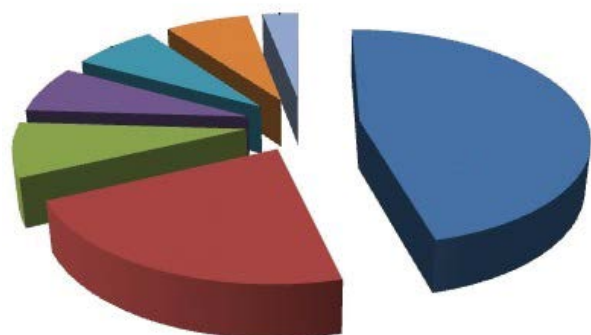
Fig. 5: Employment status of persons died of intoxication
Employment status of the persons died of intoxication deaths in Qom province, Iran during 2008-2012. ■ Non-governmental employee (46 %); ■ house wives (22 %); ■ employees (8 %); ■ unemployed (7 %); ■ students (7 %); ■ children (7%); ■ soldiers (3 %)

and smuggling of opium by Afghanistan (Iran's neighbour to the east) and many other factors[11-14]. According to the UNODC report in 2010, the largest numbers of illicit drug users in the world are cannabis users. Amphetamine type stimulants (ATS) rank second followed by cocaine and opiates[15]. Although the tendency for crystal amphetamine is increasing in Iran, opium is the most common abused drug in this country[16]. Our results provide more evidence for the other records. Official statistics from Legal Medicine Organization, Iran announced that opioid poisoning related death rate was 68 cases per one million of population (857 cases) in Tehran, Iran in 2014[10]. Per capita use of drugs in Iran is three times above global standard and Iran is among the 20 countries of the world in drug use. Iran ranks second after China in terms of drug use in Asia[17]. The difference in the pattern of drug use in different provinces of Iran was shown in previous studies[18]. Results are similar to those found in other surveys. The cause of death of three cases was attributed to concomitant use of tramadol, methadone and opium as poly substance abuse. Poly substance abuse is an attempt to reach euphoria and can result in poisoning and death[19]. Prescription opioids obtained from legitimate pharmacy channels, diverted or nonmedical sources are contributing factors to drug poisoning related deaths[20,21]. Tramadol was first introduced to Iranian pharmaceutical market as oral and injectable forms in 2002[22]. Secretory for Food and Drug Affairs, Ministry of Health and Medical Education, Iran reported that the use of tramadol increased about 5.2 fold from 2006-2007[23]. For its high potential for abuse, tramadol was classified as a controlled drug in Iran since 2007[24]. Also methadone

maintenance therapy for opioid addiction was first used in Iran in 2001[25]. Whereas methadone has been used for opioid addicts as maintenance protocol in some ropean countries such as Italy since 1980[11]. Drug abusers use tramadol, methadone and other opioids with each other[26-28]. Deaths due to prescription opioids (methadone and tramadol) were reported by previous studies too[21,29,30]. Since the ascent in the popularity and demand for abused substances among drug adults, drug dealers adulterate illicit drugs with pharmaceutical and inert substances in order to increase weight of final product. Occasional or regular use of adulterated illicit drugs have some health consequences related to active ingredients or adulterants[12,13,31,32].

Methamphetamine poisoning was the cause of death of one case in the present study. One explanation for the high prevalence of opioid poisoning related deaths compared to ATS is that the tendency for natural opioids such as crude opium is more than synthetic psychoactive drugs. This result is in agreement with the National Center for Health Statistics report, demonstrating that nearly 40 % of opioid related deaths were deemed to be related to the natural and semisynthetic opioids[33]. Iranian common border with Afghanistan have aroused a great dilemma of opium abuse for Iran. Although in recent years methamphetamine is a crucial issue[14].

A total of 30 accidental deaths due to CO poisoning were reported in 5 y period of investigation in Qom province, Iran. The results are in agreement with those of previous studies[34-37]. The average annual of CO poisoning related deaths was 5.62 per one million of Qom population in the present study. This reporting death rate was significantly higher than the studies in China and Portugal[36,37]. However our results were significantly lower compared to the results published by WHO European Member States[38]. These differences may be due to the fact that the average air temperature is not the same in all regions of the world. The difference in heating appliances systems, types of fuel used, use of clean and solar energy technology are important factors that explain the difference in obtained results[36-39].

Five cases of intentional organophosphate poisoning were reported during five year study. Human exposure to pesticides especially organophosphorus compounds is a global health challenge particularly in developing countries[40-44]. Amount of pesticide production in each area, variation in agricultural products and pesticides accessibility are factors affecting pesticide poisoning[45].

Although ethanol poisoning is the major cause of death in Eastern European countries[46], ethanol poisoning contributed to only six deaths in the present study. Suicide with ethanol and other drugs were reported in previous studies[47-52]. However all alcohol poisoning related deaths in the present study were related to accidental poisoning as a result of binge drinking, which is of course related to the availability of cheap alcohol drinks. Cultural and religious beliefs have impressive effects on person's attitude towards alcohol use. That is why that the rate of alcohol related deaths has lower rate in Qom province in comparison to other studies.

There are many reports regarding the involvement of specific drug types in accidental and intentional poisoning[53-55]. Suicide is one of the most common causes of death in individuals suffering psychiatric disorders[50-52,56]. In the present study the underlying cause of death in all cases was drug or other toxic agents poisoning. In agreement with the results of the present study opioid poisoning was the predominant cause of death in Nordic countries in 2012[28]. Yet the most important cause of drug related deaths in France was benzodiazepines overdose[57].

Intoxication deaths were notably prevalent in young population. This finding was confirmed by previous studies[9,50,58,59]. In line with the results of the present study, Kordrostami *et al.* in their study on deliberate self-poisoning in Tehran, Iran demonstrated the predominance of young male population in these deaths[59]. In consistent with the results of the present study some other studies reported that there was no significant difference in drug related deaths between single and married cases[58]. Men showed higher rates of drug poisoning related deaths than do women, which has also been observed in the previous studies[52]. But our findings do not support those of Reydel *et al.* study, in that, they found that drug poisoning related deaths were more likely to occur in females[57]. The majority of cases were non-governmental employees. As random workplace drug testing are performed by governmental organizations for assuring accuracy and monitoring employees' performance, therefore drug related deaths would be lower in governmental employees. It should be taken into account that subjects have difference with regard to demographic parameters such as age, sex, employment status, marriage status, religious beliefs, salary and economic variables. These differences are important to investigate when considering tendency to illicit substances, commit suicide and other antisocial behaviours[50,58].

Many drug exposures occurred at home. This is possibly due to several factors such as self-medication at first, free access to all kinds of drugs in most homes and direct selling without prescription from a healthcare professional. Also the geographical location of Iran, has turned it into one of the major transit countries for opioids and consequently their high abuse rate[3,6].

Opioids abuse and its associated harm have resulted in a huge burden on public health. The demographic characteristics regarding substance abuse in Iran point to trend of younger population. Therefore a national system of management and intervention for opioid access restriction needs to be established in Iran.

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Conflict of interest:

There are no conflicts of interest.

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