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Systematic Review

Ranking the acute poisoning etiologies in Iran: A systematic review and meta-analysis

Saeedeh Derhami[1], Ehsan Bolvardi[2], Reza Akhavan[2], Mahdi Foroughian[2], Behzad Shahi[3], Arman Hakemi[1], Zhila Rahmanian[4], Samaneh Abiri[5*]

[1]Department of Emergency Medicine, Mashhad University of Medical sciences, Mashhad, Iran
[2]Department of Emergency Medicine, Faculty of Medicine, Mashhad University of Medical sciences, Mashhad, Iran
[3]Department of Emergency Medicine, Faculty of Medicine, Zahedan University of Medical sciences, Zahedan, Iran
[4]Department of Internal Medicine, Jahrom University of Medical sciences, Jahrom, Iran
[5]Department of Emergency Medicine, Jahrom University of Medical Sciences, Jahrom, Iran

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***Corresponding author:**
Samaneh Abiri; Department of Emergency Medicine, Jahrom University of Medical sciences, Jahrom, Iran.
Email: Samaneh.abiri@gmail.com

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Abstract

Objective: Acute poisoning is a major health problem and one of the most common causes of emergency visits worldwide. Since most poisoning subjects present with a decreased level of consciousness and due to unreliable disease history, recognizing the etiological cause of the poisoning represents a critical part in arranging the treatment strategy. This study aimed at examining the prevalence of etiological causes of poisoning in Iran in a systematic review and meta-analysis.

Method: This systematic review and meta-analysis investigated the cross-sectional studies published from 1990 to 2020, reporting specific poisoning agents among acute poisoning cases in Iran. Persian and English articles on this subject were collected by searching the Scientific Information Database (SID), ScienceDirect, PubMed, Medlib, IranMedex, Scopus, Magiran, and Google Scholar databases. The heterogeneity of the studies was investigated using the I2 index and the probability of bias in the publication was assessed by the Begg and Mazumdar test with a significance level of 0.1. Data analysis was performed by Comprehensive Meta-analysis software version 3 (Biostat, Englewood, NJ, USA).

Results: In our review, 19 studies appraising 143,251 cases of poisoning were included. The ranking of the OR of each agent was done; Opium poisoning was the most prevalent poisoning case followed by benzodiazepine, acetaminophen, antipsychotic medications, organophosphates, aluminum phosphide, amphetamine, pesticide, tricyclic antidepressant (TCA), alcohol, chemicals, carbon monoxide (CO), nonsteroidal anti-inflammatory drugs (NSAIDs), and selective serotonin reuptake inhibitors (SSRIs).

Conclusion: While proper judgment on the cause of poisoning and selection of suitable treatment manners could be followed by a very good prognosis in patients with acute poisoning; this demands an epidemiological perception of the prevalence of the etiological poisoning agents. Our study ranked the most likely agents leading to the poisoning, to be at the top of the list of differential diagnoses of physicians.

Keywords: Acute poisoning, Iran, Meta-analysis

Introduction

Decreased level of consciousness can be an acute and potentially life-threatening state that necessitates prompt management to sustain life and restore normal brain functions (1). One of the most important skills that emergency physicians should have is how to manage patients with an altered level of consciousness (ALC) (2). Having a clear diagnostic and treatment algorithm in the face of these patients is vital to save their lives (3,4). The non-traumatic decreased level of consciousness is an important emergency due to the high mortality rate if not properly managed (5). Decreased levels of consciousness can be started with drowsiness or get progressed to stupor (severe drowsiness) or coma. In a coma, the patient is unable to communicate verbally so there would not be a reliable history of the disease. Data on the prevalence of common causes of ALC in each region can help diagnose the etiology of the disease (6). The etiology of decreased level of consciousness plays an important role in predicting the prognosis (7). Poisoning is one of the most serious etiologies to reduce the level of consciousness. Also, unknown drug toxicities may contribute to a decreased level of consciousness with an urgent need for early diagnosis, treatment, and special care. In examining the causes of decreased consciousness and coma, major etiologies include poisoning and

metabolic disorders (8). Finding the poisoning etiology is the most important part of ALC management, which should be conducted through a precise history taking and performing accurate clinical examinations (9). However, there may not be much information in the patient's history with a decreased level of consciousness. The toxin is a substance that, if ingested in sufficient amounts, can interfere with health and lead to temporary or permanent damages to the body. Toxins may be solid, liquid, or gaseous. Toxins cause adverse effects after entering the body, which is called poisoning. The signs and symptoms of poisoning vary depending on the type of toxin and the way it enters, and they appear quickly or over several days (10). Due to the different treatment methods and antidotes for different toxins, it is very important to diagnose the type of poisoning (11). Opioids, medications, Rice pill (aluminum phosphate) and various toxins that may be mistakenly or intentionally used for suicide are common causes of poisoning. To prevent the potential dangers of poisoning, epidemiological information is of particular importance and the epidemiological pattern of poisonings on a national scale should be examined to give a clear view to physicians.

Methods

This systematic review and meta-analysis was undertaken to investigate the prevalence of poisoning etiology in Iran based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

The search strategy embedded in this study was based on both English and Persian researches conducted in Iran. Scientific information databases of Jihad Daneshgahi University (SID), Medlib, IranMedex, Google scholar, and Magiran for Persian studies, and PubMed, ScienceDirect, and Scopus for articles in English were queried based on the various combinations (AND/OR) of Medical Subject Headings (MeSh) keywords [acute poisoning, Iran, "Agent" poisoning, Drug Overdose]. The query was limited to peer reviewed English or Persian language studies, mainly conducted in Iran. Two researchers independently selected eligible studies and in case of incompatibility in each step of the study, a third researcher was negotiated to make the final decision. The inclusion criteria for studies were (1) the cross-sectional studies reporting etiology of the poisoning in acute poisoning cases having the ICD10 criteria of the poisoning definition; (2) quality assurance based on the STROBE checklist statement (Table S1). STROBE Statement—checklist of items that should be included in reports of observational studies, based on the latest version (https://www.strobe-statement.org), had 32 items and studies which had at least 29 items were included in study. Item of "Describing any efforts to address potential sources of bias" was considered indispensable.

Initially, all articles related to poisoning in Iran were collected and after the search, a list of abstracts was prepared by the researchers and duplicates were removed (n=31). At this stage, all the articles in which the prevalence of poisoning was mentioned in the abstract were included in the initial list for full-text evaluation. A checklist was used to assess the inclusion criteria of our study and the data collection (including items of researcher's name, title, year of publication, city, sampling method, sampling number, study type, total prevalence, and toxicology etiology). Based on these steps, 185 articles were detected in the primary search, and 78 articles with related title and abstract were included in full-text evaluation. In addition, the reference lists of all selected articles were screened for potentially relevant publications. Finally, 19 eligible articles were entered into the meta-analysis stage (as shown in Figure 1). The ratio of each poisoning

Table 1. Included studies in the meta-analysis

Author, year	Female: Male (n/%)	Number of cases	Death rate	Mean age
Sadeghieh Ahari, 2012	66.1%:33.9%	245	33.5%	30.52
Torkashvand, 2015	45.4%:54.6%	260	1.90%	23.10±15.16
Najari, 2017	16: 39	7732	0.9%	49.84 ± 20.28
Dehghani, 2015	47.6%: 52.4%	163	2.4%	NA
Hashmnejad, 2014	102: 102	204	5.8%	29.8 ± 13.4
Ahmadi, 2011	NA	2057	1.3%	NA
Afzali, 2008	69: 349	418	3.6%	40.5
Masoumi, 2013	95.1%: 4.9%	402	2.0%	19-44
Eslami, 2014	34.9%: 65.1%	988	2.8%	NA
Jafarzadeh, 2017	36.72%: 63.28%	275	0%	28.20 ± 18.60
Feiz Disfani, 2019	130: 113	243	3.8%	Under 15 years
Shokrzadeh, 2017	45.9%: 54.1%	800	1.6%	19.53 ± 14.39
Sobhani, 2000	51.4%: 48.6%	1215	1.06%	Under 15 years
Islambulchilar, 2009	55.7%: 44.3%	1342	2.3%	26.83 ± 12.59
Abdollahi, 1997	≈ 4500: 2500	7000	NA	NA
Vatandoost, 2002	12233: 7278	19511	NA	>13 years
Afshari, 2004	53.4%: 46.6%	71589	22.3	22.3 ± 14.38
Gorgi, 2016	89:103	17, 342	NA	NA
Hassanian-Moghaddam, 2008	5583: 5818:64 unknown	11,465	1%	>12 years

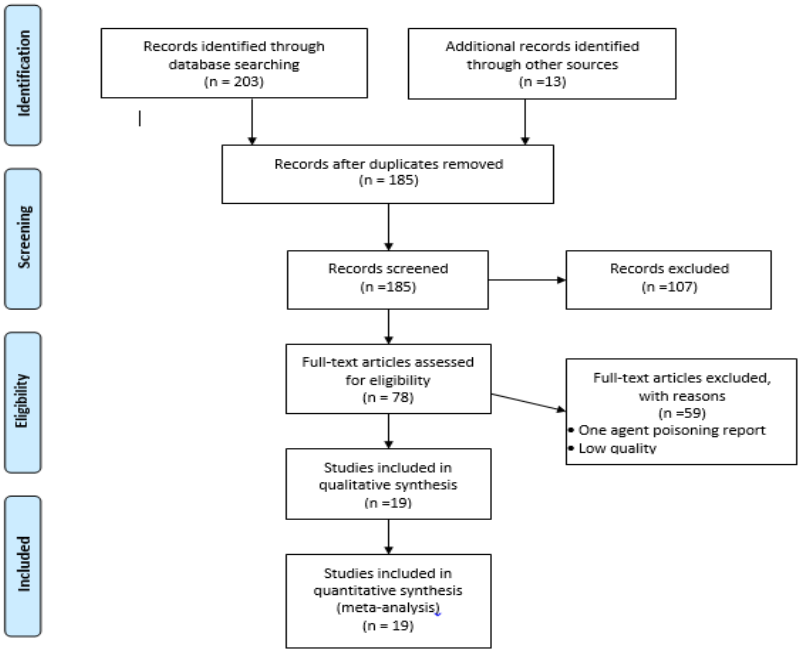

Figure 1. Study search strategy (PRISMA flow diagram).

agent to all of the poisoning cases was used to calculate the odds ratio (OR). The variance of each study was calculated according to the fixed-effect model. Studies were combined according to the number of samples and variance. Due to the heterogeneity of the studies, random effects were used to combine the studies. Cochran's test was used to evaluate the heterogeneity of studies using the I2 index. Begg and Mazumdar test revealed no possibility of the publication bias for each poisoning agent analysis (P>0.05).

Results

As shown in Table 1, in our review, 19 studies evaluating 143,251 cases of poisoning were included (12-30). The age of most subjects was between 12-45 years old. In 8 studies, the number of female poisoning cases was dominant. The average death rate was 5.39% (range: 0%-33.5%).

To evaluate the incidence rate of the poisoning by each agent, a meta-analysis of studies reporting the number of poisoning by a specific agent from a whole poisoned subject population was conducted.

As shown in Table 2, five studies reported the prevalence of acetaminophen poisoning. Among 10 985 evaluated cases, acetaminophen poisoning was responsible for 1043 cases (9.49%). Pooled incidence OR for acetaminophen poisoning was 0.164 (95% CI: 0.155-0.174; P=0.001, I^2=99.67%). The total incidence of alcohol poisoning was 698 cases in 16413 poisonings (4.25%) with pooled OR of 0.054 (95% CI: 0.051-0.058; P=0.001, I^2=98.00%). Also, incidence of aluminum phosphide poisoning was 10.9% (984/8950) with polled OR of 0.115 (95% CI: 0.109-0.122; P=0.001, I^2=95.09%). Incidence of amphetamine poisoning was 8.4% (831/9908) with polled OR of 0.091 (95% CI: 0.085-0.097; P=0.001, I^2=98.05%). Besides, incidence of antipsychotic poisoning was 10.9% (1232/11241) with polled OR of 0.139 (95% CI: 0.130-0.149; P=0.001, I^2=99.06%). In addition, incidence of benzodiazepine poisoning was 19.9% (6312/ 31 692) with polled OR of 0.204 (95% CI: 0.200-0.209; P=0.001, I^2=98.92%). Among 1 2401 evaluated cases, chemical poisoning was responsible for 383 cases (3.1%). Pooled incidence OR for chemical poisoning was 0.033 (95% CI: 0.030-0.037; P=0.001, I^2=96.61%). Incidence of carbon monoxide (CO) poisoning was 1.8% (375/20 648) with polled OR of 0.027 (95% CI: 0.024-0.029; P=0.001, I^2=98.5%). Nonsteroidal anti-inflammatory drugs (NSAIDs), opium, pesticides, selective serotonin reuptake inhibitor (SSRI), organophosphate and tricyclic antidepressant (TCA) poisoning incidences were 1.7% (40/2261), 25.1% (4960/19794), 6.7% (1894/27943), 1.3% (33/2475), 12.7% (690/5426), 5.7% (174/3045), respectively. The Forrest plots of the meta-analysis are

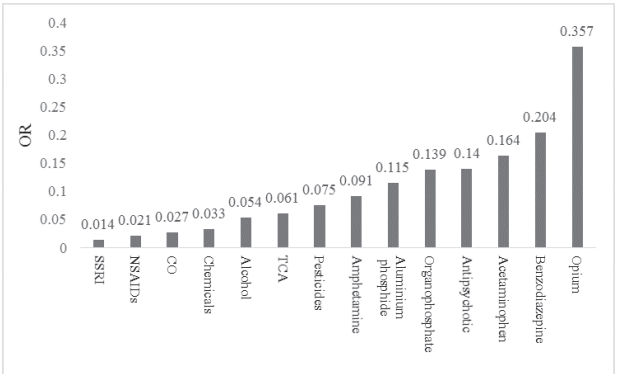

Figure 2. Ranking of each poisoning agent OR.

Table 2. Meta-analysis of poisoning ratio based on the agent

Agent	Number of studies	OR	95% CI		I^2 (%)
			Lower limit	Upper limit	
Acetaminophen	5	0.164	0.155	0.174	99.670
Alcohol	6	0.054	0.051	0.058	98.000
Aluminum phosphide	3	0.115	0.109	0.122	95.090
Amphetamine	3	0.091	0.085	0.097	98.050
Antipsychotic	7	0.140	0.133	0.148	99.060
Benzodiazepine	8	0.204	0.200	0.209	98.920
Chemicals	4	0.033	0.030	0.037	96.610
CO	5	0.027	0.024	0.029	98.500
NSAIDs	2	0.021	0.015	0.028	94.530
Opium	10	0.357	0.348	0.365	99.720
Organophosphate	4	0.139	0.130	0.149	97.800
Pesticides	6	0.075	0.072	0.078	99.330
SSRIs	2	0.014	0.010	0.019	28.02%
TCAs	2	0.061	0.053	0.070	95.980

Abbreviations: CO, Carbon monoxide; SSRIs, selective serotonin reuptake inhibitors; TCAs, Tricyclic antidepressants; NSAIDs, nonsteroidal anti-inflammatory drugs.

provided in Supplementary file 1.

As shown in Figure 2, the ranking OR of each agent was done; Opium poisoning was the most prevalent poisoning followed by the benzodiazepine, acetaminophen, antipsychotic medications, organophosphates, aluminium phosphide, amphetamine, pesticide, TCA, alcohol, chemicals, CO, NSAIDs, and SSRIs.

Discussion

Due to the increasing use of medications in recent years, drug poisoning is a common cause of the level of consciousness (LOC) and in most cases can be treated with timely diagnosis and prompt treatment. Poisoning is one of the most common causes of emergency department visits, which can cause serious injuries and even death (31).

Acute poisoning refers to exposure to a toxic substance accidentally or over a short period, which can be intentional or unintentional (3). Unintentional or accidental poisoning is common and can lead to increased complications and mortality (2,3). Most acute poisonings referred to the hospital are intentional poisonings that, regardless of their intentions and motives, potentially threaten a person's life and sometimes lead to death. Awareness of the pattern of poisoning in a particular area will play an important role in identifying risk factors and early detection of poisoning (2-4).

Due to this, the present study investigated the prevalence of etiological causes of poisoning in Iran in a systematic review and meta-analysis. We found out that opium poisoning was the most prevalent poisoning in Iran. In a study by Haghgou (32), it was stated that the pattern of intentional poisoning for suicide has changed from opium to pharmaceutical pills and chemical pesticides (1969-1974). While our analysis from 1997 to 2019 revealed opium as the most common cause of poisoning in Iran.

Drug poisoning has also been reported as the most common cause of poisoning in other studies (31). Among the causes of poisoning, narcotics and painkillers accounted for the largest share (33). The most common cause of poisoning in the United States was analgesic medication poisoning, including acetaminophen (34). While in our study opium poisoning was the most prevalent.

Access to painkillers as over-the-counter medicine is easy and acetaminophen is responsible for a significantly higher rate of poisoning in comparison to other over-the-counter (OTC) medications like NSAIDs. Also, the ranking of medications in our study shows that OTC-medication or non-OTC-medication does not seem to be responsible for the rate of consumption. This is a warning for health policymakers regarding the management of the drugs and medication available to the public; while many other factors may have an effect on our results as well as intentional or accidental poisoning.

The main issue investigated in the present study is the identification of the causes of toxicity in cases of intentional poisoning or suicidal attempts. With the increasing prescription of antidepressants in many countries, suicide rates have increased. Studies have shown that with the increased rate of the prescription of antidepressants; while being effective in controlling depression as one of the most important risk factors of suicide, they are causing an increased incidence of poisoning through suicide or drug overdose. However, in some countries increased prescription of the antidepressants was beneficial (35,36). Findings showed that benzodiazepines were the second agent responsible for the poisoning in Iran. But the results regarding the TCA and SSRIs are contradictory as those are ranked as the least common causes of poisoning. One reason elucidating this issue could be due to the fact that benzodiazepines like diazepam are better known by the Iranian people than TCA or SSRI. Also, the low rank of TCA and SSRI toxicity in Iran may happen because of a

higher prescription rate of benzodiazepines in comparison to the TCA and SSRIs. As a result, it is necessary to design and present an appropriate training program regarding the considerations of how to prescribe medicine in medical education. In prescribing medications, the patient's mental state, and the number of pills prescribed should be taken into account.

There are shreds of evidence regarding the effect of the type of medications available in the market on the suicide pattern. For example, in Sweden, the replacement of SSRIs instead of TCAs was effective in the prevention of SSRIs poisoning but increased the benzodiazepine poisoning rate (37).

In our study, the average death rate was 5.39%. Rapid access to medical centers for poisoning can justify low mortality rates. In most cases, hydration, gastric lavage, activated charcoal, antidotes, and laxatives are being used to treat the poisoned patients. There are often issues regarding the management of the poisoning cases in the emergency department as well as inadequate knowledge of physicians dealing with the poisoned patient (38).

Also, there are concerns about the high incidence of organophosphate and aluminum phosphate poisoning. In this regard, it is suggested that public education be conducted to increase the level of public awareness through mass media to prevent drug poisoning.

The findings of this study are limited in generalizability due to various factors like age, sex, culture, etc. The substance used for intentional poisoning is related to various factors. Thus, age, sex, place of birth, and access to the substance of poisoning have a profound effect on this option in attempting suicide.

Conclusion

Due to several influential factors, further research is needed to implant preventive public policies on the education of the people or market availability of medications. Our study has been conducted on a national scale without any time constraints. Although the generalizability of the results may be influenced by the mentioned confounding factors, the results of this study provide a viewpoint on the cause of the poisoning in the country as we have provided a ranking of the most possible poisoning etiologies that may refer to the emergency department and this would be useful for physicians in cases of poisoning with unknown sources.

Authors contributions

The study was designed by MF, AH, and SD. The search strategy protocol was determined by EB, MF, BS and ZH. Searching was conducted by SA, SD, and RA. RA and BS did the analysis. All authors contributed in draft preparation and its revisions.

Ethical issues

All sources used to conduct this study were rederived based on the permissions of research authors in sharing the data.

Supplementary Materials

Supplementary file 1 contains Figure S1 and Table S1.

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