Epidemiological Aspects of Opioid Poisoning in Northern Iran: A Registry-Based Clinical Study

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ABSTRACT: Opioids are a class of drugs that are commonly used to manage pain due to their analgesic and sedative effects. However, the high consumption of opioids in the community has led to an increase in the incidence of overdoses and poisonings caused by various types of these drugs, whether intentional or unintentional. Therefore, comprehending the epidemiological features of patients experiencing opioid poisoning is crucial. We decided to investigate various epidemiological aspects of patients with opioid poisoning in the Mazandaran province, located in northern Iran, during the period of 2020 to 2021. The present investigation was conducted as a descriptive cross-sectional study, wherein we collected data on patients registered in the Mazandaran Registry Center of Opioid Poisoning (MRCOP) who had a history of using any kind of opioid. We collected information on various parameters, including patient demographics, the type of opioid consumed, the mode of consumption, and clinical outcomes. A total of 240 patients were initially registered at the registry center. However, 17 cases were excluded with personal consent, and eventually, a total of 223 patients were included in the investigation. The majority of the patients 70.9% (n = 158) were male, and the average age was 34.4 ± 16.55 years. The most common cause of poisoning reported in our study was intentional, which was mainly due to a suicide attempt. Furthermore, the most prevalent type of opioid consumed was methadone. The most frequently observed symptoms of poisoning among the patients were drowsiness, a decreased level of consciousness, and reduced arterial oxygen saturation levels. Based on the results of our study, several factors were found to be significant in methadone poisoning, including addiction, age, gender, suicide attempt, and a history of psychiatric disorder. These findings highlight the need for public education and awareness campaigns on the risks associated with opioid use, particularly methadone.

KEYWORDS: Intentional, poisoning, opioid, epidemiological, registry center

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Background

The terms "opioid" or "narcotic" refer to substances extracted from poppy seeds, as well as semi-synthetic and synthetic compounds with similar properties that can interact with opioid receptors in the brain.[1] Opioids are often used to treat pain since they contain analgesic and sedative properties. Opioid drugs such as opium syrup, methadone, and buprenorphine are used to treat addiction. Opioids can induce euphoria when consumed, which is one of the main reasons they are used for non-medical purposes.[2] Due to their medical properties, these substances can make breathing difficult, and an overdose can lead to death.[3]

Individuals begin consuming opioids for a variety of reasons. Some patients initially request opioids from their physician to relieve acute or chronic pain. Others may utilize opioids prescribed by someone other than a physician (a friend, relative, or even a stranger) for psychotherapy.[4] Finally, the majority of people who develop opioid use disorder turn to heroin since it is less expensive and easier to obtain.[5,6] Consumption of other drugs, particularly alcohol and benzodiazepines, is an important factor that aggravates drug poisoning among heroin users.[7] Approximately 500 000 fatalities have been reported worldwide as a result of drug usage, with overdose and poisoning from these opioids accounting for more than 30% of these deaths.[8]

Opioid abuse and overdose have steadily increased in the United States over the last 2 decade. Between 1990 and 2010, opioid overdose mortality quadrupled, and it is estimated that over 100 individuals die each day from opioid-related overdoses.[9-11] Unintentional poisonings, which are currently the leading cause of the mortality in the United States for adults aged 25 to 64, are mostly caused by prescription and illegal opioid overdoses.[10-12]

According to a United Nations assessment, Iran is among the nations with the highest rates of drug-related crime in the

world due to its geographical position and shared border (almost 2000 km) with Afghanistan and Pakistan.[13] Opioids were the most common type of drug causing poisoning in elderly patients admitted to hospitals in Iran during the years 2008 to 2013.[14] In recent years, studies have shown that the incidence of poisoning with opium and its derivatives is increasing in society because it can lead to loss of consciousness, respiratory depression, apnea, coma, and finally death.[15-17]

To counter this alarming trend and save more patients' lives, hospitals must enhance the availability of antidotes, assure the prompt deployment of emergency medical services, and the police should act more proactively and provide programs to educate the community and family members.[18] Every community must have a thorough understanding of its members in order to improve treatment and prevent drug overdose.[19] Given the significant rates of opioid consumption and the incidence of overdose and poisoning, both intentional and unintentional, we conducted a study examining various epidemiological aspects of opioid poisoning in patients registered at the Mazandaran Registry Center of Opioid Poisoning (MRCOP) in Mazandaran province during the period of 2020 to 2021.

Methods

This cross-sectional research was approved by the Mazandaran University of Medical Science Ethics Committee (NO: IR.MAZUMS.REC.1400.13954) and carried out in accordance with the Helsinki Declaration Principles. Also, written informed consent was obtained from all of the participants.

The statistical population of this study included all patients with a history of poisoning with various types of opioids, such as heroin, opium, methadone, tramadol, opium syrup (tincture), and buprenorphine. The information of the patients registered in the registry center was reviewed, and they were included after being admitted to the emergency department (ED), poisoning ward, or intensive care unit and matching the clinical symptoms of poisoning. The patients who did not agree to participate in the study for any reason were excluded. The registry center comprises a team of multiple individuals, including a registry official. The project manager is responsible for entering the patient's information into the system, following the checklist that has been approved by the University of Medical Science Ethics Committee. Its primary objective is to provide feedback and maintain control over the distribution of opioids, in line with ethical guidelines and regulations.

Rapid urine toxicology tests, encompassing morphine, methadone, tramadol, and other substances, were conducted for all patients, particularly those with questionable or ambiguous histories, as well as patients exhibiting a diminished level of consciousness (LOC). The data collection checklist was completed after obtaining informed consent and providing a thorough explanation to both the patients and their families regarding the importance of privacy. Variables were characterized using percentages, means, standard deviations, medians, and interquartile ranges. The normal distribution assumption was assessed using the Shapiro-Wilk test. To compare the frequency of findings and other grouped variables between 2 groups, the *t*-test or Mann-Whitney test was employed. Additionally, a multivariate regression test was conducted to adjust for potential confounding variables. Data analysis for this study was performed using SPSS v. 24 software and a *P*-value level less than .05 was considered statistically significant.

Table 1. The prevalence order of opioid types consumed.

VARIABLES	NO	FREQUENCY (%)
Methadone	140	64.4%
Tramadol	47	21.1%
Opium	19	8.2%
Tincture	11	4.2%
Heroin	6	2.1%

Results

Two hundred forty patients were included in the study, 17 of who were withdrawn with personal consent, and, finally, 223 of whom were studied. The majority of the patients 70.9% (n = 158) were male, and 29.1% (n = 65) female patients. The average age of the patients was 34.4 ± 16.55 years. The majority of patients are uneducated and unemployed. Half of the patients were married. The most common cause of poisoning, at 126 (59.2%), was intentional (a suicide attempt), and was caused by methadone consumption (Table 1).

Among the patients, the most commonly reported symptoms of poisoning included drowsiness, a decrease in LOC, and reduced arterial oxygen saturation (SpO2) levels. Specifically, a decrease in LOC, as measured by the Glasgow Coma Scale between 8 and 13, along with a SpO2 level below 90% and respiratory depression (ie, a respiratory rate below 8 breaths per minute) and systolic blood pressure below 90 mm Hg, were considered as hypotension.

Most patients had no family arguments or family or individual addictions. There was an underlying disease in 62 of the individuals. Only 11 individuals experienced electrocardiography abnormalities, and 31 had pulmonary involvement. In this study, the diagnosis of all cases was established by obtaining a comprehensive medical history from the patients and their families. This information was further validated through urine drug screening. It is important to note that all patients were admitted only once during the 2-year duration of the study.

Out of a total of 240 patients, who were admitted to the ED within the first 6 hours after consumption and subsequently treated with the infusion antidote naloxone in the poisoning ward, the duration of hospitalization for all 240 patients was less than 1 week. Among these patients, 194 (91.08%) showed improvement without experiencing any side effects. Regrettably, 4 (5.63%) of the patients did not recover from their condition and unfortunately passed away. The results of laboratory tests

Table 2. The results of laboratory tests.

VARIABLES	MEAN	SD	REFERENCE VALUE
Cr	0.97	0.43	0.6-1.2 mg/dl
BUN	21.21	9.97	9-26 mg/dl
BS	130.10	71.2	<200 mg/dl
Na	139.62	3.68	136-145 mEq/L
K	4.07	0.50	3.5-5.1 mEq/L
pH	7.29	0.30	7.35-7.45
PaCO2	54.61	14.65	35-45 mmHg
HCO3	28.3	6.05	22-28 mEq/L

Abbreviations: BS, blood sugar; BUN, blood urea nitrogen; Cr, creatinine.

Table 3. The common clinical manifestations.

VARIABLES	NO	FREQUENCY (%)
Drowsiness	146	68.54
Decreased LOC (GCS: 8-13)	91	42.72
Decreased SpO2 (<90%)	87	40.85
Miotic pupil	62	29.11
Apnea	37	17.37
Coma	27	12.68
Convulsions	22	10.33
Nausea and vomiting	19	8.92
Dizziness	15	7.04
Agitation and restlessness	11	5.16
Respiratory depression (RR < 12)	7	3.29
Itching	4	1.88
Abdominal pain	4	1.88
Fever	4	1.88
Hypotension (SBP <90 mmHg)	4	1.88
Mydriatic pupil	2	0.94
Arrhythmia	1	0.47

Abbreviations: GCS, Glasgow coma scale; LOC, level of consciousness; RR, respiratory rate; SBP, systolic blood pressure; SpO2, arterial oxygen saturation.

and also the clinical manifestations of the patients are shown in Tables 2 and 3.

Discussion

Acute poisoning is one of the most common causes of ED visits, with annual rates ranging from 0.1% to 0.6% worldwide.[20,21] Meanwhile, drug poisoning is one of the most frequent concerns, with many patients admitted to the ED each year and some dying.[14] The current study has shown that the most common cause of poisoning was the use of methadone, and most people used drugs orally or in pills. Most of the poisonings were intentional (a suicide attempt) and occurred at home. Most of the patients did not have family arguments, a history of suicide, an underlying disease, or an addiction. Most of the people were admitted to the ward. The time interval from poisoning to visiting the treatment center was within the first 6 hours for most patients.

In the study of Afzali et al, the most common poisonings were opium, methadone, and methamphetamine, respectively. Also, cases lived in urban areas with a ratio of 6.3 to 1 compared to rural areas, and the main drug used in both areas was opium, which was different from our results. Patients in urban areas were between the ages of 31 and 45, while those in rural areas were between the ages of 46 and 60.[14]

In our study, the cases of opium poisoning were lower than in this study, and most cases were poisoned with oral methadone. The remarkable point in our study was that, despite the fact that most people were transferred to the ED within the first 6 hours; most of the patients were discharged from the hospital with a full recovery.

Also, cases of methadone poisoning in Farzaneh et al's study were less than in our study. It seems that in our study, the incidence of methadone poisoning was much higher than in other studies.[22,23] These studies have provided insights into the diverse patterns of opioid consumption observed in 3 distinct provinces of Iran. While our study found methadone poisoning to be more prevalent, their study reported a higher incidence of opium poisoning. These variations in findings highlight the regional differences in opioid usage and poisoning cases within Iran. Understanding these differences can contribute to the development of targeted interventions and strategies to address specific opioid-related challenges in each province.

Considering that most Iranians are traditional, the use of traditional drugs such as opium and its derivatives is still

prevalent. Also, due to the numerous methadone maintenance treatment (MMT) centers and the unsafe storage of methadone syrup in mineral water bottles and containers for other drugs, methadone syrup poisoning is very common. On the other hand, cases of poisoning with synthetic drugs are increasing, which is probably due to their low price and easy supply.

Maddi et al carried out a study on a population of Ontario adults during the period from 2006 to 2008. The objective of their research was to identify patterns and characteristics among opioid users, as well as the underlying causes of fatalities resulting from opioid poisoning. Among the total of 2330 drug-related deaths in Ontario, approximately 58% (n = 1,359) were attributed, either wholly or partially, to opioids. Interestingly, one-third of all opioid-related deaths were specifically caused by oxycodone, which differs from the focus of our study.[24]

In a retrospective cohort study conducted by Tadros et al in 2015, it was demonstrated that the majority of opioid poisoning cases, accounting for 53.50%, were unintentional. The study also revealed that the average age of the patients was 45.5 years, and a slight majority of the patients were females, comprising 52.37% of the total cases.[25] In this study, the mean age of patients was 34.4 ± 16.55 years, and the majority of the patients were males (74.2%). In addition, in recent years as well as in Gholami et al's study, cases of AKI and rhabdomyolysis following tramadol-induced seizures have been reported.[26]

In a 10-year descriptive-analytical study conducted by Taheri et al, a total of 385 methadone poisoning patients were examined. The study revealed that the majority of the patients were men and individuals with a history of opioid addiction who were under the supervision of a MMT center. Moreover, the majority of patients in the study had intentionally poisoned themselves. During their admission, it was observed that most of them exhibited symptoms such as decreased LOC, respiratory depression, and hypotension.[27] In our study, the most common clinical manifestation in patients was drowsiness, followed by decreased LOC and SpO2 levels. The duration of hospitalization for most patients is less than 1 week, with 194 (91.08%).

During a 5-year retrospective study conducted by Sharif and Nouri, the prevalence of methadone toxicity in Iranian children under the age of 12 was investigated. The study found that there were more boys than girls among the affected children. Additionally, it was noted that all of the patients had been poisoned with methadone syrup. The most frequently observed symptoms in these children were drowsiness, meiosis, vomiting, and ineffective breathing, respectively, with the majority of children experiencing this symptoms.[28]

One of the important limitations of this study was the misconception of some people in society during the COVID-19 pandemic about the use of opioids to prevent contracting this disease, which can have a significant effect on the increase in poisoning with these substances. The COVID-19 pandemic had a notable impact on the study's findings, as patients exhibiting symptoms of poisoning were less likely to seek medical attention at healthcare centers. Consequently, this factor could have significantly influenced the registration statistics at the registry center. Another limitation of the study was the absence of precise recording of information regarding these patients in other medical facilities, which could have affected the comprehensiveness and accuracy of the data collected.

It is suggested to keep methadone syrup in standard bottles and keep it out of the reach of children in order to prevent poisoning. Due to the existence of a suitable antidote (naloxane), it is essential to transfer patients to the ED immediately in the case of poisoning with opioid compounds.

Conclusion

The results of the current research showed that most of the opioid poisoning patients were young, married men with low education, and their poisoning was often intentional (a suicide attempt). The most common symptoms of poisoning were drowsiness, decreased LOC, and SpO2 levels. Addiction, age, gender, attempts at suicide, and a history of psychiatric disorder were among the most important factors in methadone poisoning, which should be considered in public training and prevention of poisoning. Thus, these analyses underscore the need for health care providers to assess suicidal risk in patients receiving opioids. Future studies should evaluate preventative measures, optimal screening, and intervention programs for these patients.

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Authors' Contributions

HR and ZZ designed the study, wrote the manuscript, and analyzed and interpreted the data. NKh and SMH involved in writing, editing and preparing the final version of manuscript. ZZ, MM, and MS involved in interpretation and editing the manuscript. All authors reviewed the paper and approved the final version of the manuscript.

Ethics Statement and Consent to Participate

The protocol of the study was proved by the Ethics Committee of Mazandaran University of Medical Sciences (NO: IR.MAZUMS.REC. 1400.13954). Written informed consent was obtained from all of the participants.

Consent for Publication

Not Applicable.

Availability of Data and Materials

The data is available to the correspondent author and can be obtained upon request.

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