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RESEARCH ARTICLE **OPEN ACCESS**

Symptoms, Consequences, and Action Across of Methadone Poisoning in Children Referred to a Hospital in the South of Iran

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Abstract:

Introduction: The aim of this study is to investigate the consequences of children with methadone poisoning referred to the emergency department of Imam Khomeini Hospital in Jiroft in 2020. Methadone poisoning in children is one of the major public health problems and one of the most common causes of emergency room visits.

Methods: This research is a case series study. The study population included all children under 15 years old. Data were collected through interviews with the child's parents or companions, as well as a medical examination of poisoned children in the hospital, and by reviewing the records of past patients and recorded in the data registration form. Data were analyzed using SPSS software version 21.

Results: Of the 90 children surveyed, 66.7% were in the age range of 2 months to 3 years, the mean age of the children was 2.49 ± 0.89 years old, and 51.1% of patients with poisoning in the morning and autumn were the highest number of patients. Education level of parents, 50% of men and 38% of women were illiterate. 76.7% had taken 1 to 5 mg of methadone. The most common side effect of methadone poisoning was vomiting (41.1%).

Conclusion: Incidental use of methadone in children is very high so that families and surroundings, doctors, and health personnel have sufficient knowledge of the most dangerous complications of methadone and proper maintenance, keeping this dangerous substance from the reach of children should be trained to parents.

Keywords: Symptoms, Consequences, Methadone, Poisoning, Children, Hospital.

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1. INTRODUCTION

The toxin is a substance that can usually lead to damage or death of the organism, and poisoning is an event during which the body absorbs a substance through

the mouth, respiration, mucous membranes, arteries, *etc*. This process leads to a series of complications caused by poisoning, and these side effects can cause damage or be life-threatening [1].

Substance abuse and its poisoning are known as the most common type of poisoning in the world. Due to the increase in population and increase in the number of drug users, the resulting poisoning is spreading [2]. It has also been reported that the mortality rate in people who use drugs regularly is 13 times higher than in normal people [3].

According to the International Narcotics Control Board, 2.7 percent of the total population of Iran used drugs in 2011. The drugs used included 34 percent opium, 27 percent crack, and 19 percent. Heroin was 4% opium syrup, 4% methamphetamine, and 2% cannabis [4].

Methadone is a diphenylmethane derivative and a μ-receptor agonist that is used to prevent the symptoms of drug withdrawal in short-term detoxification, long-term detoxification, and as a maintenance treatment in people with opioid dependence in MMT (Maintenance methadone therapy) method [5]. Methadone is an opioid receptor agonist that has several effects on the central nervous system (CNS) and smooth muscle. Methadone poisoning has life-threatening effects and may cause delayed coma [6]. Respiratory depression is a symbol of serious methadone poisoning and is seen in 50% of patients with central nervous system depression [7].

Methadone use for more than a year causes many problems, such as severe loss of libido, indigestion, problems with male fertility, neurological problems, stomach and digestive problems, and many others [8]. After the first use, people may become ill or constipated. Methadone use can cause fatty liver [9].

Opioids increase the risk of miscarriage or the birth of children under standard or prematurely, and their sudden cessation during pregnancy may cause opioid withdrawal syndrome in the fetus, a syndrome common in newborns of addicted mothers. It also affects opioids and requires medical attention [10, 11].

In a U.S. study of methadone poisoning children, out of a total of 30,000 methadone poisonings reported to the US Centers for Disease Control, 684 deaths occurred, 19 of which occurred before the child was rushed to the emergency room [12].

Winchester *et al*. found that 88% of methadone ingested was accidental, 92% of which occurred at home, 82% had no or mild symptoms, and 1% were fatal [7]. Methadone poisoning in children is one of the major public health problems and one of the most common causes of emergency room visits [13]. In their study of children, Mamouri *et al*. showed that the average age of children who had taken methadone was 5 years and that the onset of symptoms from the time of methadone use was 55 minutes. Clinical symptoms included drowsiness in 92.4%, Bradypenea in 83.5%, Myotic pupils in 64.6%, nausea and vomiting in 63.3%, and pruritus in 43%. The most common laboratory findings were leukocytosis (41.9%), metabolic acidosis (30.7%), and hyperglycemia (11.7%) [14]. Alikhani *et al*., in the study, examined demographic, clinical, and autopsy findings on deaths due to acute methadone poisoning. The results showed that most women were under 20 years old, and methadone abuse was 55%. The cause of death was methadone poisoning in 37% of people with respiratory failure. With the use of autopsy, 43% of the deceased had more than one limb involved [15].

Due to the change in the picture of drug intoxication and the significant increase in methadone use in homes in the form of addiction treatment and methadone maintenance programs in recent years, the seriousness and novelty of the phenomenon of methadone poisoning in children and its possible causes and consequences. The results were used to provide solutions to prevent this type of poisoning in children.

In this research, the questions that were investigated were: demographic information of patients with poisoning, common symptoms of poisoning, when to go to the hospital, the prevalence in what season of the year, how to access methadone, the interval between methadone consumption and hospitalization and the number of days in the hospital. The aim of this study is to investigate the consequences of children with methadone poisoning referred to the emergency department of Imam Khomeini Hospital in Jiroft in 2020.

2. METHODS AND MATERIALS

This is a case series study. The study population included all children under 15 years old who were admitted from March 20, 2020, to February 19, 2021, to the emergency department of Imam Khomeini Hospital in Jiroft City.

The data were collected in such a way that by referring to Imam Khomeini Hospital in Jiroft and with the permission of hospital officials and parents of children, demographic information (including the age of the child, sex of the child, education of parents) and other related data (Such as emergency department, methadone preparation and maintenance, methadone intake, methadone intake to a hospital stay, and naloxone intake) by reviewing past patient records or by telephone interview to complete incomplete data files with parents and also, the medical examination of the poisoned children in the hospital were collected and recorded in the data registration form. Inclusion criteria included age under 15 years and diagnosis of methadone poisoning, which were excluded in case of dissatisfaction and lack of cooperation from the child or his companions. The ethics committee is affiliated with Jiroft University of Medical Sciences and approved this study with the ethics code IR.JMU.REC.1400.021. Afterward, explanations were given for the purpose of the study and obtaining informed consent to participate in the research and to keep the secrets and confidentiality of each individual's family.

In this study, after collecting and extracting the questionnaires, the data were analyzed using SPSS software version 18. Descriptive statistics, including frequency tables, standard deviation, and mean, were used

to analyze the data.

3. RESULTS

In the time duration of the study, poisoning occurred in 90 children; 66.7% were in the age group of 2 months to 3 years, and the lowest number was in the age group of 9 to 12 years 1.1%, and the results showed that the mean age of the children 2.49± 0.89 years old. Boys accounted for 54.4% of children with poisoning. The results also showed that 50% of fathers and 38% of mothers were illiterate (Table **1**).

The results show that 51.1% of patients were referred in the morning and 28.9% in the Autumn. Among children, 48.9% had taken 5 to 10 mg of naloxone, and 76.7% had taken 1 to 5 mg of methadone. Also, 40% of poisoning patients needed oxygen therapy. The most common side effect of methadone poisoning was vomiting (41.1%). Regarding the method of preparation and access to methadone, the results showed that 35.6% got sick through the people around them (Table **2**).

There was a statistically significant relationship between the season and hospitalization in the ICU ($p = 0.041$). There was also a statistically significant relationship between methadone use and the number of days of hospitalization ($p < 0.008$) and hospitalization in the ICU ($p < 0.000$). The results of the present study showed a statistically significant relationship between the need for oxygen therapy and hospitalization in the ICU ($p = 0.008$) and the number of days of hospitalization ($p = 0.001$) (Table **3**).

Table 1. Demographic information on methadone poisoning patients.

Variable	Categories	Number	Percent
Age	2 months - 3 years	60	66.7
	3-6 years	23	25.6
	6-9 years	3	3.3
	9-12 years	1	1.1
	12-15 years	3	3.3
Sex	Male	49	54.4
	Female	41	45.6
Mothers literacy	Unliberated	35	38.9
	Middle school	28	31.1
	Diploma	12	13.3
	Associate degree and above	15	16.7
Fathers literacy	Unliberated	45	50
	Middle school	28	31.1
	Diploma	7	7.8
	Associate degree and above	10	11.1
Total		90	100

Table 2. Clinical information on patients with methadone poisoning.

Variable	-	Number	Percent
Referral time	Morning	46	51.1
	Noon	31	34.4
	Night	13	14.4
Season of the year	Spring	24	26.7
	Summer	18	20
	Autumn	26	28.9
	Winter	22	24.4
Methadone intake	1-5 mg	69	74.6
	5-10 mg	13	14.4
	Above 10 mg	8	8.9
Interval between methadone consumption and hospitalization	One hour	28	31.1
	Two hour	32	35.6
	Three hours and above	30	33.3
Need oxygen treatment	Yes	36	40
	No	54	60

(Table 2) contd.....

Variable	-	Number	Percent
Complications of methadone poisoning	Arrhythmia	11	12.2
	Vomiting	37	41.1
	Convulsions	25	27.8
	Asphyxia	17	18.9
How to prepare and access methadone	Family	20	22.2
	Those around them	32	25.6
	Accidental	38	42.2
Total		90	100

Table 3. Status of the relationship between hospitalization in ICU and hospital with the season, amount of methadone consumption, the distance between methadone use and hospitalization, and oxygen requirement (n = 90).

Variables		Hospitalization in the ICU	Number of days of hospitalization		
			1-2	3-4	More than 5 days
		Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)
Season of the year	Spring	4 (80)	9 (37.5)	7 (29.2)	8 (33.3)
	Summer	0 (0)	4 (22.2)	9 (50)	5 (27.8)
	Autumn	0 (0)	14 (53.8)	8 (30.8)	4 (15.4)
	Winter	1 (20)	6 (27.3)	12 (54.5)	4 (18.2)
p-value	0.041		0.194		
Methadone intake	1-5 mg	0 (0)	28 (40.6)	28 (40.6)	13 (18.8)
	5-10 mg	0 (0)	4 (30.8)	7 (53.8)	2 (15.4)
	Above 10 mg	5 (100)	1 (12.5)	1 (12.5)	6 (75)
p-value	0.000		0.008		
Interval between methadone consumption and hospitalization	One hour	1 (20)	11 (39.3)	11 (39.3)	6 (21.4)
	Two hours	1 (20)	11 (34.4)	16 (50)	5 (15.6)
	Three hours and more	3 (60)	11 (36.7)	9 (30)	10 (33.3)
p-value	0.427		0.434		
Need oxygen treatment	Yes	5 (100)	9 (27.3)	11 (30.6)	16 (76.2)
	No	0 (0)	24 (27.7)	25 (69.4)	5 (23.8)
p-value	0.009		0.001		

4. DISCUSSION

The results of the present study showed that the mean age of the children was 2.49± 0.89 years old, and the number of boys with methadone poisoning was higher than that of girls. The results also showed that the highest frequency was in the age group of 2 months to 3 years; 50% of fathers and 38% of mothers were illiterate, and the fall season was the most methadone poisoning.

In the study of Masoudpour *et al*., the results were similar to the present study; the mean and standard deviation of the age was 3.75±3.14 years, and 58.8% of poisoned boys and the level of education of most poisoned children were below the diploma, and most cases of methadone poisoning were seen in autumn and winter [16]. In the study of Besharat *et al*., Bagheri *et al*. had more male children poisoned with opium and its derivatives than female children [17, 18]. In the study of Martin *et al*., the mean age of methadone poisoning was 2.61 years old [13], and in the study of Binchy *et al*., the mean age was 2.08 years old [19]. In the study of Farnaghi *et al*., the mean age of patients was 33 months, of which only 19% of patients were under 1 year old, and the number of male patients was more than the number of female patients [12].

In the study of Heratipour *et al*., the most common age range of poisoned children was between 1 and 5 years, the highest level of education of mothers of poisoned children was under a diploma, and the lowest level of undergraduate education and the highest level of education of fathers was below diploma [20]. In Golestan's study on opium poisoning and its derivatives in children under 5 years old, 84.6% and 80% of parents were illiterate or had undergraduate education, respectively [21].

The average hospital stay in patients with methadone poisoning is 2 hours. This delay may be due to parents' misconception that methadone is less dangerous or that they are more afraid of the social stigma of this type of poisoning due to the small study environment. In the study of Masoudpour *et al*., the time interval between methadone use and emergency department visits was between 2 to 3 hours [16]. In Memouri *et al*.'s study, the average time interval between methadone use and referral to a medical center was 153.5 minutes [14]. In the study of

Farnaghi *et al*., the mean time from the onset of symptoms to medical referral was 2.34 hours, which indicates a relatively long time from the time of consumption to the onset of symptoms [12]. Fortunately, few children died at the time of this study, but other studies have shown that methadone poisoning in some cases has resulted in the death of the child, so parents or others reaching the hospital quickly and promptly can be very effective in reducing mortality.

Most children with methadone poisoning used 1 to 5 mg of methadone, which is much less than 33 mg in a study conducted in Tehran [12], but in the study of Masoudpour *et al*., the minimum amount of methadone used was 0.5, and the maximum amount was 13 mg with an average of 2.19 mg, which is consistent with the findings of our study [16]. The most frequent visits of patients with methadone poisoning are in the morning and evening, which is consistent with the results of Binchy *et al*. that most of the poisonings (95%) occurred during the day [19]. In Memouri *et al*.'s study, the maximum poisoning time was from 12 noon to 6 pm [15]. Among the studied complications, vomiting (41.1%) was seen in most children with methadone poisoning. In Farnaghi *et al*.'s study, most children had vomiting [12]. In another study, 63.3% of nausea and vomiting were reported compared to the other complications [14].

There was a statistically significant relationship between the season and hospitalization in the ICU ($p = 0.041$), so the rate of hospitalization in the ICU in autumn and winter is higher than in other seasons. Similar to our study, Lotfalizadeh had the highest prevalence of preeclampsia in winter [22]. There was also a statistically significant relationship between methadone use and the number of days of hospitalization ($p < 0.008$) and hospitalization in the ICU ($p < 0.000$). People with 5 to 10 mg of methadone were hospitalized for 3 to 4 days, which had the highest percentage of hospitalization. In the confirmation of the present study, in the study of Memory *et al*., on average, patients were hospitalized for 31 hours and 46 minutes [13]. The days of hospitalization in the Martin study were one to seven days. Therefore, the results show that hospitalization due to methadone poisoning depends on the amount of methadone used [11].

Similar to our study, in the study of Bargagli *et al*., The mortality and hospitalization rate of people who used drugs regularly was 13 times higher than that of normal people [16].

In the study, Massoudpour and colleagues were associated with methadone volume and severity of complications [16]. Therefore, the results indicate that the volume and amount of methadone are effective in raising the number of days of admission.

There was a significant relationship between the need for oxygen therapy and hospitalization in the ICU and the number of days of hospitalization in the hospital. There was a significant relationship, so the children of addicted mothers had an average of one day more than the sons of non-addicted mothers in the hospital, indicating that maternal addiction was significantly associated with increasing the days of hospitalized children. In the study of Asgarzadeh and colleagues, late time and high doses of methadone in poisoning people at hospitals caused patients to use emergency services and respiratory services and mortality [23].

CONCLUSION

This study showed that incidental use of methadone in children is very high so that families and surroundings, doctors, and health personnel have sufficient knowledge of the most dangerous complications of methadone and proper maintenance, keeping this dangerous substance from the reach of children should be trained to parents.

LIMITATIONS OF THE STUDY

In this study, data recorded in the health sector were used. The researchers were not involved in data collection and were not aware of the accuracy of the information.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This article reports the results of a research project approved by Jiroft University of Medical Sciences with the code of ethics (IR.JMU.REC.1400.021.).

HUMAN AND ANIMAL RIGHTS

All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1975 Helsinki Declaration and its later amendments or comparable ethical standards.

CONSENT FOR PUBLICATION

In order to comply with ethical considerations in this research, the information of the participants was kept confidential, and other people were not able to access this information. The names and surnames of the participants were not used for data collection, and data collection was done after obtaining the code of ethics from Jiroft University of Medical Sciences.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available from the corresponding author [K.R] upon reasonable request.

STANDARDS OF REPORTING

STROBE guideline has been followed.

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CONFLICT OF INTERESTS

The authors declare no conflict of interest, financial or otherwise.

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