

A Cross Sectional Study on Pediatric Methadone Poisoning in Northeast of Iran

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Abstract

Introduction: Methadone is a product derived from heroin that is available in drug stores as a 1mg/ml syrup. Methadone is a long acting drug with a roughly 24-hour half-life. Poisoning from opiates is one of the most dangerous and prevalent causes of poisoning in Imam Reza hospital (North-East of Iran), and its pattern has changed in the form of increased poisoning from methadone in recent years. The goal of this study is to evaluate why methadone poisoning in children under 6 years old have been increasing in recent years

Methods: This cross-sectional study was done on all children referred to Imam Reza Hospital's pediatric emergency room for cause and agent of poisoning during 2015, to identify the number and the most common cause of poisoning; evaluated demographic data showed methadone poisoning as the most common cause of accidental poisoning in children.

Results: In one year 3395 child admitted in the pediatric emergency room, including 409 cases (12%) of intoxication; 256 of these cases had different opium poisoning (62.5%) and 69 cases (16.8%) had methadone poisoning. In methadone poisoning 39 cases were male and 30 female. 25-48 months and 4-24 months age groups had the most cases of methadone poisoning, respectively.

Conclusion: In the emergency center the most common poisoning is opioid compounds especially methadone, likely due to the availability of methadone syrup in pharmacies. Parents use methadone to give up addiction. Poisoning occurred because children like to open bottles and accidentally consume its contents.

Key Words: Children; Iran; Methadone; Poisoning

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INTRODUCTION

Poisoning is one of the most common causes of children referral to hospital emergency departments especially in the pediatric emergency room of Imam Reza hospital, Mashhad, Iran(1-3); most of which occurring in the primary years of life and happens as a result of accidental consumption of hazards and drugs (3-5).

Poisoning from opiates is one of the most dangerous and prevalent causes of poisoning in the hospital (North-East of Iran), and its pattern has changed in the form of increased poisoning from methadone in recent years (6); Methadone is derived from heroin as a long-acting synthetic mu-opioid agonist; this product is available in drug stores in the form of 1mg/ml syrup and used for opioid addiction for 50 years(7). Due to respiratory depression and other symptoms, hospitalizing and monitoring of all patients with methadone toxicity is advised (8-10).

According to contradictory results of some studies and the need for more valid information about methadone poisoning of children in this society, this study was performed to

evaluate why methadone poisoning in children under 6 years old has been increasing in recent years.

METHODS

This cross-sectional study was done on children admitted to the emergency room of Imam Reza hospital in Mashhad with accidental poisoning during the year 2015; type of poisoning was identified based on subjective data asked from parents and urine analysis.

Urine samples of children were gathered in urine bags or sampling containers according to child cooperation, and sent to laboratory for evaluation of poisoning with other similar opiates like morphine, tramadol, benzodiazepines, barbiturates, three cyclic anti-depressants, or amphetamines and meth-amphetamines, ecstasy, cocaine.

Laboratory findings confirming methadone toxicity were necessary to include the patient in this study. Children with severe failure to thrive (FTT), renal failure, addicted to methadone and other opiates, children receiving other medications simultaneously or children of addicted mothers whom received breast milk were excluded of this study.

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Information on children with confirmed methadone toxicity including age, gender, severity of symptoms, time intervals between ingestion and presentation of symptoms and admittance in hospital, symptom relapse post-termination of treatment, hospitalization time and mortality were registered in a questionnaire. Data were statistically analyzed in SPSS version 16.

RESULTS

There were 956 cases of poisoning admitted to Imam Reza hospital in the 1 year period, of which 256 were cases of opium poisoning and 79 of them who had methadone poisoning met the inclusion criteria, and 6 other with methadone poisoning had FTT, one known case of Barter syndrome with nephrocalcinosis and 3 receiving other medications were excluded from study; 43% (34) of which were female and 57% (45) were male, age means were 59.88±40.93 months and 52.47 ± 38.7 months for female and male children, respectively. No significant difference was observed between age means of two genders (P = 0.413).

The most common time of poisoning was between 1-7 P.M, and the mean time of methadone ingestion was 15:46 with standard deviation of 36 minutes. The mean time interval from methadone ingestion until presentation of symptoms was 55 minutes 47 seconds with standard deviation of 6 minutes and 53 seconds, in the most acute case only 1 minute after ingestion symptoms of poisoning were presented and the longest time interval between ingestion and presentation of symptoms was 5 hours. The mean time interval from methadone intake until admitting to a treatment center was 153 minutes and 5 seconds with a standard deviation of 19 minutes and 4 seconds. Delayed referral to hospital resulted in increased bradypnea and need of naloxane infusion significantly (P = 0.007).

Of all cases of this study, 27.8% (n= 22) were admitted to Imam Reza's hospital emergency room and 72.2% were referred from another treatment center, of whom 16 children had no significant therapeutic measure performed. The other 41 children had some treatments like administration of naloxane and gastric lavage performed.

Methadone was ingested in the form of syrup by 88.16% (70) of patients, and methadone tablet by 11.84% (9) of patients. According to the questionnaire filled by parents at the time of admittance, in 59.46% (47) of cases the child's parents were using methadone. In the rest of the cases parents

did not use methadone. Methadone was ingested accidentally by children themselves in 42 cases and was accidentally given to children by parents in 28 cases. In 4 cases methadone was used for treatment, and 4 cases had an unknown source (parents denied methadone ingestion of their children); only 1 patient had committed suicide using methadone. In 30.4% (24) of patients there were other diseases at the time of admittance.

Nausea and vomiting, seizure, miotic pupils, bradypnea, decreased O2 saturation level, drowsiness and itching were observed as signs and symptoms between children, who were categorized into four age groups (table 1). Drowsiness was the most common symptom with 92.4% (73) prevalence, of which 32 were female and 41 male. Itching was shown by 43% of children. Nausea and vomiting reported in 50 patients (63.3%). In 64.6% of children miotic pupil was reported; 16.5% of patients had normal breathing but in the other 83.5% bradypnea was reported. O2 saturation level was normal in 17 cases (25%), and 52 cases (75%) showed decreased O2 saturation levels. There was no significant correlation between any of the symptoms and sex (P > 0.05).

According to Chi-square statistical analysis the only significant correlation was between age and nausea-vomiting. (Chi-square = 11.21, P = 0.011)

Prolonged loss of consciousness of more than 24 hours was reported in 7 cases, and more than 3 days was reported in one patient who expired. Mechanical ventilation was reported in 7 patients; presentation of seizure and vomiting was significantly associated with the need for mechanical ventilation (P = 0.008). Aspiration pneumonia happened in 2 patients during hospitalization; both of them experienced seizure at the time of admittance.

During the hospitalization period an average of 8.7 milligram naloxone was administered for poisoned children, ranging from 0 to 64 milligrams. Naloxone was administered for 91.2% (62) of patients and not administered for 8.8% (7) of patients. Ten out of 79 patients in methadone poisoning due to lack of inclusion criteria (FTT, Bartter syndrome, etc.) were excluded. None of the hospitalized children received charcoal.

Patients were hospitalized for 31 hours and 46 minutes on average with a standard deviation of 15 hours and 43 minutes, ranging from 2-87 hours of hospitalization. Four patients needed to be hospitalized again, all of them had initially left the hospital at their own will.

Table 1. Signs and symptoms on the age basis

Signs and symptoms	0-12 months	1-5 years	5-10 years	10-15 years
Drowsiness	77.8%	93.3%	94.1%	100%
Itching	22.2%	42.2%	58.8%	37.5%
Nausea and vomiting	33.3%	55.6%	88.2%	87.5%
Seizure	0	26.7%	5.9%	37.5%
Miotic pupils	57.1%	65.8%	53.8%	85.7%
Bradypnea	55.6%	84.4%	94.1%	87.5%
Decreased O2 saturation level	55.6%	85%	70.6%	75%

There was one case of methadone toxicity leading to death due to prolonged hypoxia, another case of death occurred before transporting the patient to the hospital. Also, one case of death was excluded for positive urine analysis of tramadol simultaneous to methadone poisoning.

DISCUSSION

Poisoning is one of the common reasons for children's admittance to emergency rooms and an important cause of children hospitalization and death in Iran.

The average patient's age in this study was 39 months, comparable to that of Anselmo and Farnaghi studies(11, 12); the higher average of age compared to this study with Sachdeva and Martin et al(9, 13) can be explained by accidental ingestion of methadone instead of water or other drinking by children of this age.

This study showed no significant difference between two genders in terms of methadone toxicity, which is comparable with the results of Martin et al(13). the most prevalent symptoms of children in this study were drowsiness followed by bradypnea ; comparable to the results of Bazmamoun et al which reported decreased level of consciousness, respiratory disorder, cyanosis, and seizure(3). Also in the study of Alotaibi et al the most common symptoms were CNS depression (92%), respiratory depression (58%) and meiosis (50%)(6). Maamouri et al also reported respiratory and CNS depression in 66% of patients(4). Aspiration pneumonia occurred in 2.89% of patients however Bazmamoun et al. reported aspiration pneumonia in 17%; this difference may result from difference between emesis management (3).

In the study of Bazmamoun et al seizure, hypotension, and cyanosis were considered as acute warning symptoms of an increased mortality and morbidity(3); also in this study seizure and bradypnea associated with long-term hospitalization.

According to the high prevalence of bradypnea and low prevalence of miotic pupil in children with methadone poisoning in this and other studies, it is suggested to consider respiratory rate instead of miosis for diagnosis and treatment of patients.

Poisoning was reported in this study to be most prevalent during 1-7 P.M, similar to result of Sachdeva et al which reported most of poisoning cases occurring during day time (95%)(9); it seems that time of poisoning is when parents are napping and do not monitor their child. The average time interval from methadone ingestion to presentation of symptoms was fifty-five minutes and forty-seven second; Farnaghi et al reported a mean time interval of 93 minutes(12), the difference of time interval between two studies can be due to difference in methadone dose ingested. Lo Vecchio et al reported a mean time interval of 192 minutes in patients over 18 years old, the higher possibility of addiction in this age group can explain more time or higher dose for presentation of symptoms(14).

Methadone was ingested in the form of syrup by 88.16% of patients and methadone tablet by 11.84% of patients; comparable to the studies by Farnaghi et al and Shadi-nia et al showing similar findings(12, 15).

According to the statements of parents, methadone was ingested accidentally by children themselves in 42 cases

and was accidentally given to children by parents in 28 cases, in 4 cases methadone was used for treatment, 4 cases of unknown source (parents denied methadone ingestion of their children); only one 13-year-old patient had committed suicide using methadone. In 30.4% of patients there were other diseases at the time of admittance. In this study, 59.46% of cases children were accidentally poisoned by methadone prescribed for their parents. This result was parallel to Sachdeva et al's study. In the study by Sachdeva et al, in most of the cases (73%) methadone was prescribed for parents(9). In the studies of Martin and Ghasempouri, in most cases the source of methadone was from family members(13, 16).

One of the patients of this study died due to methadone poisoning. Sachdeva et al reported 2 out of 44 patients(9), Alotaibi et al 29 out of 62(5), Sharif et al 1 out of 18(17), Maamouri et al 5 out of 13 and Anselmo 2 out of 15 deaths, respectively(4,11).

CONCLUSION

Opioid poisoning, one of the dangerous and most common causes of children's poisoning in Iran, has changed in terms of a remarkable increase in methadone poisoning in recent years; this is due to accidental exposure of children because of the unsafe availability of methadone in houses which are provided from addiction centers in containers different from factory containers. Because of insufficient knowledge and experience about methadone poisoning in children, inappropriate approach for treatment is not a rare incident; this research showed that methadone in the form of syrup increases the risk for accidental use by children in comparison to other forms.

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