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Methadone toxicity in a poisoning referral center

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Abstract

Objective: Methadone poisoning can occur accidentally among addicts or member of their families or intentionally for suicide. The aim of this study was to evaluate the epidemiological and clinical manifestations of Methadone poisoning. Methods: A descriptive analytical study was performed from 2013 to 2014 in the poisoning emergency and clinical toxicology departments of Imam Khomeini hospital affiliated with Kermanshah University of Medical Sciences (Kermanshah, Iran). All patients with Methadone poisoning within this period of time were investigated. Different variables were recorded in a checklist. Findings: A total of 199 patients were studied. Most of the patients were males 62.8% and the rest were females 37.2%. Mean \pm standard deviation of the age was $33.86 \pm 13/33$ years (range: 18-85). The mean interval between Methadone ingestion and the first medical care was 5.6 h with

median of 4h with the range of 0/5-24h. 101 patients (50.8%) were narcotic addicts. Intentional poisoning was observed in 56 patients (28.1%). Accidental poisoning was observed in 42 patients (21.1%). 183 patients (93%) consumed syrup of Methadone. Besides low level of consciousness, apnea, meiosis, and nausea and vomiting which are observed as the most common symptoms of methadone poisoning and also are common symptoms among poisoning with other opiates, we focused on other acute and more serious complications of methadone poisoning. 99 patients (49.7%) had hypotension, 79 patients (39.7%) had aspiration pneumonia, 35 patients (17.6%) had rhabdomyolysis, 23 patients (11.6%) had acute kidney failure, 14 patients (7%) were in hypoglycemic condition. 11 patients (5.5%) were in deep coma, 9 patients (4.5%) had cardiac arrest, 6 patients (3%) had seizure, 3 patients (1.5%) had acute liver failure, 1 patient (.5%) had anoxic encephalopathy, 1 patient had (.5%) disseminated intravascular coagulation and finally 1 patient (.5%) died because of Methadone poisoning. Mean length of hospital stay was 2.46 d (range: 1-17 d, median: 2 d). Conclusion: Addiction, attempt to suicide, accidental poisoning, age, gender, delayed hospital presentation, acute toxicity in patients who were on daily dose of Methadone (acute on chronic toxicity) were of the most important factors effective in Methadone poisoning, which should be considered in the public training and prevention of poisoning. Rhabdomyolysis can be considered as a great risk factor for genesis of acute kidney failure in patients with Methadone poisoning. **Keywords: Methadone, complications, poisoning, toxicity**

Introduction

Neurobiological evidence and medical experiences show that opium dependence is a common problem. Agonist maintenance therapy is one of the present therapies for opioid dependency. One of these opioid agonists used to treat addiction is Methadone. Despite the effectiveness of this agonist, comprehensive care facilities for the people under this treatment are not still enough. Although Methadone is not a new medicine, its use to reduce pain and treat addiction has increased rapidly. Pharmacological characteristics of Methadone indicate lethal and dangerous effects of Methadone poisoning. Methadone poisoning can occur accidentally (resulting from overdose due to abuse of narcotic substance or accidentally by children or elderly) or intentionally for suicide. Methadone poisoning is a common poisoning observed in poisoning emergency and clinical toxicology department of Imam Khomeini hospital (Kermanshah, Iran). This may be due to the large number of addicted patients under Methadone maintenance therapy (MMT) protocol and also Methadone availability to other family members. Pharmacy companies usually prepare Methadone for the purpose of MMT as a solution with a fruit taste. In this way, the good taste of Methadone makes it attractive for the children. Because of easily availability of Methadone in our country, and increasing MMT centers for addicted patients, there is a need for epidemiological study on this poisoning to improve both the quality of care and imposing better program on prevention methods. Therefore, the epidemiological and clinical manifestations of Methadone poisoning in the mentioned hospital have been investigated.

Methods

A descriptive analytical study was performed from 2013 to 2014 in the poisoning referral center of Imam Khomeini hospital, Kermanshah, Iran. All patients poisoned with Methadone who was hospitalized in the poisoning ward and intensive care unit during the above mentioned period were investigated. Patients who consumed

Methadone and were under 18 years old were excluded from this study. Patients who had been discharged by their own consent were excluded from the study. Patients who consumed Methadone in concomitant with other medications, which may affect our study, were excluded. After admission of patients to the hospital different variables including gender, age, clinical symptoms on admission, time interval from ingestion to admission, type of Methadone used (tablet or syrup), kind of exposure (addiction, accidental, intentional), hospitalization time and complication including aspiration pneumonia, hypotension, seizure, rhabdomyolysis, disseminated intravascular coagulation, anoxic encephalopathy, acute kidney failure, acute liver failure, cardiac arrest, deep coma and decreased blood sugar, and death) were investigated and recorded in a checklist. Data was analyzed by statistical package for the social sciences for windows (SPSS, Chicago, IL, USA) version 20.0. Mann-Whitney U Test, Chi-square, and Fisher Exact Test were used. *P* value less than 0.05 was considered to be significant.

Results

A total of 199 patients were studied. Most of the patients were males 62.8% and the rest were females 37.2%. Mean \pm standard deviation of the age was $33.86 \pm 13/33$ years (range: 18-85). The mean interval between Methadone ingestion and the first medical care was 5.6 h with median of 4h with the range of 0/5-24h. 101 patients (50.8%) were narcotic addicts. Intentional poisoning was observed in 56 patients (28.1%). Accidental poisoning was observed in 42 patients (21.1%). 183 patients (92%) consumed syrup of Methadone. Besides low level of consciousness, apnea, meiosis, and nausea and vomiting which are observed as the most common symptoms of methadone poisoning and also are common symptoms among poisoning with other opiates, we focused on other acute and more serious complications of methadone poisoning. 99 patients (49.7%) had hypotension, 79 patients (39.7%) had aspiration pneumonia, 35 patients (17.6%) had rhabdomyolysis, 23 patients (11.6%) had acute kidney failure, 14 patients (7%) were in hypoglycemic condition. 11 patients (5.5%) were in deep coma, 9 patients (4.5%) had cardiac arrest, 6 patients (3%) had seizure, 3 patients (1.5%) had acute liver failure, 1 patient (.5%) had anoxic encephalopathy, 1 patient (.5%) had disseminated intravascular coagulation and finally 1 patient (.5%) died because of Methadone poisoning. Mean length of hospital stay was 2.46 d (range: 1-17 d, median: 2 d).

Discussion

The general purpose of this study was to determine epidemiological and clinical characteristics of the patients poisoned with Methadone. According to the results obtained from this study, Mean \pm standard deviation of the age of Methadone poisoned patients was $33.86 \pm 13/33$ years (median 30) which is compatible with other studies. Most of the poisoning cases were narcotic addicts (50.8%). In this manner, the most important factors in poisoning with Methadone is its availability, namely the addicts receive it through MMT centers or buy it from the free markets. Moreover, in this way, the addict makes it accessible to his/her other family members. Therefore, limitation of access to Methadone and prevention of its sale in the free market can be an appropriate approach to prevent and reduce Methadone poisoning. Moreover, Methadone poisoning occurs either with the intention of suicide or accidentally. In our study, 28.1% of the patients had intentionally used the drug and 21.1% accidentally. According to results analysis by Chi-square Test we found significant relationship between sex and purpose of consumption ($p < 0.001$). The main purpose of

consumption in men was addiction and the main purpose of consumption in women was suicide. Our study showed that most type of consumed Methadone was syrup in both men and women (92%). According to results analysis by Chi-square Test we couldn't find significant relationship between sex and type of consumed Methadone. It may be because the type of Methadone which was more available in Kermanshah from 2013 till 2014 was syrup. According to data analysis by Mann-Whitney u Test, we found significant relationship between time interval from consumption till admission and complications such as aspiration pneumonia and rhabdomyolysis and acute kidney failure. We found out that with decrease of the time interval the risk of above mentioned complications was decreased. We strongly believe that time interval from consumption till admission plays great role in genesis or prevention of these complications. According to data analysis by Mann-Whitney u Test, we found significant relationship between time interval from consumption till admission and sex ($p=0.004$). Mean time interval from the time of consumption till admission was 6.6h (median 4h) for men versus mean time interval from the time of consumption till admission was 3.85 (median 2h) for women. With considering that mean time interval for women was significantly much lower than men and also frequency of acute complications in women was much lower compared to men so the time interval plays an important role in genesis of acute complications of MTD poisoning. This is supported by another research which has been done in Tehran, Iran. According to data analysis by Mann-Whitney u Test we could not find any significant relationship between duration of admission and sex ($p=0.551$). Our study is one of the first reports on Methadone-related poisoning complications from the Kermanshah of Iran. The results which were analyzed with Mann-Whitney u Test showed that there is significant relationship between age and sex ($p<0.001$). We found significant relationship between age and methadone poisoning complications such as acute kidney failure and hypotension by Mann-Whitney u Test. we saw frequency of acute kidney failure increased with increase of mean age and frequency of hypotension increased with decrease of mean age. Mean age for men was 36.97 ± 14.56 (median 33) versus mean age for women was 28.56 ± 8.79 (median 25). With considering that mean age of women was significantly much lower than men and also frequency of acute kidney failure in women was much lower compared to men. We can conclude in addition to delay in hospital admission, the risk of genesis of acute kidney failure related to methadone poisoning increased with increase of patients age. It can be concluded that Methadone poisoning can contribute to acute kidney failure in older ages and surely needs more medical attention in them. The mean age of our patients was similar to a Norwegian study. According to analysis of relationship between complications and sex by Fisher Exact Test we found significant relationship between sex and rhabdomyolysis ($p<0.001$). Rhabdomyolysis was more among men and also by Fisher Exact Test we found significant relationship between sex and acute kidney failure ($p=0.003$). Acute kidney failure was more among men. By Fisher Exact Test we found significant relationship between sex and aspiration pneumonia ($p=0.027$). Aspiration pneumonia was more among men. By Fisher Exact Test we found significant relationship between sex and hypotension ($p=0.001$). Hypotension was more among women. This is so because as we mentioned above the mean age of women was significantly much lower than men and we showed hypotension as complication of methadone poisoning decreased with decrease of age. We could not find a significant relationship between sex and other complications of Methadone poisoning by Fisher Exact Test. We found significant relationship between rhabdomyolysis and acute kidney failure ($p<0.001$). We found that frequency of acute

kidney failure was more among patients with rhabdomyolysis so we can consider rhabdomyolysis as a great risk factor for genesis of acute kidney failure. Meanwhile our study showed that most of the complications occurs in men so we believe in addition to age and time interval between Methadone consumption and admission there is another factor that plays an important role in genesis of complications related to Methadone poisoning. In men 91 patients (72.8%) were addicts and in women only 10 patients (13.5%) were addicts. According to analysis with Chi-square Test we found significant relationship between addiction and some complications of Methadone poisoning such as aspiration pneumonia and rhabdomyolysis. In addicts compared to non addicts these two complications were more and with consideration of this fact that rhabdomyolysis plays a great role in genesis of acute kidney failure subsequently addicts are in greater danger of Methadone poisoning complications compared to non addicts. So we can conclude that acute toxicity in patients who were on daily dose of Methadone (acute on chronic toxicity) can cause much more complications in contrast to women who consumed it accidentally or for suicide and probably for the first time. One important limitation in our study was different amounts of Methadone ingested by studied patients, which may definitely affect the clinical manifestations and also outcome.

Conclusion

In conclusion, considering the Methadone toxicity this study showed that narcotics addiction, attempt to suicide, accidental poisoning, age, gender, delayed hospital presentation, acute toxicity in patients who were on daily dose of Methadone (acute on chronic toxicity) were of the most important factors effective in Methadone poisoning, which should be considered in the public training and prevention of poisoning. Rhabdomyolysis can be considered as a great risk factor for genesis of acute kidney failure in patients with Methadone poisoning.

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