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The Evaluation of Clinical and Paraclinical (Laboratory or ECG) in Methadone Toxication

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ABSTRACT

Background

Nowadays, drug abuse is increasing globally, and methadone toxicity, which is also available as addiction treatment, has also increased. Therefore, due to the increased availability of methadone and the novelty of its toxication phenomena, this study aimed to determine the prevalence of methadone toxicity and its Clinical laboratory findings was done.

Materials and Methods

In this study, the cases of 214 patients who had referred to Razi Hospital in Guilan province due to methadone toxication were investigated. The researcher recorded the necessary information through the patients' files. Analyzing the collected data using SPSS software version 19 and using central indicators and dispersion of statistics, including Mean, standard deviation and statistical samples, were estimated significantly ($P < 0.05$).

Ethical Considerations

Honesty and fidelity in writing the text have been observed.

Findings

In this study, the patients' mean age was 30.52 years and 75% of the male patients. Nearly 40% of the patients were drug addicts, 25.5% of the addicts were under the supervision of methadone maintenance centres, and 34.5% were none addicted. The average dose of methadone in these cases was 35.5±35.7 mg. The most common clinical finding was respiratory depression and then decreased consciousness. The most common result of the ECG in these patients was prolonged QT. 34.6% of the patients had high SGPT.

Conclusion

Methadone toxicity can lead to serious clinical and Para clinical symptoms that require accurate and comprehensive evaluations to reduce these complications.

Key words

Methadone, Toxicity, Heart Disease.

How to Cite this Article

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INTRODUCTION

Today, drug abuse is on the rise worldwide, and no age group, not even children and infants, is immune to its destructive and even fatal effects. The picture of drug use in society is constantly changing, and every day we encounter new and more dangerous compounds. Methadone toxication, which is available as an addiction drug to addicts, is rising [1],[2]. Opium dependence is a common problem in various societies, and maintenance therapy with its agonists is currently used for opium dependence. One of these agonists is methadone [3]. Methadone is a synthetic opioid with a long half-life and is the drug of choice for opioid addiction and pain control [4]. methadone replacement therapy in Iran's centres (MMT)[1] has been started since 2003 and has gradually expanded [5]. Increased methadone use, on the one hand, and not taking adequate measures for prevention, makes this toxication a serious threat to all society members [6].

Symptoms of methadone toxication, like those of other opioids, include decreased level of consciousness, decreased respiratory rate, and myotid pupils. Another symptom of methadone toxication is acute non-cardiac pulmonary edema. Therapeutic measures in methadone toxication include vital and supportive measures and stabilization of the patient, and then, the second antidote administration is Naloxone and, if necessary, gastric lavage and administration of Charcoal [7].

Numerous studies have been performed on patients with methadone toxication in different age groups (children and adults) that showed differences in the incidence of clinical symptoms and outcome treatment [8],[9]. In the history of methadone therapy, methadone was first used as a heroin replacement therapy in 1964 in New York. Methadone therapy has also been introduced in Europe since the late 1960s in response to the widespread use of heroin. Sweden then pioneered methadone therapy in 1967 and the Netherlands and the United Kingdom in 1968. But the official start of methadone treatment in some countries, such as Belgium, was delayed until 1967. In 2002, approximately 215,600 patients in the United States were treated with methadone, and in 2004, about 47 countries began the program, with 500,000 patients worldwide [10]. In Iran, this drug has been included in the country's medical system since 2005, and currently, more than 3,000 centres in the country provide this drug to patients based on the national treatment protocol. Since 2009, methadone has been used only in maintenance therapy [11].

This medicine may cause side effects in consumers. Complications of methadone include cerebrospinal complications (12), gastrointestinal complications, genitourinary complications, skin complications, ENT[2]

[1]- Methadone Maintenance Treatment

[2] - Ear, Nose and Throat

complications, and cardiovascular complications [13]. At present, few studies on the side effects of methadone in the Iranian population are available in our country, and most of these studies have been performed on a specific complication. Also, because currently, the national protocol does not prescribe methadone to evaluate drug side effects as part of the work process, while in clinical evaluation and during interviews with patients, physical complaints are raised in this regard. On the other hand, patients themselves may tolerate annoying symptoms due to the need to take medication. While this can severely affect their quality of life, it seems necessary to first evaluate the side effects of methadone to provide an introduction to a targeted questionnaire to assess the physical side effects of methadone. Therefore, we designed this study to review clinical and Para clinical findings (laboratory and ECG) in patients admitted to Razi Hospital in 2016 due to methadone toxication.

MATERIALS AND METHODS

The present study is a retrospective cross-section. The study population is all patients referred to Razi Hospital in Guilan province in 2016 due to toxication and were over 12 years old. Methadone toxication and age over 12 years were considered inclusion criteria, and suspicious cases or cases associated with other toxications were considered exclusion criteria. The required information was counted by sampling so that all the files of patients diagnosed with methadone toxication who were admitted to the toxication ward of Razi Hospital in 2016 were included in the study. The prevalence of methadone toxication in the ward of poisoned patients admitted to the hospital and its demographic information, including age, gender, patients' education, intentional or accidental, mortality rate and disease outcome, was recorded by the researcher information forms and finally statistically analyzed.

On the other hand, all information related to laboratory findings and ECG findings were extracted from patients' records. The collected data were analyzed using SPSS software version 19 and using central indicators and dispersion of statistics: Mean, standard deviation, and 95% confidence interval. Independent T and ANOVA tests with a significant level ($P < 0.05$) were considered statistically significant. Data collection was performed during the approval and licensing process and obtaining the code of ethics with the number IR.GUMS.According to the entry and exit criteria, REC.1397.382 from Guilan University of Medical Sciences between Aprils to March 2016. The information obtained from the patients' files and the patient's name remained confidential, and the research results are only to prepare the relevant article and statistical analysis.

FINDINGS

In this study, the files of 214 patients were included in the study. The mean age of

patients was 32/10±29/35 years, with a minimum age of 17 and a maximum age of 56 years. In this study, patient mortality was observed that out of 214 patients studied, 34 (16%) patients had died due to methadone toxication. Examination of patients' cognitive information showed that 75.2% were male, 35.5% were aged 31-40 years, 58.9% were married, 76.1% were urban, 64% were self-employed, and 44.8% had undergraduate education. 40.1% addicted, 57% of methadone toxication was arbitrary, 91.2% had no history of suicide, 61.2% had syrup toxication, and 54.3% had no naloxone. Other cognitive information of patients is given in Table (1).

Table (1): Distribution of demographic variables

	Component	Number	Percent
Gender	Male female	161 53	75/2 24/8
Age	20 ≥ 21-30 31-40 41-50 51-60	18 42 76 57 21	8/4 19/6 35/5 26/2 9/81
Marital Status	Married Single	126 88	58/9 41/1
Address	City Village	163 51	76/1 24/7
Job	Free Employee Retired Unemployed housewife	137 8 10 39 20	9/3
Education	High school Diploma University	96 79 39	44/8 36/9 18/2
History of substance use	Non-addicted Under the supervision of methadone storage centres Addicted	74 54 86	34/5 25/2 40/1
How to poison	Self-consumption by accident Suicide Under treatment and under the supervision of a physician	122 73 15 ٤	57 34/2 7 1/8
Suicide history	Has a history of suicide No history of suicide	19 195	8/8 91/2
The type of methadone used leads to toxication	Injectable Tablet Syrup	8 75 131	3/7 35/1 61/2
Use of Naloxone	Naloxone onsumption Do not take naloxone	98 116	45/7 54/3

Clinical findings show that mean heart rate was 52/4±77/88, respiratory rate was 08/1±10/15 per minute, mean systolic blood pressure was 28/18±84/109, and diastolic blood pressure was 77/5±49/74 Mm. of mercury .Respiratory symptoms were also the most common symptom in methadone toxication patients. On biochemical evaluation (blood sugar, sodium, potassium, calcium, phosphorus, SGPT, SGOT, creatinine, bicarbonate, arterial CO2 and PH), 100% patients had arterial CO2 above 40. The electrolyte and blood status of patients and the prevalence of patients whose electrolyte and blood status was

outside the normal range are shown in Table (2) .In the evaluation of ECG findings, the most common symptom in these patients was QT prolongation. Most of the ECGs observed in this study are sinus tachycardia, U wave, T inversion.

Table (2):Frequency and electrolyte and blood status of patients

Variable	Serum level	Abundance	Percent	Average	Standard deviation
Blood sugar (mg/dl)	b) High than greater (200 Low (less than 90)	10 0	4/7 0	19/1 23	42/26
Sodium (meq / L)	(B)) Top than greater 145(Low (less than 132)	31 10	14/5 7/4	42/1 40	41/5
potassium (meq / L)	b) High 5 than greater (Low (less than 3.5)	10 0	4/7 0	46/4	4/0
Calcium (meq / L)	b) High than greater (11 Low (less than 8)	0 52	0 3/24	59/8	51/0
Phosphorus (meq / L)	the) High (6 of greater Low (less than 3)	0 0	0 0	54/4	34/0
SGOT	High (b greater than 100)	59	6/27	62/9 7	88/46
SGPT	Top (more than 100)	74	6/34	29/9 9	82/45
Bicarbonate	Top (more than 25)	104	72	29/2 4	1/3
CO2 Arterial	Top (more than 40)	214	100	17/4 7	98/2
PH	Respiratory acidosis Metabolic one acidosis Respiratory alkalosis Metabolic alkalosis	76 48 13 37	5 / 35 4 / 22 6 2 / 17	3/7	35/5 22/4 6/07 28/17
Creatinine	Top (more than 1.5)	1	4 / 0	13/1	15/0

Here was a significant relationship between ECG findings and methadone toxication directly related to the duration of methadone use ($P < 0.05$). There was no meaningful relationship between addiction, age, gender, residence, occupation and marital status with clinical and paraclinical findings.

DISCUSSION

Methadone toxication is one of the most common toxications, and many patients go to emergency rooms and toxication clinics due to methadone toxication [3]. This study aimed to determine the frequency of clinical and paraclinical findings (laboratory and ECG) in patients admitted to Razi Hospital in Rasht in 2016 due to methadone toxication and reviewing the files of 214 patients. In this study, the patients' median age was 35.29 years, and 75% were male. Also, most of the patients were married and lived in the city. 70% of patients had no history of methadone use, and 45% had a university degree. According to this and other studies, the prevalence of methadone use is higher among young people [14]. Reasons for young people to use methadone include misconceptions such as "methadone is not a drug", "methadone is a cure for addiction", "methadone does not test positive for addiction", "methadone use has no side effects" among young people, and it is common for people with low levels of

education. Therefore, more research is needed in this area.

More than 60% of methadone toxication has been through methadone syrup. In recent years, the use of methadone syrup to quit addiction has been increasing. Supply and packaging of this drug are usually non-standard, and beverage bottles or containers of other drugs are used to store it. Also, some pharmaceutical companies often produce methadone with a fruit flavour. Therefore, this drug delivery method, along with its colourless appearance, has often caused mistakes in the use of drugs instead of water or other drugs, especially by children [15],[16]. Methadone has become popular because of its unique properties in the treatment of pain and drug addiction. But patients are at risk for the resulting cardiotoxicity.

The effectiveness of methadone against these side effects should be weighed, and physicians should consider ways to minimize these side effects. In this study, nearly 40% of drug addicts, 25.5% of addicts were under the supervision of methadone maintenance centres, and 34.5% were non-addicts. Arbitrary consumption was observed in 57% of patients. This indicates the important issue of educating and informing people in the community to prevent methadone toxication, especially those treated with methadone in addiction treatment centres. The most common symptom in patients with methadone toxication was respiratory symptoms, which was the most common clinical finding of respiratory depression in line with other studies [18],[20]. Because overuse of methadone leads to dangerous side effects such as slowing down the breathing and eventually stopping it, which if not treated properly and promptly, may lead to suffocation and death of the patient.

Other common symptoms in these patients were decreased consciousness level, so that the consciousness of 19.6% decreased. Gradual disturbance of consciousness level such that the patient initially becomes confused and drowsy, and gradually the disturbance of consciousness becomes deeper and may even lead him to a coma. Another common clinical symptom was 19.2% of myotid pupils, which is consistent with the study of Sidlo et al. [21].

Laboratory findings show that 100% of patients had arterial CO2 above 40. This result indicates acidosis in these patients. Findings from Farnaghi et al. Indicate that the most common laboratory finding is respiratory acidosis [22]. Also, 27.6% of patients had high SGOT enzyme, and 34.6% had high SGPT enzyme, which is probably due to hepatitis. Hepatitis is inflammation of the liver, and in a study by Alikhani et al., Which was performed on deaths due to methadone toxication, it was reported that 45% of the deceased had positive pathological findings in the pathological examination of the liver [23]. Darke et al. Also reported a pathological prevalence of 80.7% in their study [24]. Chronic liver

disease is common in people who take methadone frequently. Due to this drug's hepatic metabolism, which is via cytochrome P450, it is necessary to adjust the therapeutic dose for liver patients in people treated with methadone [17].

The most common ECG finding in the studied patients was a prolongation of QT interval, and a significant relationship was found between ECG findings and methadone toxication, which was directly related to the duration of methadone use. The reason for the longer QT interval is that methadone interferes with voltage-dependent potassium channels in the heart [25]. Also, high levels of plasma methadone and their combination with other drugs and stimulants lead to prolongation of QT interval and various arrhythmias [19]. Studies also show that the most common finding on the ECG increased the QT interval between methadone toxication [26],[28]. In the study by Geoffrey et al., Although more than a third of patients had a longer QT interval, no significant relationship was found between methadone dose and QT interval [27]. Also, in the study of Sheibani et al., No significant relationship was found between methadone toxication and ECG findings [29]. Lack of information about patients, signs and symptoms of toxication and actions taken in patients' files were among the limitations of this study. Therefore, incomplete files were excluded from the study.

DISCUSSION

Methadone toxication can lead to serious clinical and paraclinical symptoms of toxication, and it is life-threatening. On the other hand, due to increased methadone use among young people and the high prevalence of toxication, especially its abuse, methadone use management in addiction treatment centres and government of related factors in different age groups to reduce mortality seems necessary. Therefore, accurate and comprehensive evaluations should be performed to reduce the side effects of methadone.

ETHICAL CONSIDERATION

Authenticity of the texts, honesty and fidelity has been observed.

AUTHOR CONTRIBUTIONS

Planning and writing of the manuscript was done by the authors and Co-author.

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CONFLICT OF INTEREST

No conflict of interest was reported by the author.

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