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Investigating the relationship between blood lead concentrations and kidney function tests in drug abusers admitted to Babol Hospital, Iran: A short report

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Short report

Abstract

BACKGROUND: The amount of impurity and addition of lead in drugs has grown increasingly. This study investigated the relationship between blood lead concentrations and kidney function tests.

METHODS: This cross-sectional-analytical research was conducted between October and March 2016 in Babol City, Mazandaran Province, Iran. 25 patients who were addicted to opium (case group) and 25 patients who had no history of drug use (control group) (30-60 years old) were randomly selected and paraclinical tests of the patient's blood and urine were performed. SPSS software, Pearson's correlation coefficient test, independent samples t-test, and Mann-Whitney test were used to analyze the data.

RESULTS: Between blood lead concentration and uric acid ($r = 0.33$, $P = 0.01$), glomerular filtration rate (GFR) ($r = 0.6$, $P = 0.07$), protein (24-hour urine) ($r = 0.46$, $P = 0.001$), 8-hydroxy-2'-deoxyguanosine (8-OHdG) ($r = 0.67$, $P < 0.001$), and total creatinine (24-hour urine) ($r = 0.3$, $P = 0.03$), there was a direct and significant relationship. There was an inverse and important relationship between GFR and protein (24-hour urine) ($r = -0.31$, $P = 0.02$) and serum creatinine ($r = -0.66$, $P \leq 0.001$). There was a direct and significant relationship between GFR and creatinine urine ($r = 0.5$, $P < 0.001$) and total creatinine (24-hour urine) ($r = 0.4$, $P = 0.002$).

CONCLUSION: Drug users had higher levels of lead than the control group. The high concentration of lead in the body harms the kidney function.

KEYWORDS: Blood Lead Concentrations; Kidney Function Tests; Drug Abusers

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Introduction

The issue of addiction in Iran has been growing in recent years. In 2014, the prevalence of addiction in different provinces varied from 2.5% in Tehran Province to 17% in Hormozgan Province. The highest frequency of addiction was reported in the age group of 20-35 years, and about 60%-70% of addicts were illiterate or low-educated people.[1] People who use narcotics suffer from chronic lead poisoning due to the presence of lead impurity in narcotics in long-term consumption of narcotics.[2] Lead levels of 30 to 60 grams per deciliter in the blood of the renal system cause kidney failure in severe conditions.[3] Oxidative stress leads to oxidative damage to deoxyribonucleic acid (DNA). 8-hydroxy-2'-deoxyguanosine (8-OHdG) is the most common stable product of oxidative DNA damage caused by reactive oxygen

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species (ROS).[4]

Soltaninezhad et al. showed that the amount of lead in opium was 214.6-266.3 mg/L.[5] Abdou and Hassan showed that lead acetate increased oxidative stress in tissues and increased urea and creatinine levels.[6] Ghasempouri et al. reported that the most common clinical symptoms of lead-poisoned addicts were abdominal pain (91%), constipation (54%), and weakness due to anemia (53%), respectively. The average serum lead level was reported to be 95.03 mg/dl before treatment and 56.33 mg/dl after chelator drug treatment.[7] Sabzevari et al. reported that the serum level of lead in the blood of opium-addicted mothers was 9.22 ± 30.40 µg/dl and in healthy mothers, it was 1.5 ± 3.2 µg/dl.[2]

Opium and its derivatives are the most commonly abused drugs in Iran. Intentional contamination of drugs with lead is a serious and dangerous fact that has been revealed recently, but there are no reliable findings regarding the abundance and effects of this criminal act on the health of addicts. Lead is present in the form of impurity and adulteration in illegal opium that is smuggled and distributed in Iran. Moreover, related studies have been done less in the northern provinces of Iran. This research aims to evaluate blood lead concentration in addicted and non-addicted patients in Babol City, Mazandaran Province, Iran.

Methods

This cross-sectional-analytical study was conducted in 2016 (during 6 months, October to March) in Babol City, on 50 male patients (age group of 30-60 years old) hospitalized in Ayatollah Rouhani Teaching Hospital, Babol City, who were suspected of lead poisoning and for whom the doctor had requested a blood lead concentration test and a test to confirm the consumption of opioids. 25 men who were addicted to drugs (opium) were selected as the case group and 25 men who had no history of opium use were selected as the control group. The formula for calculating the sample size was determined based on the first type of error at the 0.05 level and the second type at the 0.20 level.

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 \left[P_1(1-P_1) + P_2(1-P_2)\right]}{(P_1 - P_2)^2}$$

Male and hospitalized patients whose lead test was positive were included in the study. Patients who had underlying diseases related to the kidney were excluded from the study.

Detailed history of the patient, blood sampling, urine test, and blood test of the patients were done by the laboratory technicians. Urine tests for testing protein (24-hour urine) (mg/dl), urine creatinine (mg/dl), and total creatinine (24-hour urine) (mg) (Pars Azmoon Kit, Iran) were performed. A multi-drug 10-panel test (Hannan Teb Pars Kit, Iran) was used to perform an addiction test using urine samples.

The patient's blood was taken for tests related to 8-OHdG, uric acid (mg/dl), serum creatinine (mg/dl) (Pars Azmoon Kit, Iran), and glomerular filtration rate (GFR). An atomic absorption-6200 device (Shimadzu, Japan) was used to measure lead in blood samples. The lead calibration curve was previously drawn in the machine, and the amount of lead in the samples was calculated by the machine with the help of the calibration curve at a wavelength of 217 nm. The minimum detectable amount of lead in samples by this method is 0.1 ng/ml. To measure serum 8-OHdG, an enzyme-linked immunosorbent assay (ELISA) (Pars Azmoon Kit, Iran) was used.

Pearson's correlation coefficient was used to check the normal distribution of data from the Kolmogorov-Smirnov test and the correlation of quantitative variables with each other. Independent samples t-test and Mann-Whitney (non-parametric test to

compare the mean of two independent groups) were used to compare the average of different variables in the case group with the control group. Data analysis was done by SPSS software (version 20, IBM Corporation, Armonk, NY, USA) ($P < 0.05$).

Results

The average blood lead concentration in the case group (77.85 ng/ml) was higher than the control group (12.24 ng/ml). The average concentration of uric acid (6.73 vs. 4.19), GFR (65.77 vs. 65.73), 8-OHdG (2.20 vs. 0.26), serum creatinine (1.50 vs. 1.17), total creatinine (24-hour urine) (1.50 vs. 1.17), urine creatinine (2700 vs. 1500), and protein (24-hour urine) (520.00 vs. 161.60) were higher in the case group than the control group, and a significant correlation was seen between the two case and control groups with all variables ($P < 0.05$) (Table 1).

Between lead concentration with uric acid ($r = 0.33$, $P = 0.01$), protein (24-hour urine) ($r = 0.46$, $P = 0.001$), 8-OHdG ($r = 0.67$, $P < 0.001$), and total creatinine (24-hour urine) ($r = 0.3$, $P = 0.03$), there was a direct and significant relationship. There was an inverse and significant relationship between GFR with protein concentration (24-hour urine) ($r = -0.31$, $P = 0.02$) and serum creatinine ($r = -0.66$, $P \leq 0.001$). There was a direct and significant relationship between GFR with urine creatinine concentration ($r = 0.54$, $P < 0.001$) and total creatinine (24-hour urine) ($r = 0.42$, $P = 0.002$) (Table 2).

Discussion

This study aimed to investigate the relationship between lead blood concentration and kidney function tests in hospitalized drug addicts. The results showed that blood lead concentration in the group of people poisoned with lead (people with drug addiction) was significantly higher than the control group (case group: 77.85 ng/ml and control group: 12.24 ng/ml). These results indicate that the drugs used by these people were contaminated with lead. Lead increase in blood and urine are related to kidney failure and disorders and preventing the excretion of excess substances through the kidney. Moreover, there was a statistically significant difference between the concentration of various blood and urine parameters in the case group and the control group; it was significantly higher in the case group than the control group.

Table 1. Comparison and correlation of lead averages, factors related to blood and urine in case (n = 25) and control (n = 25) groups

Variables	Group	Mean ± SD	P
Lead (µg/ml)	Case	77.85 ± 47.18	< 0.001
	Control	12.24 ± 3.77	
Uric acid (< 0.6 mg/dl)	Case	6.73 ± 2.75	< 0.001
	Control	4.19 ± 0.84	
GFR > 60 ml/min/1.73m^2	Case	65.77 ± 26.50	0.994
	Control	65.73 ± 12.80	
8-OHdG (ng/ml)	Case	2.20 ± 0.31	0.001
	Control	0.26 ± 0.23	
Serum creatinine (0.9-1.3 mg/dl)	Case	1.50 ± 0.50	0.003
	Control	1.17 ± 0.72	
Total creatinine (24-hour urine) (500-2000 mg/day)	Case	2700.00 ± 1200.00	0.040
	Control	1500.00 ± 600.00	
Urine creatinine (955-2936 mg/day)	Case	3200.00 ± 1500.00	0.040
	Control	2500.00 ± 1000.00	
Protein (24-hour urine) (< 150 mg)	Case	520.00 ± 378.00	< 0.001
	Control	161.60 ± 78.00	

GFR: Glomerular filtration rate; 8-OHdG: 8-hydroxy-2'-deoxyguanosine; SD: Standard deviation

Table 2. The relationship between the mean factors related to blood and urine with lead and glomerular filtration rate (GFR) in case (n = 25) and control (n = 25) groups

Variables	Lead (µg/ml)	GFR (ml/min/1.73m^2)
Uric acid (< 0.6 mg/dl)	r = 0.33*, P = 0.010	r = -0.02, P = 0.870
Protein (24-hour urine) (< 150 mg)	r = 0.46**, P = 0.001	r = -0.31*, P = 0.020
8-OHdG (ng/ml)	r = 0.67**, P < 0.001	r = 0.52**, P = 0.010
Total creatinine (24-hour urine) (500-2000 mg/day)	r = 0.30*, P = 0.030	r = 0.42**, P = 0.002
Serum creatinine (0.9-1.3 mg/dl)	r = 0.17, P = 0.220	r = -0.66**, P < 0.001
Urine creatinine (955-2936 mg/day)	r = -0.23, P = 0.100	r = 0.54**, P < 0.001

*The relationship is significant at the 0.05 level; **The relationship is significant at the 0.01 level
GFR: Glomerular filtration rate; 8-OHdG: 8-hydroxy-2'-deoxyguanosine

In line with the present study, Chen et al. showed that contact with lead harmed the protein pattern of kidneys in a mouse model.[8] Chronic lead poisoning caused an increase in the amount of 18 types of proteins in the kidneys of rats. In our study, the average protein concentration (24-hour urine) (520.00 vs. 161.60) in lead-poisoned subjects was statistically much higher than in the control group. Besides, the 24-hour urine protein concentration and GFR were inversely related. Therefore, it can be concluded that with increasing GFR, the amount of protein in urine decreases and vice versa. On the other hand, with the increase in the blood level of lead, the amount of protein excretion through the kidneys increased significantly during 24 hours. Therefore, high blood lead levels can increase protein excretion from the kidneys.[8]

In the study by Fadrowski et al., the median blood lead concentration was 1.2 µg/ml and the median GFR was 44.4 ml/min/1.73m^2. In this study, for every µg increase in blood lead concentration, the GFR decreased by about 1.2 ml.[9] In our study, the GFR in addicted patients (65.77 ml/min/1.73m^2), with a high concentration of lead in the blood, was higher than the group of non-addicted patients (65.73 ml/min/1.73m^2). However, there was no significant relationship between the blood lead concentration of people in the case and control groups with the GFR. A study by Pan et al. investigated the effect of 6-valent chromium on oxidative damage to DNA and lipid peroxidation. To investigate the genomic damage caused by oxidative stress caused by 6-valent chromium, 8-OHdG was used and measured in the urine of patients.[10]

Roy et al. reported that there was no direct correlation between blood lead concentration and urinary 8-OHdG concentration.[11] In our study, the level of 8-OHdG in the blood of people who suffered from lead poisoning (people with drug addiction) was statistically significantly higher than the control group (2.20 ng/ml vs. 0.26 ng/ml). Moreover, the investigation of the relationship between the level of lead in the blood of people and the level of 8-OHdG showed that with the increase in the level of lead in the blood of people, the amount of this substance in the blood also increased.

This difference in results could be because Roy et al. study was conducted on children and our study was conducted on addicted and non-addicted adults. A high concentration of lead in the body can harm the balance of parameters such as creatinine, protein, and uric acid and cause oxidative stress in the DNA of cells, which is indicated by the appearance of substances such as 8-OHdG in the blood. An increase in lead can cause the destruction of nucleotides and the genetic material of cells, which is indicated by the appearance of nucleotide metabolites (8-OHdG) in the blood.[11]

According to the results of Mohammadi et al., chronic exposure to lead poisoning played a role in the occurrence and change of the pattern of gallstones and appendicitis.[12] In our

study, the amount of uric acid (6.73 mg/dl vs. 4.19 mg/dl), serum creatinine (1.50 mg/dl vs. 1.17 mg/dl), total creatinine (24-hour urine) (1.50 mg/dl vs. 1.17 mg/dl), and urine creatinine (2700 mg/dl vs. 1500 mg/dl) in the case group was higher than the control group. The direct relationship between blood uric acid concentration, urine creatinine, and urine total creatinine with GFR shows that the increase in creatinine causes an increase in GFR. Therefore, it can be concluded that the high concentration of blood lead can increase the concentration of uric acid and creatinine, and as a result, kidney dysfunction. Consequently, the presence of lead in the blood can harm the internal organs of the body that are responsible for the elimination of waste materials.[12] Finally, similar to the study of Fatemi et al.,[13] who showed that there were oral drugs containing lead in Iran, it can be concluded that drug users have a higher blood level of lead than other people and the negative effect of high concentration of lead has a significant effect on kidney function.

Therefore, the necessary information to increase the level of awareness of the people in society about the use of drugs, especially drugs contaminated with lead, more monitoring and control over the illegal distribution of drugs, and coordination between the emergency department and the poisoning department in cases of poisoning caused by the use of drugs. Contaminated with lead, it is suggested that more studies be carried out in the field of identifying other contaminants in drugs, including opium. The limitations of the present study included the small number of examined samples, geographical and hospital limitations (in one region), and the study of men. In this regard, it is better to conduct investigations in a larger sample size, on women and men, and in a larger number of medical centers.

Conclusion

The average concentration of blood lead, uric acid, GFR, 8-OHdG, serum creatinine, total creatinine (24-hour urine), urine creatinine, and protein (24-hour urine) in the case group was higher than the control group and there was a significant relationship between the two case and control groups. There was a direct and significant relationship between lead concentration and uric acid, protein (24-hour urine), 8-OHdG, and total creatinine (24-hour urine). There was an inverse and significant relationship between GFR, protein concentration (24-hour urine), and serum creatinine. Moreover, there was a direct and significant relationship between GFR with urine creatinine concentration and total creatinine (24-hour urine).

Conflict of Interests

Authors have no conflict of interests.

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