Original Article

Blood Lead Levels, Hemoglobin, and Liver Enzymes in Opium-Dependent Addicts

Farzaneh Montazerifar, Mansour Karajibani[1], Maryam Lashkaripour[2], Manijeh Sayyad Mollashahi[3], Abbas Ali Niazi[4], Moghgan Soltan Mohammadi[5], Samaneh Rahimi Helari[5]

Department of Nutrition, Pregnancy Health Research Center, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran, [1]Department of Nutrition, Health Promotion Research Center, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran, [2]Department of Psychiatric, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran, [3]Department of Psychiatric, Baharan Psychiatric Hospital, Zahedan University of Medical Sciences, Zahedan, Iran, [4]Department of Pathology, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran, [5]Department of Nutrition, Student Scientific Research Center, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

Address for correspondence:
Dr. Farzaneh Montazerifar, Dr. Mansour Karajibani, Department of Nutrition, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran.
E-mail: fmontazerifar@gmail.com

Access this article online

Website: www.ijpvmjournal.net/www.ijpm.ir

DOI: 10.4103/ijpvm.IJPVM_303_18

Quick Response Code:

Abstract

Background: Opium addiction, as a major health problem, has been reported in Middle East countries. Recently, contaminated opium has been reported as a probable source of lead poisoning. Thus, the aim of this study is to evaluate blood lead levels (BLL), liver enzymes, and hemoglobin (Hb) concentrations in opium-dependent addicts with healthy controls. **Methods:** In a cross-sectional study, 75 opium-addicted men (case group) referred to Zahedan Baharan Hospital were evaluated. A group of 75 nonaddicted men were selected as a control group. BLL, Hb, and liver enzymes levels were measured. Body mass index (BMI) was also calculated. **Results:** The case group had elevated BLL compared to the controls (19.1 ± 1.6 vs. 9.1 ± 0.4; $P < 0.0001$). Hb concentrations were significantly lower in the patients compared to the controls (13.3 ± 1.6 vs. 15.1 ± 1.3; $P < 0.0001$). A positive correlation was found between BLL and opium addict duration in the case group ($r = 0.52$, $P < 0.0001$). **Conclusions:** Due to the contamination of opium to lead, it seems that opiate addicts are at risk of lead poisoning. Thus, it is recommended that the blood lead level is frequently monitored to control the adverse effects of poisoning and prevent lead accumulation.

Keywords: *Hemoglobin, lead, liver enzymes, opium addiction*

Introduction

Opium addiction in the Middle East countries is recognized as a vital health problem. There is evidence showing the toxic effects of lead in drug abusers.[1] Lead (Pb) is a poisonous heavy metal that is quickly absorbed in the body through the inhalation and ingestion and affects many organ systems in human.[2-5] In the body, lead accumulates in liver, renal, bone, and blood.[6] Blood lead level (BLL) is the most reliable index of recent lead exposure.[7] Human exposure to lead and its compounds occur more often in occupations associated with the lead with different sources such as lead gasoline, industrial processes such as lead melting, pottery, the building of boats and the lead containing pipes, battery manufacturing and, recycling, and book printing.[5,8,9] In addition, new forms of nonoccupational lead intoxication such as oral utilization, intravenous injection, or inhalation of opium pills, crushed and suspended in water can also result in the accumulative of lead in the body. The possible poisoning effects of heavy metals including lead in heroin[10] and opiate dependents[6,8,11-14] have already been reported by other authors. Long-time exposure to lead can result in constipation, abdominal pain, irritability, muscle aches, headache, anorexia impaired respiratory function, reduce fertility in males, hypertension, blood disorders, brain, and nervous system damage, and severe kidney failure.[5,8,13]

Other deleterious effects of increased levels of blood lead have been reported, which also inhibit the synthesis of heme and reduce hemoglobin.[7,8] Although, there is no threshold level of lead in the blood, which can be considered safe or to be essential or beneficial for the body,[7] however, lead poisoning is diagnosed on the basis of elevated BLL ≥25 μg/dL.[8] Since 2012, the Centers for Disease Control and Prevention (USA) have identified standard high blood lead levels for adults 10 μg/dL.[15] Chelation therapy for reduction of lead level and its chemical effects (such as toxicity or physiological activity) by using some drugs including EDTA, succimer, or dimercaprol has been

How to cite this article: Montazerifar F, Karajibani M, Lashkaripour M, Sayyad Mollashahi M, Niazi AA, Soltan Mohammadi M, Rahimi Helari S. Blood lead levels, hemoglobin, and liver enzymes in opium-dependent addicts. Int J Prev Med 2021;12:3.

reported as a treatment indication in children and adults in the USA.[16] Given the contamination of opium with lead and its adverse effects on certain organ systems, it seems that evaluation of blood lead level in opium addicts to be important. Therefore, this study was carried out with the aim of evaluation of blood lead levels, hemoglobin, and liver enzymes in opium-dependent addicts with healthy controls.

Methods

A cross-sectional study performed on 75 opium-addicted men (case group) (mean age of 40.3 ± 10.7 years old; ranged 25–55 years) referred to a self-introducer unit of Baharan hospital located in Zahedan, Iran from January 2018 to May 2018. They were selected through systematic incidental sampling. All subjects used opium orally or by inhalation. Seventy-five nonaddicted men matched by age (mean age of 38.6 ± 10.5 years old; ranged 25–55 years), with no history of opium addiction, who accompanied the patients, were evaluated as a control group.

The subjects who had industrial occupations related to batteries, car radiator repairs, printers, and non-copying machines, and also drug abusers who used methadone, tramadol, cocaine, or heroin, and other opioids during ten or more years of addiction were excluded from the study. Informed consent was obtained from all patients and control subjects. Demographic characteristics, health status, addict duration, and type and model of opium consumption were fulfilled in a personal data questionnaire by interviewer.

Weight and height were measured in a standing position. BMI was calculated by weight (kg) divided by the square of height (m^2).

About 5 ml blood samples were taken from all subjects. Out of 5 ml, 2 ml whole blood samples was obtained in tubes containing EDTA for measuring of blood lead and hemoglobin and the rest were transferred in hemolysis tubes to measure liver function tests.

Blood lead levels were assayed using an atomic absorption spectrophotometer. Hemoglobin by Coulter (Sysmex, KX-21), and liver enzymes levels) ALT "Alanine transaminase; AST "Aspartate transaminase", ALK.P "alkaline phosphatase" and bilirubin) were determined using commercially available kits (Parsazmun, Tehran, Iran) with a Technicon RA-1000 system (Miles, Inc., Diagnostics Division, Tarrytown, NY).

The protocol of the study was approved by the Ethics Committee of Zahedan University of Medical Sciences, Iran (Approval date: 1396.08.21).

Statistical analysis

Data were analyzed by using SPSS software version 21 (SPSS, Inc., Chicago, IL, USA). The results are expressed as mean ± SD and mean ± SEM with range and frequency, as appropriate. Data were tested for normal distribution using the Kolmogorov– Smirnov test.

Student *t*-test was applied to compare the mean of normal distribution variables in the two groups. Mann-Whitney U test was performed for non-normal distribution variables. Spearman correlation coefficient was used to determine the relationship between variables. *P* value <0.05 was considered significant.

Results

The demographic characteristics of the studied subjects are summarized in Table 1.

Duration of addiction was 8.3 ± 0.7 years (ranged: 2–25 years). Body mass index (BMI) was significantly declined in patients group when compared to controls ($P = 0.007$). Around 52 patients (69.3%) had a history of opium ingestion and 23 patients (39.7%) inhaled.

As shown in Figure 1, the mean of BLL in opium-addicts was markedly increased as compared with the control group ($P < 0.0001$).

About 26.1% of the patients had BLL more than 20 µg/dL. All controls had BLL below toxic level ($P < 0.0001$) [Table 2].

Table 3 demonstrates the levels of hemoglobin and liver enzymes based on BLL categories in the case group compared to the control group. No significant difference was found between the patients. While, decreased Hb concentration and elevated ALK. *P* level was found in the

Table 1: Demographic characteristics of the studied group

Groups Parameters	Case (*n*=75)	Control (*n*=75)	*P*
Age (years)	40.3±10.7	38.6±10.5	0.62
BMI (kg/m^2)	22.6±4	24.8±5.7	0.007
Opium addict duration (years) (range)	8.3±0.7 (2-25)	-	-
Model of opium consumption *n* (%)			
Ingestion	52 (69.3%)		
Inhalation	23 (39.7%)	-	-

Data were expressed by mean±SD or *n* (%). BMI=Body mass index

Table 2: Frequency of BLL categories in studied groups

Groups	BLL (µg/dL)		
Frequency	<20	20-45	>45
Control			
n	75	0	0
%	100%	0%	0%
Case			
n	50	19	6
%	66.7%	25.3%	8%

χ^2=21.6 *P*<0.0001, Data were expressed by frequency: Number (percent), BLL=Blood lead level

patients compared to the control group (both, $P < 0.0001$), no significant difference was found between two groups with respect to AST, ALT, and bilirubin levels.

Regarding the model of drug consumption, as shown in Table 4, results showed that BLL and ALT levels were higher in those who used opium orally compared to inhalation ($P < 0.001$).

In patients with more than 10 years of addiction, BLL was markedly higher ($P < 0.0001$), and Hb concentration was lower ($P = 0.05$) compared to those under 10 years of addiction. As well, the liver enzymes levels were found to be slightly increased in those with more than 10 years of addiction, but the difference was not significant [Table 5].

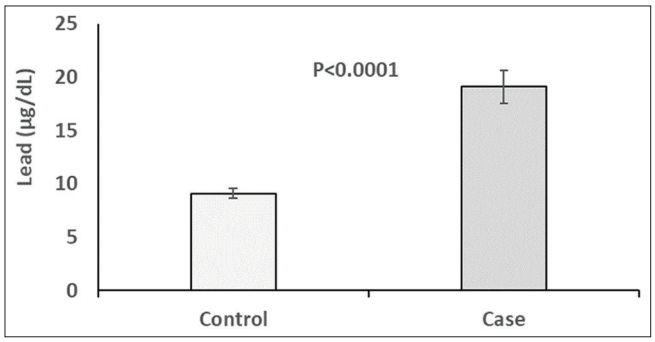

Figure 1: Mean levels of lead (µg/dL) in studied groups

A significant positive correlation between BLL and opium addict duration was found ($r = 0.52$, $P < 0.0001$). However, there was no such correlation between BLL and other parameters.

In addition, multiple symptoms including nonspecific abdominal pain, headache, weight loss, muscle aches, reduce appetite, irritability, confusion, nausea and vomiting, and constipation were presented in most patients ($n = 40$; 53.3%).

Discussion

The results of this study showed that the mean BLL in opiate patients was markedly higher compared to the control group. When the subjects were classified based on the BLL, 26.1% of the case group had BLL more than 20 µg/dL. Few studies performed on lead-contaminated opium demonstrated that opiate addicts have elevated

Table 3: Mean levels of hemoglobin and liver enzymes in studied groups based on the BLL classification

Groups BLL (µg/dL)	Case		*P*	Control	*P*
Parameters	<20 (*n*=50)	>20 (*n*=25)			
Hemoglobin (g/dL)	13.5±0.24 (8-18)	13.1±1.5 (6-17)	0.94	15.1±0.15 (10.7-17.2)	0.0001
AST (IU/L)	24.1±2.9 (6.5-143)	22.6±1.9 (12.5-152)	0.24	22.9±1 (14-80)	0.71
ALT (IU/L)	23.5±3.3 (3-130)	24.9±5.1 (9.5-137)	0.88	23.8±1.6 (14-118)	0.44
ALK.P (IU/L)	231.8±0.79 (20.4-442)	256.8±16.2 (136-542)	0.17	185.1±8.2 (105-645)	0.0001
Total bilirubin (mg/dL)	0.72±0.05 (0.1-1.5)	0.82±0.05 (0.3-1.3)	0.49	0.85±0.04 (0.2-2)	0.3

Data were expressed by mean±SEM and range because the data were not normally distributed. BLL=Blood lead level; ALT=Alanine transaminase; AST=Aspartate transaminase, ALK.P=Alkaline phosphatase

Table 4: Mean levels of Lead, Hemoglobin and Liver enzymes in opium addicts based on the method of use drug

Model of drug consumption Parameters	Ingestion (*n*=52)	Inhalation (*n*=23)	*P*
BLL (µg/dL)	28.5±6.8 (8.2-67.4)	12.6±1 (5.3-27.8)	<0.001
Hemoglobin (g/dl)	13.2±0.34 (6-14)	13.5±0.27 (8-18)	0.89
AST (IU/L)	20.1±2.6 (10.6-18.2)	21.3±1.5 (10-17.8)	0.91
ALT (IU/L)	24.5±4.6 (3-137)	19.4.1±2.5 (14-35.5)	<0.01
ALK.P (IU/L)	239.4±13.2 (88-442)	236±14.5 (20.4-395)	0.94
Total Bilirubin (mg/dL)	0.81±0.06 (0.3-1.5)	0.66±0.12 (0.1-1.2)	0.089

Data were expressed by mean±SEM and range because the data were not normally distributed. BLL=Blood lead level; ALT=Alanine transaminase; AST=Aspartate transaminase, ALK.P=Alkaline Phosphatase

Table 5: Mean levels of Lead, Hemoglobin and liver enzymes in case group based on the addict duration

Opium addict duration (yrs) Parameters	<10 (*n*=52)	>10 (*n*=23)	*P*
BLL (µg/dL)	14.2±0.7 (5.3-20.4)	30.5±2.3 (6.8-67.4)	0.0001
Hemoglobin (g/dL)	13.7±0.24 (8-18.2)	12.3±1.9 (6-17)	0.05
AST (IU/L)	22.6±1.8 (6.5-73)	24.9±4.3 (10-143)	0.08
ALT (IU/L)	22.6±3.7 (3-97)	24.9±3.8 (7.5-137)	0.09
ALK.P (IU/L)	236±11.7 (20.4-442)	247.4±18.7 (109-542)	0.083
Total bilirubin (mg/dL)	0.73±0.06 (0.3-1.5)	0.81±0.05 (0.3-1.5)	0.91

Data were expressed by mean±SEM and range because the data were not normally distributed, BLL=Blood lead level; ALT=Alanine transferase; AST=Aspartate Transferase; ALK.P=Alkaline phosphatase

BLL compared to the healthy controls.[1,14,17,18] In some studies, there is an evidence of lead poisoning in addicted patients who have an intravenous injection or inhalation of contaminated heroin/opium.[8,10,12,14,19] The cause of contamination may be related to the illicit addition of lead to opium by smugglers to increase the opium weight.[1,8,11]

The toxic effects of lead have been recognized as a health hazard for opiate abusers. The symptoms such as abdominal pain, constipation, muscle aches, headache, anorexia, irritability, confusion, nausea and vomiting, combinations of abdominal pain, anemia, and constipation are demonstrated in addicted patients. These nonspecific symptoms are similar to manifestations of lead poisoning, which change from individual to individual and have been reported in several studies.[7,8,11,19] Some of these multiple symptoms were presented in our patients. However, further researches are required in this regard.

Further adverse effects of high BLL have also shown to decrease Hb concentration and to increase levels of liver enzymes.[12,19,20]

In this study, the mean concentration of hemoglobin significantly was lower in opiate patients compared to controls. When the subjects were classified based on the BLL, no significant difference was found between increasing BLL and the levels of hemoglobin and liver enzymes in the case group.

The evidence shows that, lead by increasing the fragility of cell membranes declines the life of erythrocytes and through limiting the synthesis of hemoglobin by inhibiting various key enzymes directly effects on the hematopoietic system. The combination of these two processes results in anemia.[7]

It has been reported that lead is found in circulating red blood cells, liver, renal, and bone. 99% of lead is bound to erythrocytes and 80–95% is stored in the bone. Liver as the largest repository of soft tissue stores 33% of lead.[21] The researchers found that this toxic metal can damage the liver, increase liver enzymes,[22] and cause inflammation, malignancy and cell death by triggering signals that increase TNF-α, a substance in the liver.[21] In our study, a slightly elevated liver enzyme was demonstrated in patients, consistent with a previous study.[19] While, in another case report[8] on lead poisoning, significantly elevated liver enzymes and total bilirubin was observed.

The evidence shows that excessive exposure to lead results in the accumulation of lead in the body and increased toxicity.[7] In a recent study, opiate dependents with more than 10 years of addiction showed higher BLL and lower Hb concentrations. A positive correlation was found only between BLL and duration of drug addiction in addicted patients, consistent with an earlier study.[18] However, in some studies[8,23] no significant correlation was found.

BLL has also been reported to be related to the route of opium abuse.[9] Lead is absorbed by the body through the main paths of entry, ingestion, and inhalation, and can have deleterious effects on many organ systems in the body.[8] The results of a study revealed that lead absorbed by inhalation had much more bioavailability.[14] Other study[8] reported that ingestion of lead-contaminated opium can cause manifestations of lead poisoning. A significant correlation between BLL and the amount of ingested opium was reported in another study.[1] In a recent study, the highest BLL and ALT levels was found in those who used opium orally. The findings of our study suggest that the absorption of lead through ingestion is likely higher than inhalation.

When obese and nonobese patients were analyzed separately, no significant difference was found between BMI and BLL in the two groups. Nevertheless, the results of a study[17] showed that with an increase in body mass index, BLL increased, but there was no meaningful variation between BLL and BMI compared to the control group.

In recent years, opium contamination with lead by sellers and smugglers and lead poisoning in opiate addicts has been reported from Iran.[9] This evidence shows that opium can potentially be a source of lead poisoning.[14] Afghanistan is the largest opium producer in the world and Iran is also one of the main transportation routes for narcotics.[1] Due to the borderline between Sistan and Baluchestan province located in the southeast of Iran and Afghanistan, the people of this province are at risk of addiction.

Conclusions

It is recommended that BLL is frequently monitored to control the adverse effects of poisoning and prevent more accumulation of lead in drug addicts.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Acknowledgments

The authors are grateful to the staff of Baharan Hospital for providing facilities. We would also like to thank the experts of the Tohid laboratory, Zahedan, Iran, for their kind cooperation.

Financial support and sponsorship

This study was supported by the Zahedan University of Medical Sciences, Iran. (Approval date 1396.08.21).

Conflicts of interest

There are no conflicts of interest.

Received: 21 Jun 18 **Accepted:** 08 Aug 19
Published: 19 Jan 21

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