ORIGINAL ARTICLE

Blood Lead Level in Opium Abuse; Which Is More Dangerous? Opium Smoking or Opium Ingestion?

NADER REZAEI[1], POUYAN ALINIA[1], ABBAS AGHABIKLOOEI[1,2*], SHIRIN IZADI[1]

[1] Department of Internal Medicine, Iran University of Medical Sciences, Tehran, Iran
[2] Department of Legal Medicine, Medical Toxicology Division, Iran University of Medical Sciences, Tehran, Iran

Abstract

Background: During the recent years, risk of lead poisoning has increased in Iranian's opium users. A few researches showed that the most common route was ingestion of lead contaminated opium in these patients. However, data on lead poisoning through inhalation route in opium smokers is scarce. The aim of the current study was to determine lead poisoning in opium smokers.
Methods: In this case-controlled study, blood lead level (BLL) and clinical lead poisoning were assessed and compared between pure inhalational and pure ingestionally chronic opium users and healthy controls.
Results: There were totally 90 cases, 30 patients in each group (pure inhaler opium users, pure oral opium users, and control group). In chronic opium users (case group), mean age of the patients was 48.91±13.14 yeas (range; 22 to 79 years). Eighty-four (85%) patients were male (male to female ratio: 5.6/1). Mean BLL was 10.6±4.2 and 126.1±52µg/dL in opium smokers and ingestional users, respectively (P=0.001). The mean of BLL in healthy control group was 4.78 µg/dL±1.83.
Conclusion: In contrast to chronic ingestion of opium, the probability of absorption of lead via lungs is low when opium used by smoking and inhalation route. So, lead toxicity is not common in acute or chronic inhalational users of lead-contaminated opium.

Keywords: Blood Lead Level; Lead Poisoning; Opium Smoking; Inhalation; Opium Ingestion; Plumbism

How to cite this article: Rezaei N, Alinia P, Aghabiklooei A, Izadi Sh. Blood Lead Level in Opium Abuse; Which Is More Dangerous? Opium Smoking or Opium Ingestion? *Asia Pac J Med Toxicol* 2019;8(4):124-9.

INTRODUCTION

Contaminated soil, water, and air are the most prevalent source of lead. Lead exposure can cause poisoning after ingestion, smoking or dermal contacts (1). Lead poisoning causes severe health complications in different organ systems including the central and peripheral nervous system, gastrointestinal, cardiovascular, and renal system (2). Manifestations may be different based on being acute or chronic poisonings (3, 4).

Although the risk of occupational and environmental lead poisoning has dramatically been decreased in Iran and developed countries since 2016, we encountered an epidemic of lead poisoning among Iranian opium users (5). In 2005, lead poisoning was reported in Iranian opium users as a new source of lead poisoning (6). Many studies (7-15) also reported the existence of lead in opium and introduced contaminated opium as a new source of non-occupational lead toxicity (8, 9).

Although several studies (5, 6, 8) have proven the ingestion of lead-contaminated opium as the cause of associated toxicity, few researchers supposed the opium smoking to be the prevalent route of lead toxicity (16). However, this opinion is under question and it is still not clear whether inhalational exposure to lead- contaminated opium causes lead poisonings. The aim of the current study was to determine the probability of lead poisoning in opium smokers.

METHODS

Participants and procedures

This case-control study was performed from March to September 2017 in Firoozgar Hospital affiliated to Iran University of Medical Sciences, Tehran, Iran. The study protocol was approved by the local ethics committee (Ethical Number IR.IUMS.FMD.REC 1396.9411160021). All patients provided written informed consent forms before filling out the questionnaires and checking for blood lead level (BLL).

All patients who were hospitalized due to medical or surgical causes and had positive history of chronic daily opium usage for at least one year were included in the study. All chronic opium users were first visited by a medical toxicologist as a consultant. Variables recorded by a toxicologist in a self-made questionnaire included demographic data, job and previous history of exposure to lead, route of exposure to opium, daily dose and duration of opium usage, concurrent use of other substances indeed of opium, underlying disorders, patient chief complaint and cause of admission, symptoms and signs on presentation. Patients with combined

*Correspondence to: Abbas Aghabiklooei; MD. Department of Legal Medicine and Toxicology, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran.
E-mail: aghabikloo.a@iums.ac.ir; Tel/fax: +98 21 82141321
Received 20 July 2019; Accepted 26 November 2019

ingestional and inhalational exposure to opium (even one time use of opium via oral route), changing the inhalational route to ingestion in recent or previous hospital admission, previous diagnosis of lead poisoning that underwent chelator therapy and cases with the history of exposure to high-risk jobs for lead poisoning (such as automobile radiator repairers, crystal glass makers, painters, battery workers, metal welders and jewelers) were excluded from the study. A total of 60 cases of chronic opium users were included in the study. They were categorized in two subtypes groups including 30 pure opium smokers (as inhaler group) and 30 pure ingestional opium users (as oral group). In addition, 30 cases were selected from the healthy voluntary hospital's health workers without history of occupational lead exposure and opium usage as control group.

Complete blood count, RBC indexes, peripheral blood smear for basophilic stippling, serum iron, ferritin, zinc, magnesium, calcium, kidney and liver function tests were requested for all patients. Also, BLL was checked for all cases with atomic absorption technique in one laboratory. Regardless of patient symptoms, according to our laboratory reference value, BLLs below 10µg/dL and over 25µg/dL were considered normal and toxic in adults, respectively.

Finally, data including signs and symptoms on presentation, BLL, laboratory findings, and outcome were compared between groups. All patients with BLL at toxic range and those with clinically symptomatic lead poisoning underwent chelator therapy.

Data were analyzed using SPSS version 22, t-test, Mann-Whitney U test, ANOVAs, and regression analysis. P-value less than 0.05 was considered to be statistically significant.

RESULTS

There were totally 90 cases, 30 patients in each group (pure inhaler opium users, pure oral opium users, and control group). In chronic opium users (case group), mean age of the patients was 48.91±13.14 yeas (range; 22 to 79 years). Eighty-four (85%) patients were male (male to female ratio: 5.6/1). A total of thirty-two patients were excluded due to changing the inhalational route of opium to ingestion in recent or previous hospital admission in 22 patients, previous diagnosis of lead poisoning who underwent chelator therapy in 3 patients and high-risk job for exposure to lead in 7 patients (Figure 1). Table 1 shows the age, sex, mean daily dose of opium and period of addiction to opium in inhaler, oral opium use and control groups. Fifty-three of 60 opium users (88.3%) were cigarette smokers at the same time and 7 cases (11.6%) mentioned concurrent use of another drug of dependency including ethanol or stimulants.

Mean BLLs were 10.6 µg/dL and 126 µg/dL in the inhalational and oral opium users, respectively (P=0.001). All cases of healthy control group had BLL at normal range. Table 2 shows the comparison of the BLL and other lab tests between the groups.

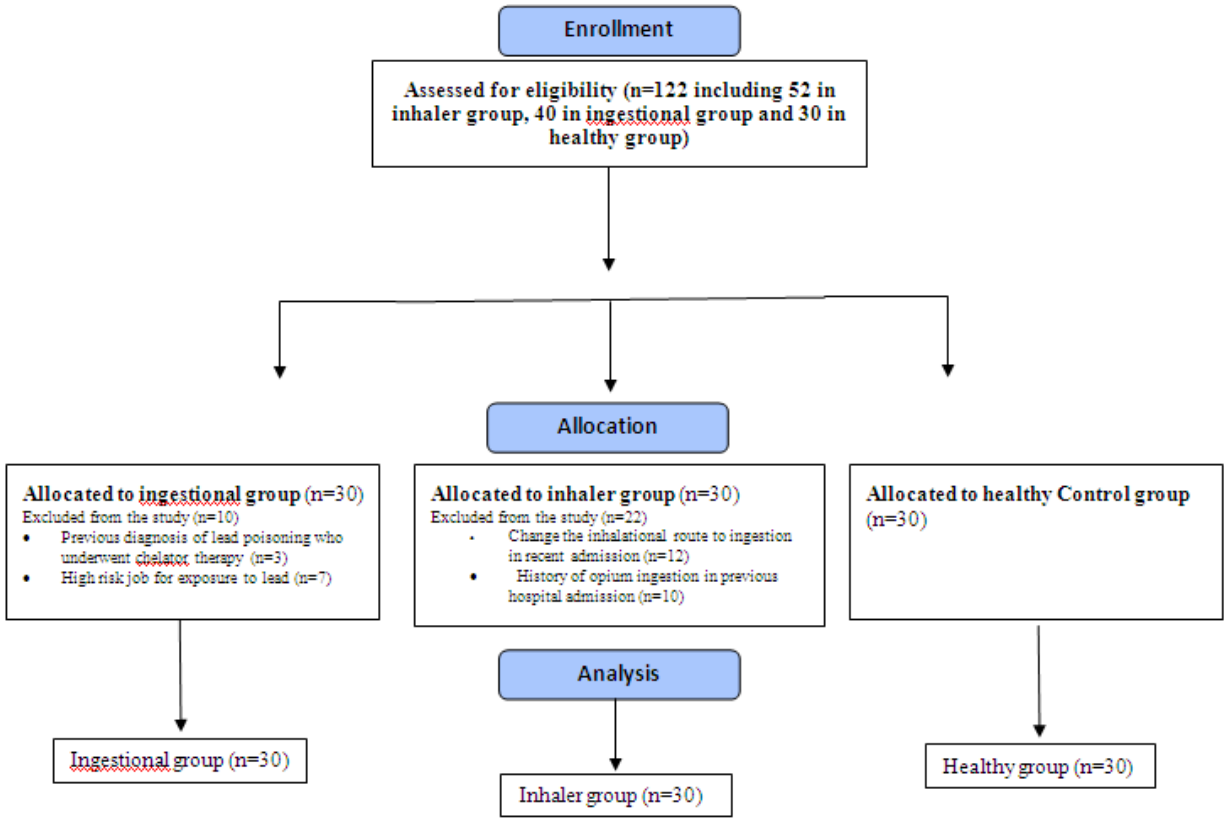

Figure 1. Flow chart of the study

Table 1. Comparison of demographic data between groups

Group	Sex		Mean Age (year)	Daily dose of opium use (gr)	Mean duration of opium use (year)
	Male	Female			
Inhaler Opium	28	2	52.9	Mean; 2.19±3.51 Min;0.3, Max;20	19.17±10.4
Oral Opium	27	3	52.4	3.04±1.88 Min;0.2, Max:7	14.8±10.5
Control	21	9	39.2	-	-

P-value of daily dose of opium use (gr) = 0.25

Table 2. Comparison of the BLL and lab tests between inhaler and oral opium exposure

Lab data	Case group		Control group	P-value
	Inhaler group	Oral group		
Blood Lead Level (µg/dL)	Mean; 10.6±4.5 Min; 5.00 Max; 26	Mean;126.1±52 Min; 58.80 Max; 358	Mean; 4.78±1.83 Min; 2.50 Max; 10	0.001
WBC	9088	6472	7850	-
Hemoglobin (mg/dL)	12.0±2.2	9.8±1.4	13.1±1.8	0.001
Hematocrit	36.7±5.4	30.3±4.2	41.3±6.7	0.001
MCV	88.7±5.3	84.2±8.3	88.9±7.2	0.01
MCH	29.2±2.0	27.2±2.9	30.1±3.0	0.005
MCHC	32.9±1.4	32.3±1.2	31.3±1.8	0.04
RDW	15.0±2.4	16.4±1.5	14.8±3.1	0.001
Platelets ×1000	209±81	243±90	268±21	0.1
Blood Urea Nitrogen	38.9±32.1	32.8±12.6	38.1±12.4	0.8
Creatinine	1.2±0.7	1.0±0.2	0.9±0.2	0.9
SGOT	76	51.9	35.1	0.09
AGPT	90	45.8	39.3	0.04
Alkaline Phosphatase	437	291	339	0.4
Total Bilirubin (mg/dL)	2.3	1.01	1.32	0.6
Direct Bilirubin	0.99	0.39	0.42	0.6
PT	12.6±1.12	13.0±1.0	13.0±1.1	0.1
PTT	31.5±6.10	34.2±17.0	29.9±2.2	0.5
INR (iu)	1.2±0.3	1.1±0.1	1.14±0.10	0.5
Iron (mg/dL)	47	99	-	-
Ferritin	178	354	-	-

In oral ingestional group, all cases (30/30) had BLL in toxic ranges (>25µg/dL) as well as clinical lead poisoning (Table 2). ANOVA test confirmed a significant correlation between the route of exposure (oral) and BLL (P<0.001). The most common signs and symptoms of lead poisoning in these patients were abdominal pain, constipation, and loss of appetite in 100, 96.6, and 93.3% of patients, respectively. Motor and sensory peripheral neuropathy, and muscle pain were other important signs and symptoms (Table 3). Encephalopathy and seizure were both detected in five of 30 patients (16.6 %) and all these patients had severe toxic level of lead with mean of 146.94 µg/dL. Diastolic hypertension was also detected in five of them (16.6%). The mean hemoglobin concentration in serum was 12 and 9.8 mg/dL in inhaler and oral group, respectively. The mean serum iron was 47 mg/dL in inhaler group (Table 2).

All patients underwent standard detoxification with methadone and those with lead intoxication who were

Table 3. Presentation of lead poisoning at oral opium users' relations to BLL

Clinical Presentation	Ingestional opium Users (Oral group)		P-Value
	No / %	Mean BLL	
Abdominal Pain	28/93.3	126.32	0.001
Anemia	21/70.0	129.08	0.001
Loss of Appetite	28/93.3	124.25	0.001
Chronic Constipation	28/93.3	127.29	0.001
Sensory Neuropathy	9/30.0	138.91	0.001
Motor Neuropathy	20/66.7	121.76	0.001
Muscles Pain	19/63.3	129.64	0.001
Chronic Fatigue Syndrome	8/26.7	125.50	0.001
Lead Gum	0/0.0	0.0	0.0
Loss of Memory	2/6.7	96.75	0.001
Seizure	5/16.7	136.40	0.002
Encephalopathy	5/16.7	146.94	-
Loss of Consciousness	2/6.7	127.35	0.04

symptomatic or those with BLL more than 70 µg/dL were treated with chelators. The mean BLL reached from 126.1±52 to 59.8±18.9µg/dL after therapy.

In inhaler group, 29 of 30 (96.6%) patients had BLL below toxic level (<25 µg/dL) and 16 cases (53.3%) had BLLs at normal range (Table 4). In addition, the patients underwent standard detoxification with methadone.

DISCUSSION

In our study, the mean daily dose and duration of opium used by cases in both inhaler group and oral group had no statistically significant differences. Surprisingly, although a few cases in inhaler group used a large amount of opium, nearly 20 g per day for a long time, they all had BLL below toxic level (BLL<25 µg/dL). Also, mean duration of opium use was 19 years in patients in inhaler group but most of them had BLL under toxic level (only one case had BLL equal to 26 µg/dL) and this finding supports the theory that inhalation or smoking of opium contaminated with lead could not lead to significant absorption of lead from the lungs.

Opium is used in two different routes; one way is ingestion (oral route) and the other is smoking via the lungs (inhalational route). The probability of lead absorption by ingestion or inhalation of opium is still a main clinical question. This study was designed to respond to this question. Recent researches suggested that lead contaminated opium is a new source of acute or chronic lead poisoning in many countries (14, 15). They showed adulterated opium with lead as a source of lead poisoning in Iran in which opium abuse is frequent concluding that it could be a new health problem in the future. Aghaee-Afshar et al showed that lead existed in opium samples collected from various sources with a mean concentration of 1.88±0.35 PPM (7). However, none of the previous studies could find the definite route for lead intake among opium users.

Table 4. Comparison of BLL between groups

Cases	Blood Lead Level (µg/dL)		Control Group
	Oral Opium	Inhaler Opium	
1	107.0	11.0	2.5
2	137.0	15.6	4.0
3	126.0	8.3	10.0
4	146.0	10.2	3.0
5	103.0	11.3	4.5
6	120.0	7.0	2.5
7	95.0	16.0	3.5
8	145.0	5.1	4.0
9	151.7	14.0	5.0
10	118.0	12.6	3.0
11	139.0	7.8	2.5
12	358.0	9.5	5.8
13	105.0	26.0	3.2
14	165.0	15.0	3.2
15	127.0	11.0	3.0
16	73.5	9.3	3.5
17	109.0	5.0	6.0
18	101.0	14.0	5.5
19	175.0	9.0	5.0
20	94.0	9.0	6.1
21	129.0	12.0	5.6
22	141.0	7.0	8.1
23	79.0	9.2	5.0
24	135.5	19.5	5.0
25	89.7	8.4	5.7
26	58.8	6.1	4.9
27	157.0	8.5	9.0
28	120.0	7.0	4.6
29	90.0	6.7	5.1
30	88.0	11.0	4.8

BLL in oral opium users

According to the results of this study, unlike the inhaler group, all patients who used opium by oral route for a long time had BLL more than toxic level (>25 µg/dL) and all of them (one hundred percent) were clinically intoxicated with lead and were symptomatic. The mean BLL in patients who used opium orally was 126 µg/dL and the minimum level of lead in blood was twofold of minimum toxic level (59 µg/dL). This means that all oral opium users had a high toxic level of lead. Surprisingly, more than seventy percent of these cases had severe lead poisoning with BLL>100 µg/dL (maximum 358). Only one case had mild toxicity (BLL=25-70) and nearly 20 percent had moderate lead poisoning (BLL=70-100 µg/dL). These findings imply that ingestion of lead contaminated opium has a very high risk for absorption of

lead via gut and the high probability of lead poisoning in oral opium users.

Many studies (14, 15) have confirmed that oral use of opium can definitely cause lead poisoning. In a case control study by Salehi et al in 2009 (8), the BLL was compared between 22 oral opium users and healthy control group. Statistically, there was a significant difference in mean of BLL in oral opium users and control group (21.9±13.2 vs. 8.6±3.5 µg/dL respectively, with P<0.0001). They also showed that BLL in opium addicted cases had a significant correlation with the amount of opium ingested (r=0.65, P<0.01) which was reported similarly in our study. Karrari et al study in 2012 (15) also showed that opium addicts have an elevated BLL in comparison to healthy subjects. Amiri et al study (17) compared BLL of 39 chronic opium users with healthy control group in 2012**.** They showed that mean BLL was significantly higher in opium abusers than control group (57.04±46.03 µg/dL vs. 16.70±12.51 µg/dL respectively, P=0.0001), but they did not highlight the oral or inhalational route of opium consumption in the subjects.

In our study, all cases in oral group had clinical signs and symptoms of lead toxicity and the most common presentation of lead poisoning in more than ninety percent of oral opium users were abdominal pain, constipation, and loss of appetite (Table 3). A significant correlation was found between the oral route of exposure and increasing the BLL (P<0.001) and toxicity.

BLL in inhaler opium users

Surprisingly, according to our data, mean BLL was very lower in inhalational opium users than oral users (10.6±4. vs. 126±525 µg/dL, respectively with P=0.001). We also know that iron deficiency has known as a predisposing factor for lead poisoning because it can increase absorption of lead from the gut. The mean serum iron level in cases at inhaler group was 47 µg/dL and it was lower than that of the normal range (65-170). In spite of that, nearly 97 percent of cases in inhaler group had BLL below the toxic range. In contrast to oral intake of opium, our study finding shows that probability of lead absorption from respiratory tract in the lungs even in the presence of iron deficiency is very lower than in the guts. However, in the inhalational opium users, the mean BLL was more than that of the healthy control group (10.6±4.5 vs. 4.7±1.8µg/dL) indicating that chronic use of contaminated lead-opium by smoking route also could increase the level of lead in the blood in comparison to healthy normal persons who did not use opium. In many Asian countries like Iran, opium is smoked by an instrument like a large pipe named "wafoor". Authors suppose that smoking opium in this way probably brings about the accumulation of lead in the big head of the *wafoor* (Hogheh).

On the other hand, few researchers supposed that inhalational use of opium smoke also can cause lead toxicity. Mahaffey et al (18) believed that inhalation of opium may cause a higher bioavailability compared to its ingestional use. A systemic review by Karrari (15) on lead poisoning in Iran in 2012 reported the probability of lead poisoning via respiratory tract. A few studies (9, 17, 18) mentioned that absorption of lead via the respiratory tract is the most prevalent route of opium abuse in Iranian adults because of high bioavailability with an average absorption of nearly 40% (16). They concluded that when opium is inhaled, the amount of absorption of lead to the blood stream will be higher than ingestion of opium. In contrast to above studies, in Nemati et al study in 2016 in southeast of Iran (17) they showed that there was no statistically significant difference between the average BLL among inhaler users and oral users (41±26 vs. 34±21 µg/dL, respectively with P=0.001).

A previous study (20) showed that BLLs may increase up to 140µg/dL in oral opium users. Afzali et al study in 2017 (21) showed that some of patients with overt lead poisoning were opium smokers, while our study's results showed that although inhalational exposure to opium can increase BLL more than normal level, it cannot increase the BLL to the toxic range, in which except one case with BLL=26 µg/dL all our opium smokers had BLL below 25 µg/dL and more than fifty percent of them had normal BLL (below 10 µg/dL). We think that, the difference between our recent study in comparison to previous researches is related to case selection in which we included definitely pure opium smokers in the study and this research showed that pure inhalation of opium did not cause lead poisoning. The difference between the type of opium and amount of contamination with lead may be the other probable cause of these contradictory results. Mean used daily dose was not significantly different between the patients with oral and inhalational exposures. In fact, although it was shown that increasing the daily used opium increased the BLL, this increase was not statistically significant.

LIMITATIONS

Our sample size is definitely a limitation in the current study. Therefore, it is recommended that prospective studies consider larger sample sizes.

CONCLUSION

In general, it can be concluded that pure inhalational exposure to lead-contaminated opium could not result in increased BLL the same as oral opium use.

ACKNOWLEDGMENTS

The authors would like to appreciate Firoozgar laboratory personnel for checking the blood lead levels. We are also grateful to Dr. Maryam Farasati-Nasab for reviewing the manuscript language before journal submission.

Conflict of interest: None to be declared.
Funding and support: None.

REFERENCES

1. Fischbein A. Occupational and environmental exposure to lead. In: Rom WN, ed. Environmental and Occupational Medicine. Philadelphia: Lippincott-Raven; 1998.
2. Lochitch G. Perspectives on lead toxicity. *Clin Biochem* 1993;26:371-81.
3. Roscoe RJ, Ball W, Curran JJ, DeLaurier C, Falken MC, Fitchett R, et al. Adult blood lead epidemiology and surveillance—United States, 1998-2001. *MMWR Surveill Summ* 2002;51:1-10.
4. Centers for Disease Control and Prevention (CDC). Adult

blood lead epidemiology and surveillance--United States, 2002. *MMWR Morb Mortal Wkly Rep* 2004;53:578-82.
5. Momtazi S. Family and addiction. Zanjan: Mahdis; 2003.
6. Masoodi M, Zali MR, Ehsani-Ardakani MJ, Mohammad-Alizadeh AH, Aiassofi K, Aghazadeh R, et al. Abdominal pain due to lead-contaminated opium: a new source of inorganic lead poisoning in Iran. *Arch Iran Med* 2006;9:72-5.
7. Aghaee-Afshar M, Khazaeli P, Behnam B, Rezazadehkermani M, Ashraf-Ganjooei N. Presence of lead in opium. *Arch Iran Med* 2008;11:553–4.
8. Salehi H, Sayadi AR, Tashakori M, Yazdandoost R, Soltanpoor N, Sadeghi H , et al. Comparison of serum lead level in oral opium addicts with healthy control group. *Arch Iran Med* 2009;12:555–8.
9. Soltaninejad K, Fluckiger A, Shadnia SH. Opium addiction and lead poisoning. *J Subst Use* 2011;16:208–12.
10. Karrari P, Mehrpour O, Balali-Mood M. Iranian crystal: A misunderstanding of the crystal-meth. *J Res Med Sci* 2012;17:96–7.
11. Beigmohammadi MT, Aghdashi M, Najafi A, Mojtahedzadeh M, Karvandian K. Quadriplegia due to lead-contaminated opium–case report. *Middle East J Anesthesiol* 2008;19:1411–6.
12. Mahaffey KR. Quantities of lead producing health effects in humans: Sources and bioavailability. *Environ Health Perspect* 1977;19:285–95.
13. Afshari R, Emadzadeh A. Case report on adulterated opium-induced severe lead toxicity. *Drug Chem Toxicol* 2010;33:48–49.
14. Jalili M, Azizkhani R. Lead toxicity resulting from chronic ingestion of opium. *West J Emerg Med* 2009;10:244–6.
15. Alinejad S, Aaseth J, Abdollahi M, Hassanian-Moghaddam H, Mehrpour O. Clinical aspects of opium adulterated with lead in Iran: a review. *Basic Clin Pharmacol Toxicol* 2018;122: 56–64.
16. Mahaffey KR. Quantities of lead producing health effects in humans: sources and bioavailability. *Environ Health Perspect* 1977; 19:285–95.
17. Froutan H, Kashefi Zadeh A, Kalani M, Andrabi Y. Lead toxicity: a probable cause of abdominal pain in drug abusers. *Med J Islam Repub Iran* 2011; 25:16–20.
18. Hayatbakhsh-Abbasi MM, Ansari M, Shahesmaeili A, Qaraie A. Lead serum levels in opium-dependent individuals. *Addict Health* 2009;1:106–10.
19. Nemati A, Jafari S, Afshari M, Dahmardeh S, Tabrizian K. Comparing Blood Lead Level among oral/inhaled opium with a non-addict control group in the southeast of Iran. *Addict Health* 2016;8:235-41.
20. Ghane T, Zamani N, Moghadam H, Beyrami A, Noroozi A. . Lead poisoning outbreak among opium users in the Islamic Republic of Iran, 2016–2017. *Bull World Health Organ* 2018; 96:165-72.
21. Afzali S, Torabian S, Taheri SK. Do opium abuser develop lead toxicity? A study on opium abusers in Hamadan, Iran. *Asia Pac J Med Toxicol* 2017;6:55-8.