ASIA PACIFIC JOURNAL of MEDICAL TOXICOLOGY
APJMT 6;2 http://apjmt.mums.ac.ir June 2017

ORIGINAL ARTICLE

# Do Opium Abusers Develop Lead Toxicity? A Study on Opium Abusers in Hamadan, Iran

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## Abstract

*Background:* Raw opium is a kind of drug, often abused in Iran. In a vast majority of cases, various impurities including lead are added to raw opium. This study aimed to evaluate Blood Lead Level (BLL) and probable clinical symptoms triggered by it among opium abusers.
*Methods:* This study was case control and conducted on 40 patients addicted to raw opium (case group) and 40 patients without any kind of addiction (control group) who were hospitalized in the poisoning ward of Farshchian hospital, Hamadan, Iran. BLL was measured by Atomic Absorption Spectroscopy (AAS) and compared between the two groups. Para clinical tests and peripheral blood smear were also assessed to check basophilic erythrocytes.
*Results:* The patients' mean age was 51.9±15.8 years in the control group and 53.2±15 years in the case group. The mean of BLL was 4.02±3.16 µg/dl in the control group and 22.41±21.14 µg/dl in the case group, and the difference was statistically significant ($p<0.001$). Moreover, routes of exposure included inhalation (72.5%), oral (12.5%), and both (15%). The results indicated no significant associations between the route of exposure and BLL ($p<0.281$).Furthermore, no special clinical symptoms were observed in most patients in both groups. Nonetheless, anemia and basophilic erythrocytes were detected in 3 patients who had high BLL.
*Conclusion:* Regarding the high BLL in raw opium abuser, it seems that poisoning with lead should be considered if patients with a history of raw opium addiction are refered to physicians.

**Keywords**: Addiction**;** Blood Lead Level; Opium

**How to cite this article:** Afzali S, Torabian S, Taheri SK. Do Opium Abusers Develop Lead Toxicity? A Study on Opium Abusers in Hamadan, Iran. *Asia Pac J Med Toxicol* 2017;6:55-8.

## INTRODUCTION

Various drugs are abused in different countries, with opioids being among the most well-known. Raw opium is one of the opioid compounds abused in Middle-Eastern countries, such as Iran, and a large number of raw opium addicts refer to clinical centers annually (1-6). In order to gain more advantage, various impurities including lead are added to raw opium in Iran (7-8). Thus, frequent opium abuse can cause lead toxicity in the long run. Lead is a heavy metal that can cause various diseases by influencing multiple organs, such as kidneys, liver, gastrointestinal, hematological, and central and peripheral nervous systems (9). Some studies showed that consumption of raw opium could result in an increase in BLL in the long run (10, 11).

According to a report published by the Center for Disease Control and prevention (CDC), BLL below 10µg/dl is acceptable among individuals in the community, and the purpose of treating poisoned cases is to reach 40 µg/dl BLL (12). The aim of this study was comparison the BLL between raw opium abusers and non-addicted patients who were admitted in the poisoning ward of Farshchian Hospital, Hamadan, Iran.

## METHODS

*Methodology*

In this case-control study, 80 male patients were selected and divided into two equal groups based on statistical calculations and inclusion and exclusion criteria. The sample size was calculated base on the formula: $n = \frac{(z_\alpha + z_{1-\beta})^2 \times (\sigma_1^2 + \sigma_2^2)}{(\mu_1 - \mu_2)^2}$ in which the following parameters were considered: $\alpha$= 0.2%, $\beta$= 1%, $z_\alpha$= 3.09, $z_{1-\beta}$= 2.57, $\sigma_1$= 13.2, $\sigma_2$= 3.5, $\mu_1$= 21.9, $\mu_2$= 8.6.

Based on the calculation, the sample size estimated as 33.7. In order to increase the power, the sample size in each group rounded up as 40 patients.

All the patients had been hospitalized in Farshchian hospital, Hamadan, Iran during September 2014 to October 2015 and signed written informed consents. Inclusion criteria included each patient who was an opium abuser (case group) and each patient who was not an opium abuser (control group) and admitted in Hospital. If any patient had a history of occupational or environmental exposure to lead such as working in mines or battery factories or exposure to paint or

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Received 22 March 2017, Accepted 25 May 2017

lead glazes in ceramic factory in both groups were excluded.

The two groups were matched regarding age, occupation and residential area.

Also, in the case group clinical signs and symptoms such as abdominal pain, constipation, central and peripheral neuropathy and paraclinical signs such as anemia, proteinuria, changes in liver enzymes and basophilic erythrocyte were assessed. BLL was measured in both groups.

*Laboratory method*

Two blood samples were drawn from the patients; 5 ml to measure BLL and 2 ml to assess peripheral blood smear. The first sample was gathered in tubes containing EDTA and was centrifuged at 5000 rpm for 7 minutes to separate its plasma. Afterwards, it was kept at -20 ºC until analysis. During analysis, the frozen samples were put in a 37 ºC water bath to be heated. Then, 1 ml sodium chloride (10% w/v) was added to plasma to settle the protein, it was mixed for 5 minutes, and the liquid at the top was separated for refining. During purification, protein- free plasma was entered into a silica gel column. To prepare the column, silica gel was kept at 240 ºC for 8 hours then cooled in a desiccator. After that, five grams of the silica gel was put into a glass dish and 5% (V/W) deionized water was added to it and shaken. The homogenized mixture was then poured into the column. Afterwards, 2 ml of the protein-free plasma was poured into the prepared column and the column was washed by 10 ml of deionized water. Also, 1 ml of pH-adjusted phosphate buffer (pH=8.2) containing $K_2HPO/KH_2PO_4$ (0.05 N) was added to the solution. Spiked human serum samples with different lead concentrations were prepared by mixing the standard stock solution of Pb $(NO_3)_2$ with freshly prepared human serum. The amount of lead in the gained solution was refined by AAS (13). To achieve this goal, the Japanese Schimadzu model of AAS was utilized. Based on definition by the Center for Disease Control and prevention (CDC), more than 10µg/dl BLL is considered significant (12).

The data were entered into SPSS statistical software, version 21 and were analyzed using t-test, ANOVA, and Spearman's correlation coefficient. A P-value less than 0.05 was considered significant.

## RESULTS

The patients' mean age was 51.9±15.8 years in the control group and 53.2±15 years in the case group. The results of Pearson's correlation coefficient showed no significant relationships between the patients' age and BLL (P=0.8).

29(72.5%) patients who had taken inhaled opium, had an average BLL of 20.17±21.07 µg/dl, 5(12.5%) patients who had oral consumption, had an average BLL of 20.08±18.2 µg/dl, and 6(15%) patients who abused opium both orally and through inhalation had an average, BLL of 32.21±22.3 µg/dl. The results of ANOVA indicated no statistically significant relationships between BLL and opium abusing routes (P<0.281).

The study patients had been abusing opium from 3 to 40 years, with most of them (47.5%) having a 15-year history of opium abuse. The results of ANOVA revealed no significant relationships between duration of opium abuse and BLL (P=0.22) (Table 1).

BLL in the two groups has been presented in Table 2. Accordingly, the mean of BLL was 3.16±4.02 µg/dl in the control group and 22.41±21.14 µg/dl in the case group, and based on t-test results the difference was statistically significant (P<0.001).

In the case group, 6 patients suffered from constipation and abdominal pain and 2 had paresthesia. No other symptoms of lead toxicity were observed. Except for 3 patients in the case group who suffered from anemia and basophilic erythrocytes, no changes in other Para clinical tests, including hepatic and renal function, were detected [illegible]

## DISCUSSION

The findings of this study revealed that although most of the raw opium abusers did not have any specific clinical symptoms of lead toxicity, 65% of them had BLL above 10 µg/dl higher than the acceptable level (12). This can

**Table 1.** The relationship between duration of addiction and BLL

| Duration of addiction (year) | N (%) | BLL (µg/dl) | P-value |
|---|---|---|---|
| <5 | 3(7.5%) | 38.37±39.37 | 0.22 |
| 5 – 10 | 11(27.5%) | 20.11±19.15 | |
| 11 – 15 | 7(17.5%) | 10.73±6.14 | |
| >15 | 19(47.5%) | 25.53±21.70 | |

µg/dl: microgram per deciliter

**Table 2.** BLL in the control and case groups

| BLL | <10 ( µg/dl ) | 10 – 20 ( µg/dl ) | 21-30 ( µg/dl ) | 31-40 ( µg/dl ) | >40 ( µg/dl ) | P-value |
|---|---|---|---|---|---|---|
| Controls (40) | 38(95%) | 2(5%) | 0(0) | 0(0) | 0(0) | <0.001 |
| Cases (40) | 14(35%) | 10(25%) | 7(17.5%) | 3(7.5%) | 6(15%) | |

indicate the existence of lead in opium as one of the reasons for contamination with this metal. In addition, no significant relationship was found between BLL and different abusing routes; i.e., inhalation, oral, and both.

Currently, lead toxicity is being mentioned less as an occupational issue, but environmental pollutions have been observed extensively. Generally, the main pollution resources include paints, dust, drinking water, parents' workplace, air, and food (14). In a study by Ahamed, the mean BLL was 9.3 µg/dl among 200 children between 3 and 12 years old in Lakno, India. Considering the fact that lead-free petrol was not used in that area, the effective factors in existence of lead in their blood were terrible socioeconomic status, living around streets with heavy traffic jam, and mothers' illiteracy (15).

Sawalha conducted another study on children in Nablus, Palestine and reported that BLL was higher in the children living in organ camps nearby industrial areas and heavy traffic streets compared to the city residents (16).

Furthermore, Sharma assessed the amount of lead in 6 foods, including leafy vegetables, leafless vegetables, fruits, pulses, grains, and milk, and indicated that the highest amount of lead was related to leafy vegetables (17).

Due to the fact that drugs, especially raw opium, are produced and distributed illegally, the involved individuals try to benefit from adding different refining materials to opium. Lead can be considered to be one of the impurities of opium (7, 8). Hence, frequent and constant opium abuse can result in emergence of lead toxicity symptoms in the long run. Various studies have demonstrated the existence of lead in blood of opium abusers (10, 11). Our study results also disclosed that opium abusers had high BLL.

In this study, the patients in the case group were between 24 and 86 years old, with the mean age of 53.2±15 years. In Salehi's report, the case group patients were within the age range of 26-50 years and their mean age was 38.8±6.7 years (10). In the present study, duration of opium abuse was more than 15 years in most of the cases, while this measure was reported to be 2-5 years in Salehi's study (10). Regarding the high average age of patients and the long-term use of opium in our study compared with the other studies, the high BLL was observed in more than 65% of patients.

The findings of the current study showed that most opium abusers' BLL was above 10 µg/dl and significantly higher compared to the control group. Similar results were also obtained by Hashemi-Domane , Amiri and Khatibi-Moghadam (11, 18 , 19). However, our study revealed no significant relationships between the opium abusers' age and BLL, which is on the contrary to the results of the research by Amiri (18). Also, our study indicated no significant relationships between the duration of opium abuse and BLL, which is in agreement with the results of the study by Salehi (10).

The present study results demonstrated no significant difference among the three different abusing routes (inhalation, oral, and both) regarding BLL. Nonetheless, BLL was higher in the patients who abused opium through both routes. This might be attributed to the inadequate number of samples. On the other hand, the study by Hashemi-Domane showed that BLL was significantly higher among oral abusers in comparison to atypical ones (11).

In general, lead toxicity affects many organs, including gastrointestinal system, central and peripheral nervous systems, hematological system, kidneys, and liver. Additionally, the main lead toxicity symptoms include abdominal colic pain, constipation, burton line, anemia, basophilic erythrocytes, and peripheral neuropathy (9, 20). In our study, no clear clinical and Para clinical symptoms of lead toxicity were observed in most of the cases. However, some studies have revealed the symptoms of lead toxicity in opium abusers although in very few cases (21-25). For instance, Masoudi performed a case report and pointed to existence of basophilic erythrocytes (22). In the current study also, basophilic erythrocytes were observed in 3 cases' peripheral blood smears. In addition, Hashemi-Domane reported anemia in 38% of the patients who abused opium orally and 43% of those who abused opium atypically (11). In our study, however, only 3 patients (7.5%) had anemia.

## LIMITATIONS

This study was conducted in only one area with a limited number of cases. Thus, future studies have to be carried out in several areas with a larger number of cases to obtain more accurate results.

## CONCLUSION

Overall, the results of the present study revealed that BLL was high in most opium abusers regardless of the duration of abuse and route of consumption. Therefore, BLL must be checked in all opium abusers even in case of absence of clinical symptoms.

**Conflict of interest:** None to be declared.

**Funding and support:** This study was conducted in the Behavioral Disorders and Substance Abuse Research Center and was approved and funded by the Ethics Committee of Hamadan University of Medical Sciences.

## REFERENCES

1. Hassanian Moghaddam H, Zamani N, Rahimi M, Shadnia SH, Pajoumand A, Sarjami S. Acute adult and adolescent poisoning in Tehran, Iran; the epidemiologic trend between 2006 and 2011. *Arch Iranian Med* 2014;17:534-8.
2. Kassiri H, Feiz Haddad MH, Ghasemi F, Rezaei M, Ghanavati F. An epidemiologic and demographic survey of poisoning in southwest of Iran. *Middle-East J Sci Res* 2012; 12: 990-6.
3. Eslami M, Kousha S, Fesharaki M, Kazemi N, Ghafarzad A, Zamani M, et al. Evaluation prevalence and causes of drug and chemical poisoning in patients referred to emergency wards of Sina Hospital of Tabriz University of Medical Sciences at 2012-13. *Int J Curr Res Aca Rev* 2014;2:187-94.
4. Besharat S, Jabbari A, Besharat M.Opium as a fatal substance. *Indian J Pediatr* 2008; 75:1125-8.
5. Ayatollahi V, Behdad SH, Oliwiaie H, Hajiesmaili MR, Dehghan M, Mehrpour O. Characteristic features of patients hospitalized with Narcotic poisoning in Yazd, Iran. *Iran J Toxicol* 2011;4:362-6.
6. Karbakhsh M, Salehian Zandi N. Pattern of poisoning in the elderly: An experience from Tehran. *Clin Toxicol* 2008; 46:211-7.

7. Soltaninejad K, Faryadi M, Akhgari M. Determination of lead in opium by flame atomic absorption spectrometry method. *Sci J Forensic Med* 2003;9:176-9.
8. Aghaee Afshar M, Khazaeli P, Behnam B, Rezazadehkermani M, Ashraf-Ganjooei N. Presence of Lead in Opium. *Arch Iran Med* 2008;11:553 – 4.
9. Hoffman RS, Howland MA, Lewin NA, Nelson LS, Goldfrank LR. Goldfrank`s Toxicologic Emergencies. 10th ed. New York: McGraw-Hill; 2015.
10. 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.
11. Hashemi Domeneh B, Tavakoli N, Jafari N. Blood lead level in opium dependents and its association with anemia: A cross-sectional study from the capital of Iran. *J Res Med Sci* 2014;19:939–43.
12. National Institute for Occupational Safety and Health. Adult Blood Lead Epidemiology and Surveillance (ABLES). Available from: http://www.cdc.gov/niosh/topics/ables/description.html.
13. Heidari Shayesteh T, Khajavi F, Ghafuri Khosroshahi A, Mahjub R. Development and validation of a novel, simple, and accurate spectrophotometric method for the determination of lead in human serum. Environ Monit Assess 2016; 188:7.
14. Hodgson E. A textbook of modern toxicology. 3rd ed. New Jersey: John Wiley & Sons; 2004.
15. Ahamed M, Verma S, Kumar A, Siddiqui MK. Blood lead levels in children of Lucknow, India. *Environ Toxicol* 2010;25:48-54.
16. Sawalha AF, Wright RO, Bellinger DC, Amarasiriwardean C, Abu Taha AS, Sweileh WM. Blood lead level among Palestinian schoolchildren: a pilot study. *East Mediterr Health J* 2013;19:151-5.
17. Sharma M, Maheshwari M, Morisawa S. Dietary and inhalation intake of lead and estimation of blood lead levels in adults and children in Kanpur, India. *Risk Anal* 2005;25:1573-88.
18. Amiri M, Amini R. A Comparison of Blood-lead Level (BLL) in Opium-dependant Addicts with Healthy Control Group Using the Graphite Furnace/atomic Absorption Spectroscopy (GF-AAS) Followed by ChemometricAnalysis. *Iran Red Crescent Med J* 2012;14:488–91.
19. Khatibi Moghadam H, Khadem Rezaiyan M, Afshari R. Comparison of serum and urine lead levels in opium addicts with healthy control group. *Hum Exp Toxicol* 2016;35:861-5
20. Patrick L. Lead toxicity, a review of the literature. Part 1: Exposure, evaluation, and treatment. *Altern Med Rev* 2006;11:2–22.
21. Fatemi R, Jafarzadeh F, Moosavi S, Afshar Amin F. Acute lead poisoning in an opium user: A case report. Gastroenterol Hepatol. *Gastroenterol Hepatol Bed Bench* 2008;1:139-42.
22. 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.
23. Beigmohammadi MT, Aghdashi M, Najafi A, Mojtahedzadeh M, Karvandian K. Quadriplegia due to lead-contaminated opium--Case Report. *Middle East J Anaesthesiol* 2008;19:1411-6.
24. Jalili M, Azizkhani R. Lead Toxicity Resulting from Chronic Ingestion of Opium. *Western J Emerg Med* 2009;10:244-6.
25. Mokhtarifar A, Mozaffari H, Afshari R, Goshayeshi L, Akavan Rezayat K, Ghaffarzadegan K et al. Cholestasis and seizure due to lead toxicity: a case report. *Hepat Mon* 2013;13:e12427.