ORIGINAL ARTICLE

Blood lead level in opium dependents and its association with anemia: A cross-sectional study from the capital of Iran

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Background: Opium dependence is one of the most challenging health problems in the developing countries as well as Iran. Among several health problems due to opium dependence, there are limited reports indicating the presence of lead in opium. The aim of this study is to investigate the blood lead level (BLL) in oral and inhalational opium dependents and its association with anemia. **Materials and Methods:** A cross-sectional study was done among 86 opium dependent patients who were referred to five large detoxification centers in Tehran city and 48 healthy individuals. BLL was assessed using the atomic absorption spectrometry technique. Multivariate analysis of variance and binary logistic regression analysis were performed for statistical assessment using SPSS version 18 for Windows. **Results:** The highest BLL was detected in oral opium dependent group (mean = 11.75, standard deviation (SD) = 6.06) in comparison to inhalational opium dependent group (mean = 7.07, SD = 3.61) and healthy control group (mean = 6.05, SD = 1.83). Anemia was detected in 38% of oral-opium dependent and 43% of inhalational-opium dependent group. Age (odds ratio (OR): 1.06, 95% confidence interval (CI): 1.03-1.09) and opium dependence (OR: 3.59, 95% CI: 1.69-7.59) were significant predictors of anemia in these patients ($P < 0.001$). **Conclusion:** The results of this study confirmed the higher BLL in opium dependents, especially with an oral form of consumption.

Key words: Anemia, blood lead level, Iran, opium dependent

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INTRODUCTION

Opium dependence is one of the most challenging health problems in the developing world as well as Iran.[1] Over many decades, opium has been the most frequently abused substance in Iran and more than 2 million people use opiates.[2] The adverse consequences of opium use were clearly described as physical, mental, and psychiatric disorders.[3]

Among several health problems due to opium dependence, there are some reports indicating unusual pathologic findings such as abdominal pain, anemia, and kidney impairment in opium addicts.[4-7] These findings suggest a non-traditional source of exposure to lead.

Lead is a prevalent heavy metal with severe toxic effects for human.[8] The major routes of exposure to lead are through ingestion and inhalation.[9] After exposure, lead will be accumulated in blood, soft-tissues and bone, and may cause several signs and symptoms such as anemia, renal failure, hearing loss, impaired immune system, and decline of neurocognitive function.[10]

The first report of the presence of lead in opium backed to 1973 due to ingestion of home-made opium.[11] In recent times, few case-report studies have reported lead poisoning as a consequence of opium addiction in Iran.[6,7] Salehi *et al*. studied blood lead level (BLL) in 22 orally opium addicted patients with 22 healthy controls. They concluded that addicted patients have an elevated BLL compared with healthy controls.[12] In another study, Hayatbakhsh Abbasi *et al*. compared BLL in 50 inhalational-opium dependent to 43 nondependents. They failed to find any significant relationship between opium consumption and serum level of lead, but the concentration of lead in dependent group was higher than controls.[13] The existence of lead was approved in 10 opium samples in Kerman province with a mean concentration of 1.88 ± 0.35 PPM.[14]

However, these studies have limited value due to the

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low sample size and comparing just one form of opium consumption (inhalation or ingestion) with a healthy population. The high frequency of opium dependence in Iran and potential severity of lead exposure, prompted us to examine BLL in three groups, consisting of two forms of opium dependence (ingestion and inhalation) in comparison to healthy individuals and to investigate its association with anemia.

MATERIALS AND METHODS

In this cross-sectional study, we studied 86 opium dependent patients who were referred to five large detoxification centers in Tehran city. Between January 2009 and February 2010, all referral opium-dependent patients were examined and participants who met the inclusion criteria were enrolled.

Eligibility criteria included diagnosis of opium dependence based on diagnostic and statistical manual of mental disorder-IV criteria[15] for at least 6 months, age more than 18 years and consenting to participate. Persons working in mines or manufacturing industries with lead exposure, such as battery factories, foundries, wire factories or working with batteries, solder, ammunitions, paint, car radiators, cable, wires, and ceramic with lead glazes were excluded. Using a simple random sampling by Microsoft Excel software, 46 patients were recruited in inhalational opium dependent, 40 patients in oral opium dependent group.

Control group was selected among healthy participants from five premarriage consultation centers in Tehran city near the detoxification centers. Participants who had no history of opium dependence and lead exposure with negative urine morphine test were included in the control group. Forty-seven participants consented to participate and recruited.

For the measurement of BLL, 5 ml of blood was obtained from the antecubital vein and was collected in heparinized lead-free tubes. BLL of participants was measured using graphite furnace atomic absorption spectrometry technique.[16] The results were obtained as μg/dl.

Hemoglobin and hematocrit of the participants were assessed using a coulter AcT Diff Hematology Analyzer (Beckman-Coulter, High Wycombe, UK).

Statistical analysis

All descriptive statistics are presented as means and standard deviations (SDs) for quantitative variables, and as relative frequencies and percentages for categorical variables.

Multivariate analysis of variance was used to compare the mean of BLL and other hematologic factors in three groups (oral opium dependent, inhalational opium dependent and healthy individuals). A *post-hoc* (LSD) analysis was then used to analyze differences between groups.

Binary logistic regression analysis was applied to assess the predictors of anemia. Anemia was defined as a definition of the World Health Organization (WHO) (hemoglobin ≤12 g/dl for women, ≤13 g/dl for men).[17] Considering the presence of anemia as the dependent variable, the independent (predictor) variables were entered in the model, starting from the age of participants and followed by the BLL and opium dependence. The level of significance was set at $P < 0.05$ and all tests were two-tailed. The analysis of data was performed by the predictive analytic software (PASW Statistics 18) for Windows.

Ethics

The design of the study was approved in Ethics Committee of Vice Chancellor for Research, Tehran University of Medical Sciences (Project No. 105). All participants received trial information and provided written informed consent. Furthermore, researchers managed the confidentiality of all information carefully.

RESULTS

Demographic characteristics

In all, 134 participants fulfilled the study's inclusion criteria and enrolled. The study population consisted of 46 patients who were inhalational opium dependents, 40 oral opium dependents and 47 healthy individuals. All of them were men. The mean age of all participants was 33.5 (SD = 16.51) with a range of 22-84 years. Using analysis of variance, there was no statistically significant difference between three groups regarding to age ($P = 0.67$).

BLL

In the healthy control group, the mean of BLL was 6.05 (SD = 1.83). The BLL mean was the highest in the oral opium dependent group. There was a statistically significant difference between BLL in these three groups ($P < 0.001$).

The *post-hoc* analysis showed a statistically significant difference between oral opium dependent group with inhalational group and healthy participants ($P < 0.001$). However, the mean difference of BLL between healthy group and inhalational group was not significantly different ($P = 0.23$) [Table 1].

Although the mean of BLL was higher in anemic group (8.98 [SD = 4.88] as compared to non-anemic group 7.79

[SD = 4.64]), this difference was not statistically significant ($P = 0.216$).

Predictors of anemia

Using WHO definition, anemia was recognized in 35 (26.1%) participants. Among them, 20 participants were in inhalational group and 15 were oral opium-dependents. No one in the control group showed clinically and laboratory anemia manifestations. Chi-squared analysis showed a statistically significant difference in these groups ($P < 0.001$) [Table 2].

Binary logistic regression analysis showed that age and opium dependence was significant predictors of anemia. The lead level has no predictive role in the presence of anemia. The overall model was significant at the <0.001 level according to the model Chi-square statistic and explained 40% of the variation of the anemia [Table 3].

Table 1: Mean of lead level in inhalational and oral opium dependents in comparison to the healthy group

Group	Mean	SD	Mean difference	*P* value
Oral-opium dependent	11.75	6.06	5.70	<0.001
Healthy control group	6.05	1.83	1.02	0.235
Inhalational-opium dependent	7.07	3.61		

SD = Standard deviation

Table 2: Frequency of anemia in in inhalational and oral opium dependents in comparison to the healthy group

Group	With anemia *N* (%)	Without anemia *N* (%)	*P* value
Oral-opium dependent	15 (38)	25 (62)	0.001
Inhalational-opium dependent	20 (43)	26 (57)	
Healthy control group	0 (0)	48 (100)	
Total	35 (26)	99 (74)	

Anemia was defined as definition of the WHO (hemoglobin ≤12 g/dl for women, ≤13 g/dl for men); WHO = World Health Organization

Table 3: Logistic regression analysis for variables predicting anemia

Predictors	β	SE	OR	CI	*P* value
Age	0.056	0.015	1.06	1.03-1.09	<0.001
Opium dependence	1.277	0.383	3.59	1.69-7.59	<0.001
Blood lead level	0.026	0.046	1.026	0.93-1.12	0.067

OR = Odds ratio; CI = Confidence interval; SE = Standard error

DISCUSSION

The aim of this study was to compare the BLL in two groups of opium dependents in comparison to healthy control group and its association with anemia.

The results of our study showed that the BLL was higher in opium dependent participants in comparison to the healthy group. Oral-opium dependent group showed the highest BLL. This is in line with the results of Salehi *et al*.[12] and Amiri *et al*.[18] who reported a higher level of BLL in opium dependent group.

The higher level of lead in opium dependents may have several explanations. Some authors suggest it is due to contamination of opium with lead during its processing.[19] On the other hand, Iran is one of the key neighbors of Afghanistan-the major producer of opium in the world-and Iran is one of the main routes of world-wide opium transit. This make opportunity for drug producers and sellers to add some other substances such as lead to increase its weight for more profit.[14,20] Although these explanations make a sense about the source of lead in opium, but the exact source of lead in opium is still unknown.

In our study, the BLL in inhalational group was higher, but not statistically significant different from healthy control group. Previous studies show that the heat of smoking opium can affect the amount of lead absorbed in the blood.[13] In oral form of opioid consumption, the lead is not much affected and the blood absorption of lead can be higher in this method.

Among adults, greater absorption of lead can be achieved via lead ingestion during a period of fasting.[21] Rabinowitz *et al*.[22] have reported that 35% of lead will be absorbed in fasting period, in comparison to lower amounts (8.2%) if ingested with food.[22] In another study, Maddaloni *et al*. found a great difference in lead absorption between fasting (26.1%) and after eating (2.5%).[23] In Iran, most oral opium addicted patients consume opium in fasting with the highest lead bioavailability.

Lead is easily absorbed by the gastrointestinal tract and respiratory system and into the blood, bone and soft-tissues.[24] Higher level of BLL is associated with several clinical manifestations such as nausea, vomiting, constipation, abdominal pain, extremity pains, headache, paraesthesia, muscle weakness as well as anemia. In our study, anemia was present in 35 opium dependent patients (20 participants in inhalational group and 15 in oral opium dependent group). No one in the control group had anemia. Among several factors, age and group of participation were significant predictors of anemia. The results of this study are in line with previous ones that showed a particularly noticeable increase in prevalence of anemia in the oldest subjects.[25]

However, the pathogenesis of anemia in these patients is not completely understood. Some authors suggest that improper feeding, lack of self-care, inadequate

diet would cause anemia in opium dependent group.[26] Lead absorption from the gastrointestinal tract is also increased in malnutrition and iron deficiency states.[27] Lead will produce anemia by two mechanisms: Impairment in heme biosynthesis, and increased rate of red blood cell destruction. A recent study proposed that low level of lead can induce phosphatidylserine exposure and erythrophagocytosis that may act as a mechanism underlying lead-associated anemia.[28] However, in our study, BLL was not a significant predictor of anemia. This may be due to the low frequency of anemia in our sample that reduced the power of study to investigate the role of lead in producing anemia. More research, particularly with large sample size, is warranted to direct the causation between BLL and anemia.

CONCLUSION

The results of this cross-sectional study confirmed the higher level of BLL in opium dependents, especially in oral form of consumption. Opium addiction is one of the most prevalent forms of addiction in Iran and there is a large population of opioid users who are potentially at risk of lead toxicity. The higher level of BLL in opium dependents is a warning to policy makers and health care workers about the possibility of lead poisoning in these patients. This needs a systematic effort to combat the opium smuggling-illegal opium importation and sale-to mitigate health risks by ensuring product quality; and reduce opium use by expanding rehabilitation centers.

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AUTHOR'S CONTRIBUTION

BHD contributed in the conception of the work, conducting the study, data collection, revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. NT contributed in the conception of the work, revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. NJ contributed in the conception of the work, data analysis, drafting and revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work.

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