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Lead Contamination in Opium, Opium Tincture, and Methadone Oral Solution, in Iran

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Original Article

Abstract

Background: The present study is conducted with the aim to assess the lead contamination in opium tincture, methadone oral solution, and opium.

Methods: 10 samples from each of the matters of opium tinctures, methadone oral solutions, and opium (provided by the Law Enforcement Force of the Islamic Republic of Iran) were collected. Then, an atomic absorption spectrophotometer (AAS) was used to measure lead concentration in each of the samples. Data were analyzed using the SPSS software. A P value of 0.05 or less was considered to be statistically significant (Two-tailed).

Findings: In this study, the amount of lead measured in all samples was equal or less than 5 parts per million (ppm) and the only exception was the lead level of 5.6 ppm in one of the opium tincture samples, which was slightly higher than the standard lead level.

Conclusion: The results of the current study showed that lead was present in opium tincture, methadone oral solution, and opium, but it was not in toxic levels. It is reasonable for opium derived medicinal products, but the low levels of lead in opium may need to be addressed at different times in different regions of the country.

Keywords: Lead poisoning; Methadone; Papaver; Opium

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Introduction

Nowadays, regrettably, lead poisoning in addicts has become a major consequence of the increasing number of addicts and illegal substance users in Iran. Lead is a toxic and heavy metal that has a short half-life in blood, but long half-life in bones. Epidemic lead poisoning was first introduced in addicts who had ingested opium. Later, this incidence was reported in substance users who underwent maintenance therapy at addiction treatment centers. Then, lead poisoning was demonstrated in patients prescribed with opium tincture and methadone solution to relieve the severe chronic pain or pain associated with incurable illness resulting in death.[1,2]

Not only in Iran, but also globally most drug users are financially at a lower social level, thus the vendors add many impurities in these drugs, in particular they add lead to their products in Iran. In the case of opium, adding lead will increase the weight of opium, giving the seller more profit. More importantly, this metal substance does not change the opium's color and taste. In addition, opium is not cultivated for medicinal purposes in Iran. Therefore, the main substance for procurement of pharmaceuticals is the opium discovered by the police. Unfortunately, adding lead to opium affect addicts, in addition to affecting those who are on prescription opioids.[3,4]

Maintenance treatment (substituting illegal drugs such as heroin and opium with pharmaceutical drugs with similar properties) has become one of the treatment modalities in addiction over the past three decades. In this way, a medication with certain and controlled opioid properties is given to addicts. At first, the primary medications were methadone and buprenorphine, and later the opium tincture was introduced. Opium tincture is an alcohol-based substance containing 20% of opium.[5-7]

According to the latest reports of Centers for Disease Control and Prevention (CDC), lead poisoning is defined as elevated blood lead level (BLL) to > 5 mcg/dl.[3,4] Inorganic lead absorption in adults occurs via lungs (50%) or gastrointestinal (GI) tract (50%). Lead spreads into blood (99% attaches to erythrocyte and 1% is free in plasma), soft tissues (kidneys, brain, liver, bone marrow, and placenta), and bones.[8] The mechanisms of lead toxicity are binding to and hindering of sulfhydryl-dependent enzymes,[9] modifying deoxyribonucleic acid (DNA) methylation and shortening of telomere,[10-12] impeding calcium-dependent processes, energy, and transport systems,[9] changing the blood-brain barrier (BBB) permeability,[13] and stimulating the production of hydrogen peroxide and superoxide in endothelial cells[8]. If identified early, lead poisoning can be reversible, but intoxication with high levels of lead can make permanent damage to the central and peripheral nervous system plus other organs.

From an epidemiological perspective, Salehi et al. in Kerman Province, Iran, compared serum lead level in oral opium dependent men with healthy control group. They concluded that opium dependent patients had significantly raised BLL compared to the control group (21.9 ± 13.2 vs. 8.6 ± 3.5, t = 4.56, P < 0.001).[14] In another study, which was directed in 2002 to 2007 at Loghman-e Hakim Hospital Poison Center, Tehran, Iran, revealed a mean BLL as 109.0 ± 37.6 µg/dl in opium addicts.[15] Another study in southeast of Iran showed that the average BLL concentration was significantly different among oral users, users through inhalation, and control group.[16] Apart from several studies using blood samples, there was no investigation with regard to analyzing the levels of lead in opium tinctures and methadone oral solution.

In the past couple of years, there was an increased number of lead poisoning in opioid addicts who were under treatment with opium tincture and/or methadone oral solution in Loghman-e Hakim Hospital, which is a unique referral poison center in Iran. Therefore, this study was conducted aiming to examine the amount of lead in the opium tinctures, methadone oral solution, and the source opium provided by police.

Methods

In this cross-sectional study, 10 samples from each of the matters of opium tinctures, methadone oral solutions, and opium in (provided by the Law Enforcement Force of the Islamic Republic of Iran) were collected. Lead level in each of these samples was analyzed by the atomic absorption spectrophotometer (AAS) device (AA-600, Shimadzu, Japan) with the sensitivity of 0.0114 µg/ml and the detection limit convention of 0.8 µg/l.

The scope of analytical concentrations was 5, 10, and 30 parts per billion (ppb). After obtaining the results, they were compared with the standard

level of lead in opium tincture and methadone oral solution.

With regard to the results of past studies on lead poisoning, the ministry of health of Iran has considered a 5 parts-per-million (ppm) as a standard lead level for the opium tincture and methadone oral solution. All pharmaceutical companies should analyze the lead level in their products before they are marketed.

Data analysis was performed using SPSS software (version 16.0, SPSS Inc., Chicago, IL, USA). The normal distribution of quantitative variables was tested by Kolmogorov-Smirnov test. The data was presented as mean ± standard deviation (SD) for continuous variables. One-way analysis of variance (ANOVA) was used and P values of 0.05 or less were considered to be statistically significant. Our local ethics committee at Shahid Beheshti University of Medical Sciences, Tehran, Iran, approved the study (Thesis code: M-9).

Results

In this study, a total of 30 samples of opium, opium tincture, and methadone oral solution (10 sample in each group) were analyzed to check the lead level. The amount of lead measured in all samples was equal or less than 5 ppm and the only exception was the lead level of 5.6 ppm in one of the opium tincture samples.

The mean lead level in opium, opium tincture, and methadone oral solution samples was 2.0 ± 1.4 (range: 0.5-5.0 ppm), 2.1 ± 1.6 (range: 0.5-5.6 ppm), and 1.2 ± 0.6 (range: 0.3-2.0 ppm), respectively (Table 1). The one-way ANOVA revealed that there was no significant difference among the lead levels in opium, opium tincture, and methadone oral solution (P = 0.300).

Table 1. The lead level [parts per million (ppm)] in the opium tincture, methadone oral solution, and opium

Sample number	Opium tincture	Methadone oral solution	Opium
1	0.8	0.3	0.5
2	0.5	1.0	0.5
3	2.0	1.6	1.0
4	2.0	0.5	3.0
5	3.0	2.0	3.0
6	5.6	0.8	5.0
7	0.8	1.2	2.0
8	1.0	1.0	0.8
9	3.0	2.0	2.5
10	0.6	0.6	2.0

Discussion

The purpose of this study was to investigate the amount of lead in opium discovered by the police force, which is used for medicinal purposes, as well as the amount of lead in opium tincture and methadone oral solution produced by pharmaceutical companies. In the study of methadone samples, the lead concentration in all cases was within the normal range. Of course, it was anticipated due to the semi-synthetic nature of methadone. In the opium tincture samples, only one case had lead levels higher than the standard amount, which could be due to lead contamination of opium cargo that was seized by the police force and delivered to pharmaceutical companies.

The first report of presence of lead in opium dates back to 1973 in Japan resulting from the ingestion of homemade opium.[17] Based on the World Health Organization (WHO) recommendation, an individual having body weight of 68 kg can ingest 240 µg of lead per day [tolerable daily intake (TDI)]. A study by Karimi et al. suggested that 30 g of opium includes 20% TDI.[18] Hence, based on this evidence and considering daily intake of opium, opium tincture, and/or methadone oral solution in addict cases, this concentration of lead can be dangerous.

In this study, it was confirmed that lead is present in opium. The present findings are in correlation with a brief report published in 2008.[19] They collected the opium seized by the Police Force in Kerman Province of Iran. The mean concentration of lead in their samples was 1.88 ± 0.35 ppm with a minimum and maximum concentration of 0.7308 and 3.5255 ppm, respectively. This mean level is slightly higher than the current results, but they presented a lower maximum level of lead than those in this study. This inconsistency could be related to different levels of lead contamination in opium cargo seized by police force in different periods of time and geographical locations in the country.

Finally, it was concluded that lead is present in both opium and opium derived medicinal products within the standard amount. It is acceptable that the lead level to be within normal range in methadone oral solutions and opium tinctures which are manufactured by the pharmaceutical companies, but the low levels of lead in opium cargo may need to be addressed at different times in different regions in the country.

It should be noted that symptoms of lead poisoning are analogous to opium overdose. Any delay in treatment could make permanent neurological, hematological, and GI complications as well as nephropathy. Thus, analyzing the BLL can help recognize lead poisoning in opioid addicts.[15,20-22]

Conclusion

The results of the current study showed that lead was present in opioid pharmaceuticals, but it was not in toxic levels, which is reasonable for opium-derived medicinal products.

Limitations: The authors did not have access to different samples from various parts of the country in several periods of time for more evaluation.

Conflict of Interests

The authors have no conflict of interest.

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Authors' Contribution

All authors made a substantial contribution to analyze the data and write the paper draft, and met the criteria for authorship.

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بررسی میزان آلودگی سرب در تریاک، تنتور تریاک و محلول خوراکی متادون در ایران

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مقاله پژوهشی

چکیده

مقدمه: هدف از انجام پژوهش حاضر، بررسی میزان آلودگی سرب در تنتور تریاک، محلول خوراکی متادون و تریاک بود.

روش‌ها: در این مطالعه، ۱۰ نمونه تنتور تریاک، ۱۰ نمونه محلول خوراکی متادون و ۱۰ نمونه تریاک (ارایه شده توسط نیروی انتظامی جمهوری اسلامی ایران) جمع‌آوری گردید. سپس برای اندازه‌گیری غلظت سرب در هر یک از این نمونه‌ها، از دستگاه اسپکتروفتومتر جذب اتمی استفاده شد. داده‌ها در نرم‌افزار SPSS مورد تجزیه و تحلیل قرار گرفت. $P \leq ۰/۰۵$ معنی‌دار در نظر گرفته شد.

یافته‌ها: میزان سرب اندازه‌گیری شده در تمام نمونه‌ها برابر یا کمتر از ppm ۵ گزارش گردید و تنها استثناء در آن، سطح سرب ppm ۵/۶ در یکی از نمونه‌های تنتور تریاک بود که اندکی بالاتر از سطح سرب استاندارد می‌باشد.

نتیجه‌گیری: نتایج به دست آمده نشان داد که سرب در تنتور تریاک، محلول خوراکی متادون و تریاک وجود دارد، اما این مقادیر در حد سطوح سمی نمی‌باشد. این میزان سرب برای محصولات دارویی مشتق شده از تریاک قابل قبول است، اما در خصوص سطوح پایین سرب در تریاک لازم است در زمان‌های مختلف و مکان‌های متفاوت در کشور ارزیابی‌های بیشتری انجام گیرد.

واژگان کلیدی: مسمومیت با سرب، متادون، تنتور تریاک، تریاک

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