



A Comparison of Blood Indices in Orally and Inhaled Opium Addicts with Non-addict Healthy Control

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Abstract

Background: Drug abuse and drug dependence are very common in the community, which causes complications in patients. It is necessary to identify these complications.

Objectives: The aim of this study was to compare the blood parameters of oral and inhaled opium addicts with healthy individuals in Zahedan.

Methods: This study was performed on 60 people (20 in the group of oral opium addicts, 20 in the group of inhaled opium addicts, and 20 in the healthy group). After recording demographic information, blood parameters were recorded and analyzed.

Results: The findings of our study showed that the mean of white blood cell (WBC), platelets (PLT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) was not significantly different in the three groups. However, it was found that the mean of red blood cell (RBC), hemoglobin (Hb), and hematocrit (Hct) in the healthy groups and serum lead (Pb) levels in addicts was significantly higher, but no difference was seen between the oral and inhaled groups. It was also found that in all subjects, Pb had an inverse and significant relationship with RBC, Hb, and Hct.

Conclusions: The higher levels of Pb in the blood of substance abusers may cause further anemia, and blood Pb levels must be frequently checked in substance abusers.

Keywords: Drug Abuse, Blood Parameters, Oral Opium, Inhaled Opium, Lead

1. Background

One of the most important public health problems is opiate addiction. According to the 2021 United Nations Office on Drugs and Crime (UNODC) report, global statistics show that in 2019, approximately 31 million people were current or past abusers of opiates (heroin and opium), representing 0.6% of the world's population aged 15 - 64. About 70% of the estimated global number of opiate abusers live in Asia (1). There are approximately 1.2 to 3.7 million drug abusers in Iran, among whom opium addiction is more prevalent than other drug addictions (2). Addictive substances can be abused either by injection, ingestion, or inhalation. Consumption of addictive drugs results in serious damage to the internal organs and is commonly associated with bone marrow suppression, aplastic anemia, and a variety of systemic disorders. Moreover, one of the uncommon causes of

lead (Pb) poisoning is Pb-adulterated substance abuse, such as opium, marijuana, Iranian crack, ecstasy, and methamphetamine (3). It has been suggested that Pb is added to make the substance heavier (4). It was shown that the highest Pb level was detected in opium samples then heroin and Iranian crack samples were ranked next, respectively.

As clinical symptoms of Pb poisoning are nonspecific and may be misdiagnosed with other pathophysiological situations, health professionals should be alerted and perform an evaluation of Pb poisoning in opium abusers. Early diagnosis of these disorders and the consequence of complications are important. Lead poisoning define based on the recent scientific evidence suggesting that upper limit for blood Pb for adults is set at 10 $\mu\text{g}/\text{dL}$ (5). Hematological parameters have been commonly investigated in the population of opioid abusers. However,

the difference in Pb poisoning in oral/inhalation routes of opium use remained unclear. Although the main route of Pb toxicity is gastrointestinal absorption, Pb is easily absorbed through skin and respiratory system (5). Rezaei et al. conducted a case-control study in 2019 and concluded Pb poisoning is not common in acute or chronic inhalational abusers of Pb-contaminated opium (6). Nemati et al. also investigated the Pb concentration in blood samples of oral and inhaled opium abusers and did not observe any relationship between blood Pb level and the route of opium use (7). In another study, Domeneh et al. found the mean Pb level was higher in oral opium group in comparison to inhalation opium abusers (8).

2. Objectives

Considering the high prevalence of opium use in Iran and potential severity of Pb exposure, this research was designed to investigate the hematological changes that are observed in different routes of opium consumption, including oral and inhalation, as case groups and compare them with a healthy control group. This may lead to a better understanding of the hematological effects of substance abusers.

3. Methods

This case-control study was designed and performed in August 2020, in Zahedan, Iran. Three groups were studied: 20 oral opium abusers, 20 inhaled opium abusers, and 20 non-substance-abusing control subjects (healthy group). The subjects signed written informed consent before the research. Inclusion criteria were addiction to opium meeting DSM-5 criteria from two years ago, male, and age between 20 to 50 years. Exclusion criteria were having current significant underlying disorder such as hepatic, respiratory, renal, endocrine, and hematological disease (severe anemia, minor thalassemia, white blood cell (WBC) $> 12,000$ cell/mm 3 , platelets (PLT) $> 450,000$ cell/ μ L), known job with Pb contact (e.g., pottery, battery making, plumbing, and painting), substance abusers other than opioids, and decline to participate in the research. For controls, non-substance-abusing individuals, according to a negative urine test for opium, who had no current and/or previous underlying disorder and signed the consent form, were enrolled in the study.

The required sample size according to $\alpha = 0.05$, $Z_{1-\alpha} = 1.96$, $\beta = 0.2$, $Z_{1-\beta} = 0.84$, and $d = 0.8$, and considering the prevalence average of Pb poisoning in addicts ($P = 0.5$) (9) was calculated 20 participants in each group. The sample size was measured using the following formula:

$$\text{Sample size} = \frac{2\sigma^2 (Z_{1-\alpha} + Z_{1-\beta})^2}{d^2} \quad (1)$$

The opium abusers were selected from outpatient psychiatric clinics by available sampling methods. All patients were interviewed by a psychiatrist, considering the inclusion and exclusion criteria. The control group was selected from the local community and was homogenous with the abuser group (not for substance use background). To detect the current use of opium, urine screening was conducted urine analysis at the baseline interview and before the blood sampling.

Patients' characteristics (age, sex, history of substance abuse, daily quantity consumed, and route of administration) and laboratory and clinical measures were recorded in the study baseline checklist. Blood samples (5 mL) were taken from the cubital vein into heparinized tubes and stored at -20°C. Medical laboratory exams including WBC count (10^3 cell/mm 3), red blood cell (RBC) count (10^6 cell/mm 3), hemoglobin (Hb, mg/dL), hematocrit (Hct, %), PLT (10^3 cell/ μ L), mean corpuscular volume (MCV, fL), mean corpuscular hemoglobin (MCH, pg), mean corpuscular hemoglobin concentration (MCHC, g/dL), and Pb (μ g/dL) also were measured. Blood Pb content was analyzed by atomic absorption spectrometry (Varian Co., US) according to a standard method.

All data were analyzed with SPSS 20. In preliminary analyses, we examined the normality of the data using a Kolmogorov-Smirnov sample test with Lilliefors correction, and by confirming the normality, appropriate parametric methods were used. Data of blood parameters are presented as the means \pm standard deviations (SD). The comparison between groups was examined using one-way analysis of variance (ANOVA). Fisher's exact test is used when there is at least one cell in the contingency table of the expected frequencies below five. To test the correlation between blood parameters and other variables, correlational analysis was performed using Pearson correlation method. The significance level was considered at 0.05.

4. Results

A total of 60 subjects consisting of 20 cases (inhaled opium abuser), 20 cases (oral opium abuser), and 20 controls (non-substance abuser) men were enrolled in the study. Hematological characteristics of the participants are summarized in Table 1. Our findings showed that the mean of WBC, PLT, MCV, MCH, and MCHC was not significantly different in the three studied groups. However, it was found that the mean of RBC, Hb, and HCT in the control group and serum Pb levels in opium

abusers was significantly higher, but no difference was seen between the oral and inhaled opium abuser groups. It was also found that in all subjects, Pb had an inverse and significant relationship with RBC, Hb, and HCT (Table 2). According to Tables 3 and 4, Pb had no significant relationship with any of the hematological variables in oral/inhaled opium abusers (n=20 per groups).

5. Discussion

The current research aimed to compare the blood parameters of oral/inhaled opium abusers with healthy individuals in Zahedan. Based on the results of the present study, the mean of RBC, Hb, and HCT in the opium abuser groups was significantly lower. Moreover, serum Pb levels in opium abuser groups were higher in comparison with healthy controls, but no difference was seen between the oral and inhaled routes.

In line with our finding, a case-control study conducted by Afzali et al. and reported no significant association between serum Pb levels and different consumption routes (oral, inhalation, and both) (10). However, Farnia et al. in their systematic review and meta-analysis revealed the route of administration, gender, and duration of opium abuse was associated significantly with blood Pb levels in opium abusers (11). Based on this systematic review, the serum Pb level in the opium abuser in Tehran and southern regions such as Sistan and Kerman has been reported to be much higher than in other cities of Iran (11). Recently, a cross-sectional study from southern Iran, Zahedan, by Montazerifar et al. reported increased serum levels of Pb and decreased Hb concentration compared to the controls (12). Also, the aminotransferase enzymes, AST and ALT levels, were found to be increased in abusers with > 10 years of opium use disorder, but the difference was not significant (12).

Medical literature reported that opium abusers had a significant increase in WBC count, while withdrawal group showed no significant changes. By contrast, chronic opium use did not cause major changes in erythrocyte parameters such as RBC count, Hb, and HCT levels (13). In the current study, the erythrocyte parameters significantly decreased in oral/inhaled opium abuser groups. Recent evidence has shown that opium use has been linked to high serum levels of Pb in drug abusers. The findings of the present study also showed the mean of serum Pb levels in opium abusers was significantly higher than in healthy controls, which is consistent with other studies (3, 10). Although the nature of their relationship is not completely understood, medical evidence suggests that blood Pb level and iron status are associated among adults.

Features of a common iron-Pb transporter and evidence suggest that iron deficiency may increase susceptibility to Pb poisoning. Lead can gradually accumulate in the bones over time which becomes an internal source of Pb in the blood. Recent human studies suggest that high iron intake and sufficient iron stores may reduce the risk of Pb poisoning (14).

Regarding the study limitations, due to long half-life of Pb in the body, which was reported to be up to 20 years, duration of drug abuse in the opium abuser groups was different and impacted our results. Definitely, our sample size was a limitation. Future researches are recommended to assess the effect of iron supplementation on opium abusers to prevent Pb poisoning.

5.1. Conclusions

It is important for health professionals in southeastern Iran, Baluchistan to update their information about the consequences of drug use and its changing over time to provide accurate management. The higher levels of Pb in substance abusers' blood may cause further anemia and screening of blood Pb levels in drug abusers, especially in those with nonspecific complaints, may be useful. Blood Pb levels must be frequently checked in substance abusers.

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Footnotes

Authors' Contribution: S. M. H.: Supervision, conceptualization, funding acquisition, data collection. A. R. B.: Validation, investigation, writing-review and editing. R. R.: Methodology, formal analysis, original draft preparation.

Conflict of Interests: One of the authors of the article (Alireza Bakhshipour) is the EIC of the journal. Based on the journal policy, this author was completely excluded from any review process of this article.

Ethical Approval: The present study was completed in accordance with the Declaration of Helsinki and the Ethical Guidelines for Medical and Health Research established by Ministry of Health and Medical Education and Ministry of Science, Research and Technology, Iran. We obtained approval from the Ethics Review Committee of Zahedan University of Medical Sciences, Iran (Registration No.IR.ZAUMS.REC.1398.143).

Table 1. Hematological Parameters of Participants in Oral/Inhaled Opium and Healthy Groups (n = 20 per Group)^a

Variables (Unit)	Oral Opium	Inhaled Opium	Control	P-Value ^b
WBC (× 10 ³ /mm ³)	6.75 ± 2.32	7.97 ± 3.18	6.96 ± 1.94	0.509
RBC (× 10 ⁶ /mm ³) ^c	4.75 ± 0.69	5.11 ± 0.72	5.66 ± 0.78	0.003 ^d
Hb (mg/dL) ^c	13.22 ± 1.60	13.73 ± 1.29	15.00 ± 1.35	0.001 ^d
Hct (%) ^c	40.58 ± 4.57	42.02 ± 3.29	46.01 ± 3.28	< 0.001 ^d
PLT (× 10 ³ /μL)	217.65 ± 66.32	263.05 ± 88.77	219.90 ± 45.25	0.334
MCV (fL)	86.05 ± 5.95	83.23 ± 7.45	82.22 ± 8.50	0.42
MCH (pg)	28.04 ± 2.16	27.20 ± 3.06	26.88 ± 3.56	0.82
MCHC (g/dL)	32.71 ± 1.15	32.83 ± 1.71	32.58 ± 1.36	0.71
Pb (μg/dL)	36.37 ± 11.80	33.54 ± 8.28	17.69 ± 5.41	< 0.001 ^d

Abbreviations: Hb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; Pb, lead symbol; PLT, platelets; RBC, red blood cell count; WBC, white blood cell count.

^a Values are expressed as mean ± standard deviation.

^b One way analysis of variance was used.

^c No significant difference between substance abuser groups was seen.

^d Significant

Table 2. Pearson Correlations Between Hematological Parameters of Participants in Oral/Inhaled Opium and Healthy Groups (n = 60)

	WBC (10 ³ cell/mm ³)	RBC (10 ⁶ cell/mm ³)	PLT (10 ³ cell/μL)	Hb (mg/dL)	MCV (fL)	MCH (pg)	MCHC (g/dL)	Hct (%)	Pb (μg/dL)
WBC (10 ³ cell/mm ³)	1								
RBC (10 ⁶ cell/mm ³)	r = 0.202; P = 0.122	1							
PLT (10 ³ cell/μL)	r = 0.305; P = 0.018 ^a	r = 0.175; P = 0.182	1						
Hb (mg/dL)	r = 0.038; P = 0.771	r = 0.643; P < 0.001 ^a	r = -0.094; P = 0.475	1					
MCV (fL)	r = -0.42; P < 0.001 ^a	r = -0.714; P < 0.001 ^a	r = -0.302; P = 0.019	r = -0.121; P = 0.357	1				
MCH (pg)	r = -0.032; P = 0.011 ^a	r = -0.579; P < 0.001 ^a	r = -0.292; P = 0.024 ^a	r = 0.143; P = 0.276	r = 0.856; P < 0.001 ^a	1			
MCHC (g/dL)	r = -0.021; P = 0.876	r = -0.034; P = 0.796	r = -0.190; P = 0.146	r = 0.53; P < 0.001 ^a	r = 0.156; P = 0.233	r = 0.537; P < 0.001 ^a	1		
Hct (%)	r = 0.053; P = 0.687	r = 0.828; P < 0.001 ^a	r = -0.02; P < 0.001 ^a	r = 0.88; P < 0.001 ^a	r = -0.269; P = 0.037 ^a	r = -0.171; P = 0.190	r = 0.145; P = 0.267	1	
Pb (μg/dL)	r = 0.024; P = 0.858	r = -0.390; P = 0.002 ^d	r = 0.028; P = 0.830	r = -0.39; P = 0.002 ^a	r = 0.156; P = 0.234	r = 0.080; P = 0.544	r = -0.10; P = 0.939	r = -0.44; P < 0.001 ^d	1

Abbreviations: Hb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; Pb, lead symbol; PLT, platelets; RBC, red blood cell count; WBC, white blood cell count.

^a Significant

Table 3. Pearson Correlations Between Hematological Parameters of Participants in Inhaled Opium Group (n=20)

	WBC (10 ³ cell/mm ³)	RBC (10 ⁶ cell/mm ³)	PLT (10 ³ cell/μL)	Hb (mg/dL)	MCV (fl)	MCH (Pg)	MCHC (g/dL)	Hct (%)	Pb (μg/dL)
WBC (10 ³ cell/mm ³)	1								
RBC (10 ⁶ cell/mm ³)	r = 0.195; P = 0.410	1							
PLT (10 ³ cell/μL)	r = 0.557; P = 0.011 ^a	r = 0.241; P = 0.307	1						
Hb (mg/dL)	r = -0.095; P = 0.689	r = 0.577; P < 0.008 ^a	r = -0.162; P = 0.496	1					
MCV (fl)	r = -0.428; P < 0.06	r = -0.81; P < 0.001 ^a	r = -0.400; P = 0.081	r = 0.299; P = 0.200	1				
MCH (pg)	r = -0.350; P = 0.130	r = -0.70; P < 0.001 ^a	r = -0.545; P = 0.045 ^a	r = 0.033; P = 0.891	r = 0.79; P < 0.001 ^a	1			
MCHC (g/dL)	r = -0.218; P = 0.356	r = -0.038; P = 0.874	r = -0.200; P = 0.397	r = 0.57; P = 0.008 ^a	r = 0.027; P = 0.909	r = 0.540; P = 0.014 ^a	1		
Hct (%)	r = 0.001; P = 0.997	r = 0.81; P < 0.001 ^a	r = -0.071; P = 0.767	r = -0.78; P < 0.001 ^a	r = -0.414; P = 0.069	r = -0.370; P = 0.108	r = 0.108; P = 0.651	1	
Pb (μg/dL)	r = 0.076; P = 0.750	r = -0.004; P = 0.987	r = 0.261; P = 0.266	r = -0.199; P = 0.401	r = -0.111; P = 0.643	r = -0.065; P = 0.786	r = -0.190; P = 0.421	r = -0.196; P = 0.407	1

Abbreviations: Hb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; Pb, lead symbol; PLT, platelets; RBC, red blood cell count; WBC, white blood cell count.

^a Significant

Table 4. Pearson Correlations Between Hematological Parameters of Participants in the Oral Opium Group (n=20)

	WBC (10 ³ cell/mm ³)	RBC (10 ⁶ cell/mm ³)	PLT (10 ³ cell/μL)	Hb (mg/dL)	MCV (fl)	MCH (Pg)	MCHC (g/dL)	Hct (%)	Pb (μg/dL)
WBC (10 ³ cell/mm ³)	1								
RBC (10 ⁶ cell/mm ³)	r = 0.276; P = 0.238	1							
PLT (10 ³ cell/μL)	r = 0.406; P = 0.076	r = -0.069; P = 0.772	1						
Hb (mg/dL)	r = -0.008; P = 0.972	r = 0.217; P = 0.359	r = -0.56; P = 0.010 ^a	1					
MCV (fl)	r = -0.376; P = 0.103	r = -0.75; P < 0.001 ^a	r = -0.290; P = 0.216	r = 0.336; P = 0.147	1				
MCH (pg)	r = -0.365; P = 0.113	r = -0.61; P = 0.004 ^a	r = -0.415; P = 0.069	r = 0.529; P = 0.016	r = 0.95; P < 0.001 ^a	1			
MCHC (g/dL)	r = -0.028; P = 0.908	r = -0.207; P = 0.381	r = -0.403; P = 0.078	r = 0.76; P < 0.001 ^a	r = 0.514; P = 0.02 ^a	r = 0.700; P < 0.001 ^a	1		
Hct (%)	r = 0.181; P = 0.444	r = 0.523; P = 0.018 ^a	r = -0.374; P = 0.104	r = -0.86; P < 0.001 ^a	r = -0.019; P = 0.937	r = -0.202; P = 0.392	r = 0.430; P = 0.059	1	
Pb (μg/dL)	r = 0.208; P = 0.379	r = -0.047; P = 0.845	r = -0.112; P = 0.638	r = 0.199; P = 0.618	r = 0.125; P = 0.600	r = 0.116; P = 0.627	r = -0.084; P = 0.724	r = -0.236; P = 0.317	1

Abbreviations: Hb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; Pb, lead symbol; PLT, platelets; RBC, red blood cell count; WBC, white blood cell count.

^a Significant

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