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Comparison of Blood Lead Concentration in Opium-Addicted and Non-Addicted Children in Birjand, East of Iran

Tayyebeh Chahkandi[1], *Mahdieh Hamzehnezhad[2], Bita Bijari[3], Omid Mehrpour [4], Alireza Amirabadizadeh[5]

[1]Department of Pediatrics, Faculty of Medicine, Birjand Atherosclerosis and Coronary Artery Research Center, Birjand University of Medical Sciences, Birjand, South Khorasan Province, Iran. [2] Resident of Pediatrics, Department of Pediatrics, Faculty of Medicine. Birjand University of Medical Sciences (BUMS), Birjand, South Khorasan Province, Iran. [3] Cardiovascular Diseases Reaserch Center, Department of Community Medicine, Birjand University of Medical Sciences, Birjand, Iran. [4] Medical Toxicology and Drug Abuse Research Center (MTDRC), Birjand University of Medical Sciences, Ghaffari Avenue, Vali-Asr hospital, Birjand, Iran. [5] Medical Toxicology and Drug Abuse Research Center (MTDRC), Birjand University of Medical Sciences (BUMS), Birjand, Iran.

Abstract

Background

Lead-contaminated opium is a new source of lead in the region that children can be exposed to. The acceptable blood lead concentration (BLC) in children is 5 µg/dl, and this population is more susceptible to lead's toxic effects. We aimed to evaluate and compare BLC in opium-addicted and healthy children in Birjand, Iran.

Materials and Methods: This case-control study was performed among children admitted to the pediatrics wards of two hospitals in Birjand, Iran. Thirty opium-addicted children were considered as the case group, and 30 age and gender-matched non-addicted children admitted to the hospital for other reasons were assigned to the control group. Two milliliters of venous blood was obtained from children, placed in specific complete blood count (CBC) vials, and stored at 2-8 ° C for subsequent analysis. Data were analyzed using SPSS software version 22.0.

Results: The means of BLC were 3.63±4.38 µg/dl (median: 1.75 µg/dl), and 2.09±1.21 µg/dl (median: 1.80 µg/dl) in the case and control groups, respectively. The results showed that BLC was not significantly different between the two groups (p=0.84). In the case group, 26.7% of them BLC was above 5 µg/dl, while in the control group, 2 (6.7%) children had BLC above 5 µg/dl. The Fisher's exact test revealed that BLC was not significantly different between the two groups (p=0.08). There was no significant relationship between BLC, duration of use, and opium type in the case group.

Conclusion

It can be concluded that addicted children's serum lead levels significantly increased, and this level of lead can result in unalterable problems in children. However, further studies with larger sample numbers and more specific targets are recommended.

Key Words: Children, Iran, Opium, Lead.

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Corresponding Author:

Mahdieh Hamzehnezhad, Address: Department of pediatrics, Faculty of Medicine, Birjand University of Medical Sciences (BUMS), South Khorassan, Birjand, Iran. Postal code: 971796151

Email: m.hamzenezhad@gmail.com

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1- INTRODUCTION

Drug abuse and its consequences are among the most significant and challenging health problems in the developing countries, including Iran (1). The wide range of side effects of substance abuse not only severely affect one's physical and mental health, but also it impacts family members and the society. Besides, opium and opium poppy sap (latex) are lead-contaminated hazards that threaten drug users (2-4). Lead-contaminated drugs have been considered as one of the new sources of lead exposure (5). In recent years, several lead poisoning cases have been reported due to opium addiction in Iran (6). Although the prevalence of this contamination among the public is unknown, in several studies, the rate of lead poisoning varied from 8 to 20% (6). Lead (Pb) is a metal available in four isotopes and is abundant in the environment. It is found in various materials such as batteries, cable cladding, cosmetics, mineral supplements, plastics, and toys (7).

The primary source of exposure varies among countries. For example, painting is an important source of lead in the United States (7). A study in Nigeria found that out of 850 children who lived near a battery factory in Nigeria, 311 children had BLCs above the World Health Organization (WHO) limit (8). The high accumulation of lead in the human biological system can also be attributed to gasoline consumption with a high lead concentration (8, 9). Lead and its organic and inorganic constituents are readily absorbed through the respiratory system and gastrointestinal tract. After entering the blood plasma, it crosses the blood-brain barrier and placental membranes and spreads to all soft and hard tissues (10, 11). Most lead is accumulated in the bones and may persist for many years (7). Lead poisoning risks and symptoms depend on BLC, and they may vary from person to person (11, 12). Lead poisoning symptoms include hearing loss, anemia, kidney disease, etc. (12, 13). Lead exposure can also lead to elevated BLCs and symptoms such as abdominal pain, anemia, fatigue, headache, and inability to concentrate (10). Lead is a non-essential trace element, which is very toxic, and even a small amount of lead, can be harmful to the body. Thus, there is not a normal BLC for humans. The US Center for Disease Control and Prevention has estimated the acceptable concentration of lead in children to be 5 µg/dl. It has been advised that any lead source should be removed from the children's living environment (9, 10). Lead poisoning in children does not result in immediate signs and symptoms, and the diagnosis of lead poisoning based on history taking and clinical examination is complicated (11, 14). In children, symptoms may include abdominal pain, constipation, nausea, vomiting, and gastrointestinal problems often during several weeks (7, 10).

Children with a BLC of more than 5 µg/dl are more likely to have gastrointestinal complaints than children with a low BLC (10, 15). Children are highly susceptible to lead-induced nerve damage, which is sometimes irreversible in children (9, 15). In the United States, it has been estimated that approximately 300,000 children under the age of five have reported having elevated BLCs (10). Another lead symptom in children has been reported to be stunted growth; that is, children with higher lead concentrations were shown to be shorter (11). Further, for every 10 µg/dl increase in lead concentration in children, their height was reported to be 1 cm shorter and puberty delayed (7, 10). Lead poisoning has previously been reported in adult opium addicts (16-19). However, very few studies have evaluated BLC in addicted children (20). Chouhdari et al., evaluated BLC in opium-poisoned children and found that 70% of children had a BLC of 5 μg/dl or above (20). Considering the widespread of drug and opium use in Iran as well as the reported cases of lead poisoning, especially in addicts, and since there is limited literature on children with addiction, the present study investigated BLC in children addicted to opium and its derivatives and compared it with that of non-addicted children in Birjand, Iran.

2- MATERIALS AND METHODS

2-1. Study Design and Population

This was a case-control study performed at Imam Reza and Vali-e-Asr hospitals in Birjand, Iran, in 2019. Based on the study by Khatibi et al. (5), the sample size was calculated at 60 children (30 patients for the case group and 30 patients for the control group). The case group included 30 opium-addicted children, and the control group consisted of 30 non-addicted children matched in terms of age and gender, weight, height, and cause of hospitalization. Children in both groups were hospitalized due to problems such as diarrhea and pneumonia.

2-2. Inclusion and exclusion criteria

The inclusion criteria included: Children under 12 years of age with the minimum age of one month, children addicted to opium or opium poppy sap (latex), children admitted for problems such as diarrhea and pneumonia, non-addicted and non-smoker parents in the control group, and full consent of parents or legal guardians of the children to participate in the study. Children were excluded if they did not meet the inclusion criteria.

2-3. Methods

As mentioned earlier, the acceptable BLC in children is considered 5 μg/dl or lower. Thus, patients with BLC of greater than 5 μg/dl were considered as elevated BLC. Addiction means a person continues to seek and take the drug despite negative consequences. Opioid addiction in children is a chronic and relapsing syndrome of psychological dependence, in which they take substances for psychoactive, sedative or euphoric effects, and when they cannot take substance, withdrawal symptoms such as muscle and bone pain, sleep problems, diarrhea, vomiting, cold flashes with goose bumps, uncontrollable foot movements, and intense cravings for substance will appear (21). In this study, the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) was used.

In this study, both groups were matched according to gender, age, and specifically the disease type for which they have been confined. Firstly, consent forms and demographic questionnaires (including age, gender, weight, height, type of addiction, etc.) were collected. Subsequently, 2 ml of venous blood samples were taken into CBC-specific vials with EDTA anticoagulant by the pediatric resident and stored in a refrigerator at 2 to 8 °C. Samples were transferred to the Shafa pathobiology laboratory on a daily basis with regard to compliance with the detailed kit procedure.

2-3. Laboratory Measurements

Blood lead concentration was analyzed by a particular kit (PG Instruments Limited, UK) using an atomic absorption technique (AA500 FG Atomic Absorption Spectrometer, PG Instruments Limited, UK). The results were then reported in μg/dl after the pathologist approval.

2-4 Ethical Considerations

After explaining the study to the participants' parents or legal guardians, a moral consent form was obtained from all the parents. In case of any illness or disorder in children, they were referred to a specialist immediately. The code of ethics number (Ir.Bums.Rec.1397.158) was obtained from the Ethics Committee of Birjand University of Medical Sciences.

2-7. Data Analysis

Data were analyzed using SPSS software version 22.0 (IBM Corp. IBM SPSS Statistics). Mean, standard deviation and frequency distribution were separately used to describe the research sample. Next, quantitative variables of the normal distribution were determined by the Kolmogorov-Smirnov test. Descriptive and analytical statistics were used and analyzed by Chi-square test, Spearman correlation coefficient or Mann-Whitney test, paired t-test and independent t-test. P<0.05 was considered as a significant level.

3- RESULTS

In this study, 60 children were participated in the case (30 addicted children), and control groups (30 healthy children) with mean age of 28.25±22.83 and 28.48±23.01 months, as well as 17 and 13 were girls and boys in each group, respectively. The test results showed that age and gender were not significantly different between the two groups (p>0.05). As the results demonstrate in **Table. 1**, pneumonia was the cause of most hospitalization in both case and control groups (14 children). In the case group, 27 (90%) and 23 (76.67%) of children's fathers and mothers were addicted, while based on the inclusion criteria no addicted parents were existed in the control group. In the case group, 14 fathers (46.6%) and none of the mothers were smoking as well.

Table-1: Demographic information of participants in this study.

Characteristics		Case Group Frequency (%)	Control Group Frequency (%)	P-value
Gender	Girl	17 (56.67%)	17 (56.67%)	1
	Boy	13 (43.33%)	13 (43.33%)	
Hospitalization Reason	Gastroenteritis	5 (16.67%)	5 (16.67%)	1
	Pneumonia	14 (46.67%)	14 (46.67%)	
	Croup	1 (3.33%)	1 (3.33%)	
	Convulsion	4 (13.33%)	4 (13.33%)	
	Urinary tract infection (UTI)	4 (13.33%)	4 (13.33%)	
	Common cold	2 (6.67%)	2 (6.67%)	
Addiction and Smoking Habit	Father's addiction	27 (90%)	0 (0)	<0.001*
	Mother's addiction	23 (76.67%)	0 (0)	<0.001*
	Father's smoking	14 (46.67%)	0 (0)	<0.001*
	Mother's smoking	0 (0)	0 (0)	1
	Sibling's addiction	13 (43.33%)	0 (0)	<0.001*

*Significance level of 5%. Case group: Opium-addicted children.

Table.2 shows that in addicted children (case group), 11 and 19 of children were used opium and opium poppy sap (latex), respectively. The administration methods were equally oral and Inhaler method in the case group. It should be noted that all children were addicted since their birth. The current usage and last previous use mean of opium were 0.68± 0.32 g and 0.4±0.93 day respectively. It is worth mentioning that the initial intake was 0.25 g in all the addicted children, and they had no other previous drug use than opium. No history of prior illnesses, ataxia symptoms, or abdominal pain symptoms were observed in the control group.

Table-2: Frequency of drug type and usage method in addicted children (case group).

Variables		Frequency (%)
Drug Type	Opium	11 (36.67%)
	Opium poppy sap (latex)	19 (63.33%)
Usage Method	Oral	15 (50%)
	Inhaler	15 (50%)
Previous Illnesses History	Heart diseases	3 (10%)
	Ataxia	1 (3.33%)
	Abdominal pain	1 (3.33%)

The mean BLC was 3.63±4.38 µg/dl in the case group with a median 1.75 µg/dl, while it was 2.09±1.21 µg/dl in the control group with a median of 1.80 µg/dl. The Mann-Whitney U test showed that BLC was not significantly different between the two groups (p=0.84). In the case group, 22 (73.3%) children had BLC of less than 5 µg/dl, and in 26.7% of them it was above 5 µg/dl. In the control group, 2 (6.7%) children had BLC above 5 µg/dl. Fisher's exact test showed that BLC was not different between the two groups (p=0.08; **Table.3**). According to the Spearman correlation test, there was no significant relationship between BLC and duration of use, age, weight, and height in the two groups (p>0.05).

Table 3- Comparison of serum lead level of children in two groups.

Variables	Case Group	Control Group	P-value
Lead Level (µg/dl) (Mean ± SD)	4.38 ±3.63	2.12±1.21	0.836
Existing Lead (Frequency (%))	8 (26.67%)	2 (6.67%)	0.038*

*Significance level of 5%. Case group: Opium-addicted children, SD: Standard deviation.

The mean lead was higher in children who were orally used opium poppy sap (latex), however this difference was not significant. Lead level was not significantly different in either case or control group in terms of sex and age as well (**Table.4**).

Table-4: Comparison of serum lead level of children's gender and age (less than 24 months and higher than 24 month) in two groups.

Groups		Lead Level in children		
		Mean (SD)	Median (Percentiles 25,75)	P-value
Case Group	Boy	2.5 (2.1)	1.5 (1.1-2)	Z=1.3, P=0.18
	Girl	5.1 (4.7)	2.1 (1.1-7.5)	
Control Group	Boy	2.0 (1.0)	1.8 (1.4-2.2)	Z=0.06, P=0.96
	Girl	2.1 (1.3)	1.8 (1.1-2.7)	
Case Group	<24 months	3.3 (3.1)	1.4 (1-5.1)	Z=1.1, P=0.25
	≥24months	5.4 (4.2)	1.8 (1.5-5.1)	
Control Group	<24 months	1.9 (1.1)	1.8 (1.2-2.3)	Z=0.56, P=0.59
	≥24months	2.2 (1.3)	1.8 (1.2-2.9)	

Case group: Opium-addicted children, SD: Standard deviation.

4- DISCUSSION

Our study aimed at comparing BLC in opium-addicted and non-addicted children in Birjand, Iran. We found that the mean BLC in opium-addicted children was higher than the matched non-addicted children (3.63±4.38 µg/dl vs. 2.09±1.21 µg/dl). Also, we found that 8 (26.7%) of the opium-addicted children had unacceptable BLCs, while only 2 (6.7%) children in the non-opium addicted group had BLCs above 5 µg/dl. This difference was not significant. A study was carried out in 2016 evaluating BLC in the population of 1 to 7-year-old children who were referred to healthcare centers in Birjand city. The mean BLC was reported 2.49 ± 2.64 µg/dL (median 1.85 µg/dL), and 8% of the children had a BLC > 5 µg/dL (22). The mean BLC of children in Birjand was lower than the adult population. Another study by Nakhaee et al. reported that the mean BLC in adults was 6.02 ± 7.41 µg/ dL (23).

Children are susceptible to the neurotoxicity of lead poisoning, and in some cases, it can cause irreversible neural damages in children. Many children are poisoned by lead worldwide, but these children are diagnosed much later than adults, often causing severe complications, especially in children's neurological functioning. The severity of lead poisoning in children may depend on various factors, including age, sex, nutritional status, weight, growth, underlying diseases, etc. (13, 14). Afghanistan and Iran share a common border. Afghanistan is the world's largest opium producer, and Iran serves as one of the main opium shipping routes. Therefore, Iran's population is potentially susceptible to opium abuse. Studies suggest that during opium preparation, retailers and drug dealers are most likely to add lead in order to increase the opium amount and weight and consequently, gain more profit. Opium is, therefore, a potential source of lead poisoning (2, 5).

In this study, 43.3% of the subjects were boys and 56.7% were girls in both groups. Also, 26.7% of the opium-addicted children had elevated BLCs, while in 6.7% of the control group BLC was over 5 µg/dl. Thus, a significant difference between the two groups was observed. Similar to our study, Chouhdari et al. investigated BLC in opium-poisoned children and found that in 70% of children, BLC was ≥ 5 µg/dl. Also, in their study, there was a significant difference in mean BLC between girls and boys (17.07 ± 6.57 µg/dl vs. 6.61 ± 3.22 µg/dl) (20). In addition, in a study performed by Nemati et al. in Zabol city (24), BLC of oral and inhaled drug addicts was compared with that of a healthy group, a significant difference in the BLC of oral and inhaled opioid users was found in comparison with the healthy group (24).

In a study conducted by Khatibi Moghaddam et al. (5) at the Imam Reza Hospital in Mashhad, Iran, lead (urine and serum) concentrations were compared in drug dependents and healthy controls. The results showed a significantly lower lead concentration in the healthy group's urine and serum samples (5). Moreover, Hashemi-Dameneh et al. (1) studied BLC in drug-dependent individuals and its association with anemia. They showed BLC of 75.11 µg/dl in the oral drug users, which was significantly higher than the BLC in the inhalant abusers and the healthy group. Therefore, BLC was significantly higher in drug dependents, especially in the oral method (1). The results of a study by Amiri et al. (25) aimed at comparing BLC in drug dependents and healthy controls depicted that the concentration of lead in the healthy group was significantly lower than that in the drug group (25). In the same vein, a study by Salehi et al. (26) compared BLC in men with drug dependence with that of a healthy group in Rafsanjan city, Iran. They found a significant difference in BLC between addicted and healthy individuals (26). However, in Hayatbakhsh Abbasi et al. (27) investigation, which aimed to compare BLC in opium-dependent individuals with that of an age and gender-matched control group, the mean BLC in the opium-dependent and control groups was not significantly different (27). Lead poisoning in adult addicts with abdominal pain and anemia has been widely studied (26, 28). In Abbasi et al. (28) study, BLC was significantly associated with abdominal pain, myalgia, and anesthesia in adults. In our case group, fathers of 27 children and mothers of 23 children were substance abusers, fathers of 14 children smoked cigarettes, and siblings of 13 children were addicts. None of the parents had addiction in the non-addicted children group, and nor did they smoke, and none of their siblings were addicted.

These results show that the history of addiction and smoking in parents and siblings of the studied groups was significantly different. So that, the family history of addiction was significantly higher in the addicted children compared to non-opium addicted children. Indeed, the present study's findings need to be generalized with caution as patients may be exposed to other sources and contaminants aside from lead-contaminated drugs. A study by Zardast et al. found that children whose fathers were laborers had greater BLCs than those with employee fathers (22). In future studies, it is suggested to investigate other opioids. Moreover, given the irreversible effects of lead on children's intelligence and learning capacities, the Ministry of Health officials and government agencies need to take appropriate measures to educate the public about this important matter. The youth are an invaluable part of any society, and action needs to be taken through media, social networks, and educational programs to promote public awareness and militate against child addiction.

4-1. Limitations of the study

Finding opium-addicted children was difficult because parents try to hide opium addiction in children. Thus, one of the study limitations is the small sample size, and we recommend performing future multicenter studies with larger sample sizes.

5- CONCLUSION

Based on the present results, BLC in opium-addicted children was higher than that in non-addicted children, although the difference was not statistically significant. Further studies with larger sample sizes and more specific target groups are recommended.

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7- CONFLICT OF INTEREST: None.

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