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Original Article

Clinical, Toxicological, Biochemical, and Hematologic Parameters in Lead Exposed Workers of a Car Battery Industry

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Abstract

Background: Lead is a toxic element which causes acute, subacute or chronic poisoning through environmental and occupational exposure. The aim of this study was to investigate clinical and laboratory abnormalities of chronic lead poisoning among workers of a car battery industry.

Methods: Questionnaires and forms were designed and used to record demographic data, past medical histories and clinical manifestations of lead poisoning. Blood samples were taken to determine biochemical (using Auto Analyzer; Model BT3000) and hematologic (using Cell Counter Sysmex; Model KX21N) parameters. An atomic absorption spectrometer (Perkin-Elmer, Model 3030, USA) was used to determine lead concentration in blood and urine by heated graphite atomization technique.

Results: A total of 112 men mean age 28.78±5.17 years, who worked in a car battery industry were recruited in the present study. The most common signs/symptoms of lead poisoning included increased excitability 41.9%, arthralgia 41.0%, fatigue 40.1%, dental grey discoloration 44.6%, lead line 24.1%, increased deep tendon reflexes (DTR) 22.3%, and decreased DTR (18.7%). Blood lead concentration (BLC) was 398.95 µg/L±177.40, which was significantly correlated with duration of work (P=0.044) but not with the clinical manifestations of lead poisoning. However, BLC was significantly correlated with urine lead concentration (83.67 µg/L±49.78; r^2=0.711; P<0.001), mean corpuscular hemoglobin (r=-0.280; P=0.011), mean corpuscular hemoglobin concentration (r=-0.304; P=0.006) and fasting blood sugar or FBS (r=-0.258; P=0.010).

Conclusion: Neuropsychiatric and skeletal findings were common manifestations of chronic occupational lead poisoning. BLC was significantly correlated with duration of work, urine lead concentration, two hemoglobin indices and FBS.

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Keywords ● Lead poisoning ● Occupational exposure ● Biochemical markers ● Hematologic tests

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Introduction

Lead is one of the most toxic elements which may cause acute, subacute or chronic poisoning through environmental and occupational exposure.[1,2] Common sources of lead poisoning are found in car battery industry, manufacturing of ceramic, plumbing, primary and secondary smelting,

and exposure to lead-bearing paint or contaminated food, water and fuel.[1-4] It seems that no threshold of blood lead concentration (BLC) has been defined for hazardous health effects of lead.[5] Lead poisoning affects multiple body organs. Neurological and gastrointestinal manifestations are predominant in lead poisoning. Chronic exposure among adults leads to loss of short-term memory, inability to concentrate, increased excitability, depressive mood, paresthesia of extremities, loss of coordination, generalized abdominal pain and nausea.[6] Patients may also complain of headaches, weakness and myalgia.[7] Anemia, lead line (Burton's line) and abnormal reaction time of deep tendon reflexes (DTR) are common signs in chronic lead poisoning.[8,9]

More than 99% of lead in whole blood is associated with erythrocyte. Almost 70% of total lead clearance occurs in the urine and the remainder is excreted in the feces and sweat, and may be accumulated in hair and nails. After a chronic exposure, lead removal usually follows a multicompartment kinetic model: a fast compartment in the blood and soft tissues with a half-life of 1-2 months.[3,10]

In Iran, workers of car battery, ceramic, and tile factories are heavily exposed to lead and few safety measures are being taken to reduce this exposure. Occupational lead exposure with or without symptoms, has not been thoroughly investigated in Iranian workers who are exposed to lead. The aim of this study was to investigate the possible clinical and paraclinical toxic effects of lead in workers of a car battery industry in Mashhad, Iran.

Patients and Methods

This study was in accordance with the Declaration of Helsinki,[11] and guidelines on Good Clinical Practice. It was also approved by the institutional review board and medical ethics committee of Mashhad University of Medical Sciences.

Informed consents were taken from each participant prior to the study. Pre-designed questionnaires and forms were then used to record demographic data, past medical histories and clinical manifestations of lead poisoning in workers of the car battery industry. Validated questionnaires from previous studies,[12,13] were used. Workers who were treated by chelating agents, such as Meso-2,3-dimercaptosuccinic acid (Succimer), calcium disodium EDTA (CaNa2EDTA), 2,3-dimercaptopropanol or british anti lewisite and D-penicillamine, during the last 6 months were not included in this study. Besides, those with any cardiac, hepatic and renal diseases as well as workers who took drugs that could alter hematological, biochemical and renal indices were excluded. A clinical toxicologist examined the workers just before taking blood and urine samples and prior to start working in the morning. Clinical signs and symptoms were recorded in a nominal YES/NO scale. For example, fatigue was recorded for a worker if his tiredness did not alleviate with rest; or increased excitability was considered with exaggerated response to social stressors. To evaluate workers' concentration, they were asked to count backwards from 100 to 0 in sevens, "100, 93, 86, 79 …" or fours "100, 96, 92 …" Also, short-term memory was assessed by recalling 3 to 5 most recently learned words of a list. At the same time, vital signs were evaluated by a clinical research assistant.

Brachial venous blood samples (10 ml) from each worker were collected into heparinized tubes ,in order to analyze their blood lead concentration(BLC) cell blood count (CBC), fasting blood sugar (FBS), Cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides (TG). Lead-free syringes and lead-free polyethylene containers were used to minimize the risk of lead contamination throughout the study.

Blood and urine lead concentrations were determined by an experienced technician in the toxicology laboratory of the research center using an atomic absorption spectrometer (Perkin-Elmer, Model 3030, USA) with heated graphite atomization technique. Hematologic test was performed in the hematology laboratory of Imam Reza University Hospital using Cell Counter Sysmex; Model KX21N to measure CBC. Auto Analyzer; Model BT3000 was applied to measure biochemical parameters in the biochemistry laboratory of the hospital. Workers diagnosed with lead poisoning were treated according to the guidelines.[14]

Finally, clinical and laboratory data were analyzed by the Statistical Package for Social Sciences (SPSS 18, IBM Corporation, New York, USA). Results were expressed as mean±standard deviation. Pearson correlation was applied to evaluate association between hematologic, biochemical and toxicological parameters. Besides, linear models were used to perform multivariate analysis, and a 2-sided P value<0.05 was considered statistically significant. The minimum s sample size was calculated as 96 individuals according to the following formula: Sample size=$SD^2 \times Z^2/d^2$, where Z score=1.96 for 95% confidence interval, Standard deviation (SD)=180 µg/L based on previous studies,[13,15] and desired precision (d)=0.16×SD.

Results

Out of 163 workers enrolled in the study, 112

Table 1: Demographic and background data of 112 workers of car battery plant with mild-to-moderate occupational lead poisoning

	Mean±SD	Range
Age (year)	28.78±5.17	20–48
Weight (Kg)	67.10±5.35	56–78
Duration of work (year)	3.89±2.40	1–11
Hours per day (hour)	8.67±1.41	4.5–12

workers completed the investigations. The male workers studied, aged 28.78±5.17 years, weighed 67.10±5.35 Kg, and working 8.67±1.41 hours daily for 3.89±2.40 years (table 1).

Clinical Findings

The most common symptoms among 112 workers of the car battery industry were increased excitability (41.9%), arthralgia (41.0%), fatigue (40.1%), paresthesia in feet (35.7%) and hands (30.3%), agitation (30.3%), and metal taste in mouth (26.7%). In addition, most common signs were dental discoloration to grey in 44.6%, lead line 24.1%, increased deep tendon reflexes (DTR) 22.3%, and decreased DTR in 18.7%. Mean values for systolic and diastolic blood pressure were 118.99 mmHg±11.95 and 78.55 mmHg±9.21 respectively. According to the guidelines of World Health Organization and the International Society of Hypertension,[16] the systolic or diastolic blood pressures higher than normal values were observed in 26 workers (23.2%). All clinical manifestations including symptoms and signs of lead poisoning are described in table 2.

Toxicological and Hemato-Biochemical Values

As shown in table 3, BLC ranged from 109 to 894 µg/L (Mean 398.95 µg/L±177.41). One-Sample Kolmogorov-Smirnov test for normality indicated that BLC followed normal distribution (P=0.293).

Hemoglobin and hematocrit values ranged from 14.2 to 18.3 g/dL and from 41.6 to 52.4% respectively. One worker (0.9%) had a mean corposcular volume (MCV) of 69.2% with a BLC=599 µg/L. Five individuals (4.4%) had platelet counts below 150,000 /mm^3. However, no significant correlation was found between platelet count and BLC (P=0.642). As shown in table 4, other values related to hematologic indices were normal.

Analysis of biochemical variables revealed that 5 workers (4.4%) had uric acid >7.0 mg/dL. High cholesterol (>240 mg/dL) and TG (>200 mg/dL) were found in 3 (2.6%) and 12 (10.7%) workers respectively. Besides, 48 (42.8%) workers had HDL<40 mg/dL. High LDL level (LDL>160 mg/dL) was detected in one (0.8%) individual.

Table 2: Clinical manifestations of lead poisoning in 112 workers of a car battery plant with mild-to-moderate occupational lead poisoning

Symptoms	N (%)	Signs	N (%)
Mood irritability	47 (41.9)	Dental grey discoloration	50 (44.6)
Arthralgia	46 (41.0)	Lead line	27 (24.1)
Fatigue	45 (40.1)	Impaired short-term memory	26 (23.2)
Paresthesia in feet	40 (35.7)	Increased DTR	25 (22.3)
Paresthesia in hands	34 (30.3)	Decreased DTR	21 (18.7)
Agitation	34 (30.3)	Reduced visual acuity	21 (18.7)
Metal taste in mouth	30 (26.7)	Impaired concentration	15 (13.3)
Anorexia	29 (25.8)	Abdominal tenderness	6 (5.3)
Malaise	27 (24.1)	Tremor	5 (4.4)
Headache	23 (20.5)	Temporal muscle atrophy	3 (2.6)
Somnolence	23 (20.5)	Pale Conjunctivae	1 (0.9)
Lower extremity weakness	18 (16.0)	Decreased proximal upper extremity force	1 (0.9)
Anhedonia	16 (14.2)	High systolic blood pressure (≥140 mmHg)	7 (6.2)
Upper extremity weakness	15 (13.3)		
Abdominal pain	10 (8.9)	High diastolic blood pressure (≥90 mmHg)	25 (23.2)
Insomnia	9 (8.0)		
Nausea	9 (8.0)	Mean heart rate (per minute)	79.9±8.4
Decreased libido	6 (5.3)	Mean Respiratory rate (per minute)	16.4±6.3

Table 3: Blood and urine lead concentrations of 112 workers of a car battery battery plant with mild-to-moderate occupational lead poisoning

	Mean±SD	Range
Blood lead concentration (µg/L)	398.95±177.41	109-894
Urine lead concentration (µg/L)	83.67±49.78	15-221

Table 4: Correlations between blood lead concentration and hemato-biochemical parameters in 112 patients with mild to moderate chronic occupational lead poisoning

Variable	Range	Mean±SD	r	P value
WBC (/mm^3)	4.1–11.7	6.44±1.36	-0.086	0.442
Lymphocyte Count (%)	19.7–61.9	37.76±7.11	-0.087	0.437
Neutrophil Count (%)	27.3–73.9	52.12±8.20	0.071	0.529
RBC count (/mm^3)	4.75–6.62	5.38±0.37	0.110	0.330
Hemoglobin (g/dL)	14.2–18.3	16.37±0.84	-0.153	0.169
Hematocrit (%)	41.6–52.4	46.94±2.41	-0.007	0.953
MCV (fL)	69.2–95.2	87.23±3.96	-0.156	0.163
MCH(pg)	27.6–34.3	30.47±1.69	-0.280	0.011*
MCHC (g/dL)	31.4–36.9	34.89±0.94	-0.304	0.006*
PLT (10^3/mm^3)	112–322	214.61±43.05	-0.039	0.642
Cholesterol (mg/dL)	110–309	169.35±32.92	0.186	0.124
LDL (mg/dL)	52–206	105.47±23.42	0.160	0.245
HDL (mg/dL)	33–53	40.16±4.03	0.070	0.788
TG (mg/dL)	37–423	112.93±66.03	0.090	0.842
FBS (mg/dL)	50–101	78.12±18.18	-0.258	0.010*
BUN (mg/dL)	9–25	16.61±3.32	-0.219	0.077
Creatinine (mg/dL)	0.7–1.6	1.08±0.15	0.051	0.403
Uric Acid (mg/dL)	3.5–9.1	5.37±0.94	0.172	0.264

*Significant; r: Pearson's correlation coefficient

Statistical Analyses

Bivariate correlation showed that there was a significant association (P=0.044; r=0.166) between BLC and duration of work among 112 workers. Besides, one-way ANOVA indicated that there was a significant association (P=0.008) between BLC and the level of education. Workers with post-secondary education (n=17; 15.1%) had lower BLCs (256.41±137.08;) compared to those(n=11; 9.8%) with middle- school education (473.64±194.25).

Independent-samples t test was applied to evaluate the relationship between BLC and clinical manifestations of lead poisoning. As shown in tables 5 and 6, no association was found between BLCs and signs and symptoms of lead poisoning among 112 workers of the car battery plant. In addition, no correlation was found between BLC and systolic (118.99 mmHg±11.95; P=0.473; r=0.112) and diastolic (78.55 mmHg±9.21; P=0.658; r=−0.033) blood pressures.

Urinary lead concentration (ULC) ranged

Table 5: Association between blood lead concentration and symptoms of lead poisoning among 112 workers of a car battery industry

Variable	Positive		Negative		P value
	N (%)	Mean±SD (µg/L)	N (%)	Mean±SD (µg/L)	
Headache	23 (20.5)	394.13±151.82	89 (79.5)	398.00±184.08	0.926
Decreased visual acuity	21 (18.7)	420.29±168.51	91 (81.3)	392.10±180.09	0.515
Fatigue	45 (40.1)	373.02±152.80	67 (59.9)	413.45±191.40	0.239
Malaise	27 (24.1)	370.89±147.88	85 (75.9)	405.56±185.68	0.378
Anhedonia	16 (14.2)	394.69±162.10	96 (85.8)	401.54±182.66	0.888
Somnolence	23 (20.5)	407.43±178.97	89 (79.5)	397.81±179.45	0.819
Irritability	47 (41.9)	379.13±158.79	65 (58.1)	414.47±191.28	0.302
Agitation	35 (31.2)	372.63±170.48	78 (68.8)	411.95±181.87	0.281
Insomnia	9 (8.0)	435.00±172.87	103 (92)	396.72±179.57	0.540
Anorexia	29 (25.8)	391.28±147.01	83 (74.2)	403.81±189.87	0.747
Abdominal pain	10 (8.9)	339.60±130.98	102 (91.1)	405.61±181.99	0.266
Metal taste in mouth	30 (26.7)	430.57±160.11	82 (73.3)	386.88±182.92	0.251
Nausea	9 (8.0)	448.22±212.26	103 (92)	395.58±175.96	0.399
Arthralgia	46 (41.0)	406.17±161.08	66 (59.0)	389.88±189.10	0.635
Upper extremity weakness	15 (13.3)	377.33±181.35	97 (86.7)	401.16±178.65	0.632
Lower extremity weakness	18 (16.0)	385.94±176.75	94 (84)	400.28±179.53	0.756
myalgia	22 (19.6)	392.82±195.56	90 (80.4)	401.45±175.38	0.840
Paresthesia in hands	33 (29.4)	407.27±192.19	79 (70.6)	400.32±171.87	0.851
Paresthesia in feet	40 (35.7)	400.38±169.34	72 (64.3)	399.44±184.62	0.979
Hearing deficit	13 (11.6)	339.69±116.25	99 (88.4)	407.58±184.15	0.199

Data were analyzed using Independent Samples *t* test

Table 6: Association between mean blood lead concentrations and signs of lead poisoning among 112 workers of a car battery industry

Variable	Positive		Negative		P value
	N (%)	Mean±SD (µg/L)	N (%)	Mean±SD (µg/L)	
Impaired short term memory	26 (23.2)	445.73±197.45	86 (76.8)	390.33±174.56	0.175
Impaired concentration	15 (13.3)	320.27±113.89	97 (86.7)	411.94±183.93	0.064
Pale conjunctiva	1 (0.9)	219.00	111 (99.1)	401.38±178.57	0.311
Dental caries	50 (44.6)	419.98±175.14	62 (55.4)	383.73±181.08	0.286
Abdominal tenderness	6 (5.3)	331.00±115.62	106 (94.7)	408.25±179.53	0.301
Tremor	5 (4.4)	359.60±140.74	107 (95.6)	401.63±180.47	0.609
Increased deep tendon reflex	25 (22.3)	372.72±142.29	94 (84.0)	408.90±183.61	0.431
Decreased deep tendon reflex	21 (18.7)	424.00±195.26	83 (74.2)	388.47±198.22	0.543

Data were analyzed using Independent Samples *t* test

from 15 to 221 µg/L (mean, 83.67 µg/L±49.78). Linear regression analysis revealed that BLC (beta coefficient=0.843; P<0.001; r^2=0.711) was significantly correlated with ULC. The regression equation was BLC=(3.005×ULC)+147.53. Additionally, the backward linear regression analysis showed significant correlation between BLC, MCV, neutrophil count (NC) and FBS (P=0.012; R^2=0.134) according to equation BLC=1385–(10.9×MCV)+(4.17×NC)–(2.97×FBS). Similarly ULC, as determined by ULC=197.19–(30.58×HB)+(7.87×HCT)+(1.58×NC)–(0.77×FBS), was significantly correlated with hemato-biochemical variables (P=0.002; R^2=0.207).

There was also a significant correlation between BLC and mean corpuscular hemoglobin (P=0.011; r=−0.280), mean corpuscular hemoglobin concentration (P=0.006; r=−0.304) and FBS (P=0.010; r=−0.258). No associations were found between BLC and other hematological and biochemical variables (table 4).

Discussion

Clinical Manifestations

We found no association between the clinical manifestations of chronic lead poisoning and workers' BLC. Previous studies on workers of a tile battery factory have also provided similar results.[13] Since the studied population was young, one possible explanation is the sufficient renal capacity to excrete and eliminate lead from the body. Secondly, due to economic and social issues and awareness of , the number of Iranian workers taking legal actions against employers is increasing, since workers are becoming aware of the hazardous health effects of lead. Therefore, inconsistency between symptoms of lead poisoning and BLC is probably due to malingering. In this study, the patients with chronic mild-to-moderate lead poisoning were investigated. According to Baker et al, more severe manifestations of lead poisoning, such as gastrointestinal symptoms (abdominal pain and colic), possible encephalopathy and wrist/ankle extensor muscle weakness, are found with acute exposure and high personnel turnover rate. They also found a significant correlation between signs and symptoms of lead poisoning and workers' BLC.[15]

The average working hours per week for male workers of the car battery industry was more than 50 which possibly leads to the fatigue-related impact of long working hours and occupational dissatisfaction. However, a recent study on 96915 workers in the United States indicates that although males show greater risks of injury compared to females, working hours is significantly associated with toxic risk only for women. This is probably due to the decreased recovery time and inadequate sleep, and elevated fatigue-related impact of long working hours for female workers.[17] Nevertheless, additional objective measures are warranted in order to come to a more reliable conclusion.

Chronic lead exposure is implicated in the development of hypertension.[18] Although 23.2% of workers had higher than normal systolic or diastolic blood pressures, the diagnosis of hypertension could not be made in the first-time visit. Our findings showed no association between systolic/diastolic blood pressure and BLC, which was consistent with other reports.[19,20] It seems that lead exposure was not sufficiently durable to cause hypertension in this young population.

In this study, the level of education was inversely correlated with BLC which was consistent with the reports from other developing countries.[21-23] Thus, improvement of education and socioeconomic status plays key role in the prevention of lead poisoning in these countries.

According to guidelines,[14] workers with severe lead poisoning should be hospitalized and treated with parenteral infusion. Since no severe case of lead poisoning was found among the studied population, workers were asked to avoid lead exposure and/or treated as outpatients.

Toxicokinetics

With normal renal function, lead is excreted in the urine. Random urine sample shows short-term exposure to heavy metals.[24,25] Urine and blood lead correlations are not reliable enough to substitute urine lead concentration for BLC, especially when the exposure is mild and BLC is less than 100 µg/L.[24,26] Gulson et al, believed that the inaccuracy in predicting BLC by measuring ULC mostly applies to children and female adults because of the potential contamination during sampling.[24] On the other hand, Moreira et al. claimed that spot urine test could be used to replace blood sampling for the evaluation of occupational lead exposure in both children and adults.[27]

Hematologic Manifestations

Lead poisoning is a known cause of microcytic anemia.[1] Although we failed to detect depressed Hb/Hct concentrations in workers, Mean Corpuscular Hemoglobin (MCH) and Mean Corposcular Hemoglobin Concentration (MCHC) values were negatively correlated with blood lead concentration. Other RBC indices were not significantly affected. Katavolos et al. demonstrated that MCHC and hemoglobin concentration in two avian species decreased significantly with rising blood lead concentration.[28] Shah demonstrated that direct or feedback responses of structural damage to RBC membrane account for the variations in blood parameters, whereas acute and intense lead exposure caused a significant increase in Hct, MCV and MCH, and significantly decreased RBC count and MCHC. On the other hand, moderate lead exposure resulted in a significant increase in Hct and a meaningful decrease in MCH and MCHC values.[29] In fact, an elevated or normal values of blood parameters, such as Hb, is probably due to the feedback response of body to compensate for the RBC loss.[30] According to Baker et al. anemia is more common in patients with severe occupational lead poisoning.[15] In this study, we did not find any cases with anemia, as all workers had mild-to-moderate lead poisoning.

Biochemical Manifestations

We found a negative correlation between fasting blood sugars (FBS) and blood lead concentration in this study, which was not consistent with previous reports. Akinloye et al. demonstrated that concentration of toxic elements, such as Cadmium, lead, arsenic and selenium, was positively correlated with FBS. The mean value of lead in diabetic patients was significantly more than that of control group.[31] Other studies found no significant association between BLC and blood glucose.[32,33]

Discrepant results have been reported on the association between lead exposure and lipid indices. According to some studies, lead intoxication can increase LDL,[34,35] decrease HDL,[34] and increase total cholesterol,[35] to worsen the risk of cardiovascular disease. On the other hand, Ito et al. found increased HDL in manual workers of a steel industry exposed to lead.[36] In another study, Kasperczyk et al. did not demonstrate any correlation between BLC and blood lipids (cholesterol, HDL, LDL, and triglycerides) which was in keeping with our findings.[37]

Lead accumulation in the proximal tubule leads to hyperuricaemia and gout and impaired renal function.[38] However, in this study, we found no abnormalities in creatinine, BUN and uric acid values which were consistent with our previous findings in workers of traditional tile factories.[12,13]

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Conflict of interest: None declared

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