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Correlation between Serum Lead Level and Coronary Slow Flow Phenomenon

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ABSTRACT

Introduction: While there are some reports onan association between lead exposure and cardiovascular disease,there is still no actual proof ofthe contribution of lead to specific cardiovascular diseases.

Materials and Methods: In this cross-sectional study with control group, serum lead level in 30 patients, diagnosed with Coronary Slow Flow Phenomenon (CSFP) documented by coronary angiography, was evaluated.Results were compared to thecontrol group, whichcontained 30 patients with normal coronary angiography.

Results: In this study, ageand gender were major clinical risk factors for coronary artery disease. Moreover, laboratory and echocardiographic parameters were similar in patients with and without CSFP (P>0.05).A significant differencewasobservedbetween the twogroups regarding serum lead level.

Conclusion: According to the results of this study, a significant correlation was found between serum lead level and CSFP. The suspected mechanismsareoxidative stress and inflammation.

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Introduction

Cardiovascular diseasesarethe leading cause of mortality and primary contributors to the globaldisease burden (1).

According to theliterature, approximately 10-20% of patients undergoing coronary angiography, due to typical pains of angina pectoris, have no occlusion or stenosis in coronary vessels; therefore, they are labeled as X syndrome.

This syndrome includes a heterogeneous group containing Coronary Slow Flow Phenomenon (CSFP).

The prevalence of CSF has been estimated at1-3%,whereas Mahgieri et al. has reported a higher prevalence rate (7%) (2).

CSFP is an angiographic clinical entity, characterized by delayed distal vessel opacification in the absence of significant epicardial coronary stenosis (3).

Rather than representing a simple angiographic curiosity, CSFP has direct clinical implications(similar to clinical manifestations of myocardial ischemia), such as life-threatening arrhythmias, sudden cardiac death and recurrent acute coronary syndromes.

Environmental toxins, such as lead, are potentially preventable exposures,whichmay explain population variation in cardiovascular disease rates. However, after more than 100 years from the initial reports suggesting an association between lead exposure and cardiovascular diseases(4,5), the contribution of lead to thesediseasesis yet to be confirmed.

Research on the cardiovascular effects of lead has largely focused on association of this substance with blood pressure and hypertension.

The cardiovascular effects of lead, however, are not limited to increased blood pressure and hypertension.

Lead exposure has been associated with an increased incidence rate of clinical cardiovascular end points, such as coronary heart disease, stroke and peripheral arterial disease (6-9).

Moreover, exposure to lead might result in cardiovascular abnormalities, such as left ventricular hypertrophy and alterations in cardiac rhythm.

The British Regional Heart Study (10) and two other small cohort studies (11) demonstratedinsignificant positive relationshipbetween coronary heart disease or stroke and high lead levels.

With this background in mind, this study aimedto evaluatethe association betweenlead exposure and Coronary Artery Disease (CAD),documented byangiography.

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Materials and Methods

This cross-sectional study with control group was performed at the Department of Cardiology, Mashhad University of Medical Sciences, Mashhad, Iran.

Eligible cases were patients diagnosed with CSFP, documented bycoronary angiography. On the other hand, the control group included30 patients with normal coronary angiography, who hadnotraditional atherosclerotic risk factors, such as diabetes, hypertension, hyperlipidemia or smoking habits. In addition, subjects of the control grouphad no contact withlead metal, their ischemic heart disease was confirmed by noninvasive stress test and they were candidates for diagnostic coronary angiography.

CSFPis an angiographic phenomenon characterized by the slow passage of contrast in the absence of obstructive coronary artery disease. The diagnosis of CSFP was made on the basis of a corrected TIMI frame count>27 frames.In this study, serum lead level of30patients (case group) with CSFPwas confirmed by angiography and compared with 30 healthy patients (control group). In addition, agewas adjusted with case group.

A total of three mL peripheral blood sample was collected in EDTA vial from the subjects. A PerkinElmer PinAAcle™ 900H atomic absorption (AA) spectrometer in toxicology department was used to evaluate the serum lead level of the participants. This instrument was equipped with a Massman-type/HGA graphite furnace and deuterium continuum source background correction, AS900 autosampler, water re-circulator system, high-speed automatic wavelength drive, automatic lamp selection and EDL power supply.

Data analysis was performed in SPSS Version 16 using t-test (to evaluate lead levels in the study groups) and Chi-square (to compare the study groups regarding lead level). In addition, all the values were expressed as mean ± standard deviation, and P-value of less than 0.05 wasconsidered statistically significant.

Results

In this study, the demographic, clinical, laboratory, echocardiographic and angiographic characteristics of both groups are presentedin Table 1.

It is noteworthy that thestudygroups were homogenousregarding demographic, clinical, laboratory and echocardiographic characteristics. Moreover, age, gender, major clinical risk factors for coronary artery disease, laboratory and echocardiographic parameters were similar in patients with and without CSFP (P>0.05).As expected, TIMI frame count values were significantly higher in CSFPpatients, compared to normal coronary patients (P<0.001 for all three major epicardial coronary arteries). In addition, a significant differencewasobservedbetween the twogroups regarding serum lead level. In general, less than 20 micrograms/dL of lead in blood isconsidered normal.

Table1: Clinical and laboratory characteristics of studygroups

Characteristics	CSFP N=30	Control N=30	P-value
Gender Male	21 (70%)	21 (70%)	
Age mean±SD	39±4	39±3	0.92
Serum lead level(micg/dl)	8.95±6.8	5.41±0.98	0.006
Systolic BP (mmHg)	124±12	120±14	0.17
Diastolic BP (mmHg)	75±8	72±11	0.10
Heart rate (bpm)	75±11	76±10	0.86
LV ejection fraction (%)	63 (59-65)	62 (57-65)	0.59
Diastolic dysfunction	18 (60%)	15 (50%)	0.26
Total cholesterol (mg/dL)	167±17	167±14	0.93
LDL cholesterol (mg/dL)	93±20	91±18	0.57
HDL cholesterol (mg/dL)	40±8	41±9	0.12
Triglyceride (mg/dL)	124±14	114±16	0.14
Fasting plasma glucose (mg/dL)	95±6	93±5	0.39
Coronary slow flow presence			
Left anterior descending(LAD)	21(70%)	-	
Left circumflex(LCX)	15(50%)	-	
Right coronary arteries(RCA)	18(60%)	-	

In this study, mean serum lead level in CSFP patients was11.6±8.9,whereas it was6.6±3.7 micrograms/dL in the control group (P=0.003). According to the results,a significant association was found between serum lead level and CSFP(Table 2).

Table2: Resultsof coronary angiography regarding serum lead level

Characteristics	CSFP N=30	Control N=30	P-value	OR (95% CI)
Serum lead level				
High	9(30%)	1(3%)	P=0.01	12.429 (1.461-05.737)
Normal	21 (70%)	29 (97%)		

Discussion & Conclusion

Lead is a highly poisonous metal (whether inhaled or swallowed), affecting almost every organ and system in the body.Long-term exposure to lead or its salts (especially soluble salts or strong oxidant PbO2) can cause nephropathy and colic-like abdominal pains. This substancemay also cause weakness in fingers, wrists or ankles. Lead exposure leads toincreasedblood pressure, particularly in middle-aged and older people, and can cause anemia.

Worldwide, there are six sources oflead poisoning, including gasoline additives, lead-soldered cans, lead-based paints, ceramic glazes, drinking water pipe systems and folk remedies. Lead intoxication has been knownto promote atherosclerosis in experimental animals. Depending on the magnitude and duration of

lead exposure, cardiac and vascular complications could be potentially life threatening. There are also indications of the influences ofchronic lead exposure on systemic lipid metabolism.

Current evidence on lead-induced oxidative stress has been mostlybased on in vitro experiments or studies conducted onanimals. Chronic exposure has been also linked to atherosclerosis and increased cardiovascular mortality in man. Lead-mediated impaired vasomotor tone, as a result of reduced Nitric Oxide (NO) bioavailability, may contribute to hypertension and atherosclerosis. Atherosclerosis and CSFP depend,to some degree,on the presence of inflammation.Increased expression and production of inflammatory markers in association with lead exposure have also been found in humans (12).

Although several cardiovascular effects of lead on animals have been confirmed (13), end points of greatest concern for humans are elevations in systemic blood pressure and decrements in glomerular filtration rate. These effects may be mechanistically related and can be confounders and co-variables in epidemiological studies. Decrements in glomerular filtration rate may contribute to elevatedblood pressure, which may predispose people to glomerular disease. Some othercardiovascular changes have been noted to beassociatedwith increased lead exposure in humans,including changes in cardiac conduction and rhythm, which mightbe secondary to lead-induced impairment of peripheral nerve conduction (14).

In a multivariate analysis of data from the British Regional Heart Study (7731 males, aged 40–59 years; 8% of cohort had lead (Pb)>24.9 μg/dL), no significant association was observed between covariate-adjusted risk of ischemic heart disease (OR) and Pb (15).

Nevertheless,a significant correlation was found between serum lead level and slow flow sub type of ischemic heart diseasein the present study.

A cross-sectional analysis of the National Health and Nutrition Examination Survey(NHANES) data found a significant association between Pb and risk of peripheral artery disease (16). In thisanalysis,2125 (1055 females, 1070 males) subjects aged ≥40 yearswere assessed. Geometric mean Pb was 2.1 μg/dL (25th–75th percentile range, 1.5–2.9). In addition,increasedlevel ofPb was significantly associated with increase of covariate-adjusted OR for peripheral artery disease (ankle brachial index 2.9 μg/dL), and the ORs were 4.07 (95% CI, 1.21–13.73), without adjustment for smoking status and 2.52 (95% CI, 0.75–8.51) with adjustment for smoking.

In the mentionedstudy,a significant correlation was observed between serum lead level and slow flow coronary disease. The mechanism through which heavy metals(e.g., lead) act toincrease cardiovascular risk still remains unknown; although, impaired antioxidants metabolism, oxidative stress and inflammation may play a role in this regard.

In the presentstudy,a relatively small sample size was evaluated, which can be regarded as a limitation for stratified analysis. This limitationcould result in imprecise estimates (as evidenced by the wide 95%confidence intervals). Nevertheless, the magnitude of the observed odds ratios for the association between CSFP and serum lead level is very high and unlikely to be due to a type I statistical error.

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