

Correlation between Serum Lead Level and Coronary Slow Flow Phenomenon

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ARTICLE INFO	ABSTRACT
<p>Article type: Original Article</p> <hr/> <p>Article history: Received: 30-Oct-2016 Accepted: 19-Nov-2016</p> <hr/> <p>Keywords: Cardiovascular disease Coronary slow flow phenomenon Serum lead level</p>	<p>Introduction: While there are some reports on an association between lead exposure and cardiovascular disease, there is still no actual proof of the contribution of lead to specific cardiovascular diseases.</p> <p>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 the control group, which contained 30 patients with normal coronary angiography.</p> <p>Results: In this study, age and 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 difference was observed between the two groups regarding serum lead level.</p> <p>Conclusion: According to the results of this study, a significant correlation was found between serum lead level and CSFP. The suspected mechanisms are oxidative stress and inflammation.</p>

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Introduction

Cardiovascular diseases are the leading cause of mortality and primary contributors to the global disease burden (1).

According to the literature, 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 at 1-3%, 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, which may 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 these diseases is 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) demonstrated insignificant positive relationship between coronary heart disease or stroke and high lead levels.

With this background in mind, this study aimed to evaluate the association between lead exposure and Coronary Artery Disease (CAD), documented by angiography.

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 by coronary angiography. On the other hand, the control group included 30 patients with normal coronary angiography, who had no traditional atherosclerotic risk factors, such as diabetes, hypertension, hyperlipidemia or smoking habits. In addition, subjects of the control group had no contact with lead metal, their ischemic heart disease was confirmed by noninvasive stress test and they were candidates for diagnostic coronary angiography.

CSFP is 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 of 30 patients (case group) with CSFP was confirmed by angiography and compared with 30 healthy patients (control group). In addition, age was 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 recirculator 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 was considered statistically significant.

Results

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

It is noteworthy that the study groups were homogenous regarding 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 CSFP patients, compared to normal coronary patients ($P < 0.001$ for all three major epicardial coronary arteries). In addition, a significant difference was observed between the two groups regarding serum lead level. In general, less than 20 micrograms/dL of lead in blood is considered normal.

Table 1: Clinical and laboratory characteristics of study groups

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 was 11.6 ± 8.9 , whereas it was 6.6 ± 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).

Table 2: Results of 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 (1.461-124.29)
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 substance may also cause weakness in fingers, wrists or ankles. Lead exposure leads to increased blood pressure, particularly in middle-aged and older people, and can cause anemia.

Worldwide, there are six sources of lead poisoning, including gasoline additives, lead-soldered cans, lead-based paints, ceramic glazes, drinking water pipe systems and folk remedies. Lead intoxication has been known to 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 of chronic lead exposure on systemic lipid metabolism.

Current evidence on lead-induced oxidative stress has been mostly based on in vitro experiments or studies conducted on animals. 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 elevated blood pressure, which may predispose people to glomerular disease. Some other cardiovascular changes have been noted to be associated with increased lead exposure in humans, including changes in cardiac conduction and rhythm, which might be 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).

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