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The Relationship between High Dose Lead Exposure and Serum Lipids and Lipoprotein Levels.

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Abstract:

This study sought to clarify the possible associations between serum lead level and serum cholestrol and lipoprotein levels in high dose lead exposed rabbits.

Levels of serum lead, total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein cholesterol(LDL), very low density lipoprotein (VLDL) cholesterol and triglyceride in 11 male rabbits who were exposed to high dose lead (547ppm lead acetate in drinking water) were compared with those in 9 unexposed subjects by SPSS package and student t test. Statistical significance was defined as $P<0.05$.

Mean serum lead levels were significantly elevated from 36.24±10.1 µg/L in nonexposed group to 60.55 ±8.09 µg/L in the exposed group($P<0.001$). The exposed subjects had significantly higher mean levels of total cholesterol, HDL cholesterol, LDL cholesterol ($P<0.001$). In contrast, VLDL cholesterol and Triglyceride level was decreased($P=0.012$). Serum lead level is positively associated with total cholesterol, HDL cholesterol, LDL cholesterol.

Key Words: Serum lead level, Serum cholesterol level, Serum triglyceride level, Rabbit.

Introduction:

Lead is a ubiquitous environmental and industrial pollutant that has been detected in almost all phases of environmental and biological systems. This heavy use has caused local and global contamination of air, dust, and soil[1].

Whereas, cardiovascular disease is a leading cause of disability and premature death. Extensive evidence of an association between serum lipid and lipoprotein levels and coronary artery disease has been well documented[2-5]. The positive association is continuous, with no single level of cholesterol separating those who are at risk from those who are not.

Several reports have shown that both acute and chronic lead poisoning cause impairment of heart and vessel function[6-7] and that rates of death from cerebrovascular disease are significantly increased in lead-exposed workers compared with the general population[8-10]. However, no clear data are available demonstrating a higher mortality rate from heart disease in subjects exposed to lead [11].

An association between atherosclerosis and lead exposure is biologically plausible. Microscopic analysis of lead-intoxicated animals has indicated fatty degeneration of the myocardium and sclerotic changes in the aorta and walls of the small arteries, especially the renal, cerebral and coronary arteries[12-15], and atrophy of elastic fibers in the aorta[16]. Thus, it has been suggested that one of the underlying mechanisms in the association between cardiovascular damage and lead exposure is the induction or acceleration of atherosclerosis[7].

According to Wojtczak-Jaroszowa and Kubow[7], there are at least 3 pathophysiological mechanisms whereby lead could induce atherosclerosis:

(I) inhibition of superoxide dismutase, resulting in the elevation of serum lipid peroxide[17,18]; (II) formation of atherosclerotic plaques from a single mutated proliferating cell (monoc1onal hypothesis);and (III) inhibition of the activity of cytochrome P-450 [19], leading to an increase in serum lipids and their accumulation in vessel walls. There have been few controlled studies of the effects of lead exposure with different dose on serum lipids and lipoprotein levels in either animals[14-16,20-30] or humans[31-36]. Increases [14,20,22,24,26,28,29,32,33,36], decreases[16,21,23,27,30,31] and no changes[34] in serum cholesterol levels have been reported. The aim of the present study was to elucidate the effect of lead exposure on serum lipid and lipoprotein levels.

Materials and Methods:

Animals: Twenty (20) male white rabbits, purchased from the animal house of Pasteur Institute of Iran (Tehran, Iran). Weighing about 1.91±0.21 Kg were used as experimental animals. Throughout the present investigation, animals were housed ingroups in cages at 22 ± 2 °C with free access to pellet food and water and on a 12 h light/dark cycle. They were fed a regular rabbit chow.

The animals were daily weighted. Rabbit's weight was measured with a laboratory electronic scale, which is accurate to within 1 0 g.

Experimental Design: Animals were randomly assigned into two groups:

1. Normal controls (n=9) were provided with regular drinking water.
2. Lead-exposed group (n=11) were received with a drinking water containing 547ppm(547 µg/l) lead.

Collection of Blood Sample: Blood samples were collected from marginal ear vein of overnight fasted rabbits before starting experiments and after 40 days of treatment.

The blood samples were collected in glass centrifuge tubes, then centrifuged for 15 min at 1000 × g. Sera were separated and stored at −30 °C in deep freezer till further biochemical measurements.

Biochemical Analysis: For measuring lead, a diphasic ammonium phosphate matrix modifier in the Ultrex and Triton X-100 grade was added to an aliquot of blood serum. A Perkin-Elmer Model 373 atomic absorption spectrophotometer with a Perkin-Elmer HGA 2200 graphite furnace was used together with a hollow cathode lamp and a Perkin-Elmer deuterium corrector.

Laboratory Analysis: Serum triglyceride and total cholesterol were analyzed using kits obtained from Sigma Diagnostics, and serum HDL, LDL, and VLDL cholesterol were measured using the Cholestech Lipid LDX system (Hayward, CA).

Statistical Analysis: SPSS package and student t test was used to compare the weight, serum lead, total cholesterol, HDL cholesterol, LDL cholesterol, and VLDL cholesterol and triglyceride betweens case and control groups. Statistical significance was defined as $P<0.05$.

Results:

In the recent years, many researchers have studied relationship between environmental pollutions and cardiovascular diseases[37-39].

The animals weight in two groups is shown in Table 1. A student t test showed a nonsignificant decrease in body weight in lead exposed rabbits; in comparison to controls ($p > 0.05$). The differences of serum lead concentrations between two groups were significant ($P<0.001$)(Table 2).

Mean cholesterol, lipoproteins and triglyceride values for both groups, before and after experiment are given in Table 2. Total cholesterol , HDL cholesterol and LDL cholesterol values were significantly higher in the high dose lead-exposed subjects ($P<0.001$); and VLDL and triglyceride significantly decreased ($P=0.012$).

Table 1. Changes of body weight in rabbits before and after of experiment.

Group	Mean weight before experiment (Kg)	Mean weight after experiment (Kg)
Case (lead exposed)	1.89 ± 0.19	1.82 ± 0.3
Control (Non exposed)	1.94 ± 0.24	1.96 ± 0.31

Average ± standard deviation

Table 2. Changes in lead, total cholesterol, LDL-cholesterol, HDL-cholesterol, VLDL and triglyceride following exposed with lead.

Group	Lead (µg/l)	Total cholesterol (µg/dl)	LDL-cholesterol (µg/dl)	HDL-cholesterol (µg/dl)	VLDL cholesterol (µg/dl)	Triglyceride (µg/dl)
Case (Lead exposed)	60.55± 8.09	116.81 ± 41.62	87.74 ± 36.93	17.0 ± 4.87	12.07 ± 3.24	60.36 ± 16.22
Control (Nonexposed)	36.24±10.11	60.77± 5.73	29.84 ± 2.26	10.33 ± 0.7	20.6 ± 7.67	103.0± 38.36
P	0.000	0.002	0.001	0.003	0.012	0.012

Average ± standard déviation

Discussion

Lead is dispersed throughout the environment, in ambient air, in many foods, in drinking water and in dust [40]. The major environmental sources of metallic lead and its salts are paint, auto exhaust, and contaminated food and water [41-43].

The main finding of this study is that serum cholesterol and lipoprotein levels were higher in subjects who were exposed to high dose lead than in those who were not exposed (Table 2). This relationship between serum lead and serum lipid levels in the exposed subjects, suggesting an altered lipid metabolism related to lead exposure.

The assessment of a possible relationship between serum lead level and lipids is an important step in elucidating the mecha-nisms underlying the excess cardiovascular morbidity among lead-exposed subjects[6].

The associations between serum lead level and serum total cholesterol , HDL cholesterol and LDL cholesterol reached statistical significance ($p<0.001$), but VLDL cholesterol and triglyceride levels significantly decreased in lead exposed animals ($P=0.012$);(Table.2.).

Our finding of elevated total cholesterol levels supports 3 previous reports[32,33,36] and disagrees with 2 others[31,34]

In the study by El Gazzar et al.[33] lipoproteins were not examined and in the others the results were inconsistent. An increase in HDL cholesterol was reported by Cocco et al.[34], but this increase was accompanied by reduced total cholesterol. Differences between our results and those of the studies cited may be due to differences in sample subjects or to high dose of lead acetate used in this study or an absence of control for confounding variables in the other studies.

Our results are consistent with the hypothesis that a lead induced accumulation of serum lipids is one of the underlying mechanisms in the association between lead exposure and

cardiovascular damage. Because of the positive and continuous association between serum cholesterol and coronary artery disease[5], it seems that subjects who are occupationally exposed to lead are at higher risk of coronary artery disease than those who are not exposed.

The association between lead exposure, and high serum lipid levels is biologically plausible and could be due to either increased synthesis or decreased removal of lipoproteins.

Decreased removal may occur as a result of the alteration of cell surface receptors for lipoproteins[20] or as a result of the inhibition of hepatic lipoprotein lipase activity[44]. Furthermore, lead has been shown to depress the activity of cytochrome P-450[19,45-46]. this can limit the biosynthesis of bile acids, which is the only significant route for e1imination of cholesterol from the body. Increased synthesis may be due to a lead induced increase in hepatic enzymes at important control points for de novo cholesterol synthesis, as has been found in Wistar rats[47], or it may be due to impaired feedback inhibition.

We conclude that serum lead level is positively associated with levels of serum total cholesterol, HDL cholesterol and LDL cholesterol . The positive association between serum lead level and serum cholesterol among exposed subjects may have important clinical implications.

Researchers have demonstrated the benefit of antioxidants including, vitamin E, vitamin C, vitamin B6, β-carotene, zinc, and selenium in preventing lead toxicity[48-52]. Further studies should focus on exploring the benefits of these antioxidants in prevention of lead Toxicity.

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