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ORIGINAL ARTICLE

Chronic Exposure to Lead: A Cause of Oxidative Stress and Altered Liver Function in Plastic Industry Workers in Kolkata, India

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Abstract It is well known that chronic exposure of lead leads to adverse health effects. Workers for plastic industry are generally exposed to high concentration of lead as fume, dust, and additive that protect PVC. This study was done on them to find out the detrimental effects of chronic lead exposure on hepatic and hematological toxicity. Blood and 24 h urine sample was collected from 47 plastic industry workers and matched against 42 controls for various parameters. The study group shows significant increase in blood ($p < 0.0001$) and urinary level of lead ($p < 0.0001$). Hemoglobin levels were significantly decreased ($p < 0.0001$), and the liver enzymes like ALP, ALT, AST and y-GT were significantly increased ($p < 0.0001$) in all cases exposed for >10 years. Serum lipid peroxide by quantitative assay of thiobarbituric acid reactive substances was also found increased in the study group ($p < 0.0001$). The observations point towards the acute health risk faced by plastic industry workers, in whom chronic exposure to lead increases the absorption and accumulation, over a period of time, of this highly toxic element in their body. This increases oxidative stress, causes metabolic damage to RBC and cell membranes, and also suggests necrosis of liver cell, hepatocellular injury and presence of space occupying lesions. Considering the data immediate health and hygiene monitoring and proper rehabilitation for the suffering population seem to be of paramount need in plastic industry to minimize occupational hazards.

Keywords Lead intoxication · Oxidative stress · Hepatocellular injury

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Introduction

When in developed countries the environmental problem of lead contamination is declining rapidly, in many developing countries the situations is just the reverse. As a result the environmental lead poisoning and it's effect on the health of the population are expected to increase [1]. Also, environmental and occupational lead pollution is a common problem in both developing and industrialized countries. There is increasing evidence that health may be harmed by chronic exposure to lead present in the environment at levels insufficient to produce classical symptoms of lead poisoning [2]. Lead has long been recognized as a neurotoxin that causes renal damage, neurological dysfunction, anemia, and death at high doses. For a long time, medical attention was on acute lead poisoning due to accidental and occupational exposures. Therefore, the adverse effects of chronic exposure at lower concentrations of lead were not well understood until the 1970, when scientific evidence showed that lead retarded the mental and physical development of children, causing reading and learning disabilities, changes in behavior, such as hyperactivity, reduced attention span; and hearing loss, even at low level of exposure [3].

The plastic industry always emit lead as fume and dust to its surrounding areas and workers are generally exposed

to high concentration on regular basis. The lead sulfate or lead stearate acts as a common additives or stabilizer that protects the polyvinyl chloride (PVC) from chemical degradation from heat and ultra violet radiation. Also, pigments containing lead chromate is continuously used to colour the coating. In the manufacturing process, these lead compounds are commonly used as the powder form of metal that may not be recognized as a hazard by workers. The various formulations used in the industry expose the workers to a varied amount of lead on an everyday basis.

Several chronic cases of occupational lead poisoning in adults and children have been attributed to lead fumes and lead oxide dust emanated from industry [4]. Personal breathing zone exposure samples documented that employees had a substantial airborne exposure to lead (as chromate compound).

The objective of this study is to evaluate the effect of occupational lead exposure of plastic industry workers on their systemic metabolism in terms of hepatic functional abnormalities and hematological aberrations.

Materials and Methods

Blood samples were taken from 47 factory workers, who had been employed full time, (8–12 h per day) for the last 10–25 years and exposed to the fumes and dust of lead in the plastic industry in Kolkata, West Bengal, India. A control group of 42 non-exposed men was included whose age distribution was standardized to those of the exposed group. All the workers as well as the control group were informed about the implications of this experimental study and written consents were taken from the willing subjects.

Heparinised whole blood and 24 h urine were analyzed for lead levels by atomic absorption spectrophotometer (Perkin-Elmer, 2380). Principle applied was formation of lead complex with 2 % ammonium pyrrolidine dithiocarbamate and extraction of it into methyl isobutyl ketone. Eluted Organic phase were measured at 283.3 nm wavelength with background correction and calibration by standard additions [5]. Special precautions were taken to avoid contamination by ambient lead, reagents and materials (heparinised vacutainers and urine containers). All tests were done using quality control materials of CDC, USA.

Hemoglobin was Determined by Cyanhemoglobin Method [6]

Activity of alkaline phosphatase (EC 3.1.3.1), alanine aminotransferase (ALT) (EC 2.6.1.2), aspartate aminotransferase (AST) (EC 2.6.1.1), γ-glutamyl transferase (γGT) (EC 2.3.2.2), lactate dehydrogenase (LDH) (EC 1.1.1.27) were measured using kits supplied by (Beckmann Coulter, India) in Olympus AU 480 auto analyzer. Both internal and external quality controls were measured, using control sera of Bio-Rad, USA.

Blood was analyzed for serum lipid peroxide by quantitative assay of thiobarbituric acid reactive substance (TBARS). Thiobarbituric acid was added to plasma sample under acidic condition, and the absorption of color that developed after heating was estimated by spectrophotometer at 535 nm [7]. Both external and internal quality control was measured using quality control sera of Randox Laboratories, UK. Statistical analysis was conducted using SAS software [8]. Students' t test was employed to evaluate statistical significance which was determined at p value <0.0001.

Results and Discussion

The results of analysis of the blood and urine samples of plastic industry workers and control groups in the study are presented in Table 1.

Blood lead levels in 47 samples of different category of workers have been estimated and showed a significant increase in the levels of blood lead ($p < 0.0001$); urinary excretion of lead was also increased ($p < 0.0001$). The initial interviews revealed that the workers were exposed to uncontrolled use of powdered lead sulfate stabilizer in custom compounding PVC plastic intended for commercial use. Although lead sulfate containing products were used at the current workplace for $\sim$25 years, the employer had never provided any lead related industrial hygiene monitoring or blood lead level testing. The workers are regularly exposed to smoke of lead or lead oxide or lead sulfate. The workers regularly consumed lead vapors by inhalation, ingestion; absorption through skin and hair and contamination of their clothing, food and drinking water. Air quality monitoring showed air lead level of 629–912 μg/m^3 (as an 8 h, time weight average), when the OSHA permissible exposure limit is 50 μg/m^3 in 8 h time weight average [9]. Clinical signs of toxicity depended upon the duration of exposure, the condition of the fume outlet, nutritional status of the workers and other undetermined factors. Both blood lead levels and the urinary excretion of lead in these workers was about three times the control group. This high urinary output with high blood value of lead indicates that the body has increased accumulation lead in the tissue. Most of the workers complained of constipation, weakness, metallic taste in the mouth and abdominal colic.

Hematological investigations showed a significant decrease in blood hemoglobin (Hb) levels ($p < 0.0001$). This could be either due to direct toxic effect of lead on

Table 1 Biochemical investigations in blood and urine of plastic industry workers and control population

Subject (no. of subjects)	Age (year)	Duration exposure (year)	Blood lead concentration (μg/100 ml)	Hemo globin (gm/100 ml)	Lipid peroxidation products (nmol/ml plasma)	Alkaline phosphatase (U/L)	ALT (U/L)	AST (U/L)	γ-GT (U/L)	LDH (U/L)	Urinary lead concentration (μg/day)
Plastic industry worker (47)	18–60	10–25	59.6 ± 6.5*	10.6 ± 0.8*	2.49 ± 1.04*	212 ± 13	98 ± 14	92 ± 13	63 ± 7	368 ± 36	89.8 ± 19.4*
Control group (42)	20–62	–	12.3 ± 3.2*	14.9 ± 1.2*	0.7 ± 0.05*	129 ± 22	23 ± 11	21 ± 14	19 ± 5	214 ± 22	24.8 ± 6.8
Significance			<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Values represent mean ± SD, student's *t* test was applied for determining the statistical significance between control and workers ($p < 0.0001$)

RBC or heme synthesis or to associated anemia in the subjects, as the economic conditions and the nutritional statuses of the workers are very poor and malnutrition is a common finding in the socio-demographic data of the worker. It is also not unlikely that lead could be the casual factor for depressing the heme synthesis by inhibiting its key enzymes. Lead's effect on RBC membrane includes interference with various energy and transport systems, which may explain why it can shorten erythrocyte survival time and cause anemia. Lead can also inhibit heme synthesis pathway, especially enzyme δ-aminolevulinic acid dehydratase causing accumulation of aminolevulinic acid in body and increasing urinary excretion of the same [10].

For the liver function test several enzymes were assayed. It was observed that serum alkaline phosphatase levels increased significantly ($p < 0.0001$) with increased blood lead concentration. There is a significant rise in serum levels to LDH ($p < 0.0001$), ALT ($p < 0.0001$), AST ($p < 0.0001$) and γ-GT ($p < 0.0001$) as compared to control group, while in few cases where exposure was not chronic the values were normal.

Environmental lead does make a significant independent contribution to increased serum ALP, ALT, AST and γ-GT value, which is associated with impaired liver function in general population. Increased ALP levels may be an indicator of space occupying lesions in the liver. The ALT and AST are aminotransferases that catalyze the interconversion of amino acids to alpha-oxo-acids by transfer of amino groups. The increased value of transaminases suggests necrosis of the hepatic cell by lead and lead induced hepatocellular injury. The enzyme γ-GT, a membrane bound glycoprotein involved in the metabolism of glutathione and transfer of glutamyl moiety to the amino acid receptors, is a sensitive indicator of hepatocellular damage [11]. Partially increased level of LDH may be due to associated destruction of cell by lead leading to the leakage of enzymes and appearance of the same in circulation, like ALT and AST.

The TBARS was increased in comparison to the control group ($p < 0.0001$). These data suggest that lead may have a role in the oxidative stress in the body producing lipid peroxidation at the cellular level. Also high value of y-GT suggests the same. These changes could be related to nutritional status or they could be a sequel of increased TBARS that seems to be due to lipid peroxidation of biomembranes.

Conclusion

Developing countries are continuously under threat from environmental pollution that comes hand in hand with industrialization. There is enough data to suggest that Pb,

one of the commonest elements used in plastic industry, poses a number of health hazards including hepatic and hematological function abnormalities for workers continuously exposed to the toxic metal.

Significantly high blood and urinary Pb levels and increased lipid peroxidation analyzed by serum lipid peroxidase levels suggests that excess accumulation of Pb in body also causes severe oxidative stress, which is a leading factor for carcinogenesis.

Abnormal LFT suggests hepatocellular inflammation and injury and may harbor other sinister hepatocellular pathology grossly detrimental to survival of the individuals.

Apart from this there is also evidence of workers suffering from anemia caused either by direct effect of Pb on RBC synthesis or by superimposed malnutrition or both.

Recommendation: Considering the data and the general impact of Pb on various biological systems of plastic industry workers, it is suggested that uncontrolled use of $PbSO_4$ stabilizer in PVC plastic compounding should be curtailed and there should be immediate provision of Pb related industrial hygiene monitoring in the factory with proper rehabilitation measures provided to workers suffering from any occupational hazard related to it.

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