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ORIGINAL ARTICLE

Diagnosis, Evaluation, and Treatment of Lead Poisoning in General Population

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Abstract Among the heavy metals, lead still remains the major toxic pollutant of the environment. Human exposure to lead can occur through numerous pathways including air, food, dust, soil, and water. In the present study 14 lead poisoned patients with non-occupational lead exposure were evaluated. They were followed up and compared against the controls with no history of lead exposure. The patients had high blood lead levels and symptoms of weakness, dizziness, abdominal pain, generalized body ache, loss of appetite, and anxiety. Repeated course of chelation therapy helped to bring down their body burden of lead. Alternative sources for lead exposure can cause severe lead poisoning in general population. Screening and medical management of such individuals is very important to identify and eliminate sources of lead. The treatment and management requires a thorough medical evaluation and environmental intervention.

Keywords Lead exposure · Blood lead level · Chelation · ZPP · D-penicillamine

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Introduction

Lead is ubiquitous in human environment, because of its excellent physico-chemical properties, low cost and easy workability and is widely used in many industrial and domestic activities. The lead dispersed through gasoline exhausts, smelter emission, peeling paint, etc., never disappears completely from our environment. Human exposure to lead is from numerous sources and a myriad of pathways including air, food, dust, soil, and water. Exposure of the general population to lead mostly occurs through the ingestion of contaminated food and drinking water, and by the inhalation of particulate lead in ambient air. Exposure can also occur due to high lead levels in dust and soil in residential areas near high-density traffic, smelters or refineries, and the consumption of vegetable, fruit and grains grown on high lead soils or near sources of lead emissions containing lead in excess as a result of direct deposition of lead onto plant surfaces apart from plant uptake of lead from soils. Gunshot wounds received through bullet injury either accidentally or due to reasons of crime act as long-term sources. Several times these type of lead poisoned cases go undiagnosed and untreated or may receive only symptomatic treatment because of lack of proper diagnosis. Screening and medical management of lead-exposed individuals is very important to identify and eliminate sources of lead.

Materials and Methods

The present study we evaluated 14 lead poisoned patients, out of the many cases referred to our National Referral Center for Lead Poisoning in India (NRCLPI), during 2002–2007. All patients (mean age 28 years, range

23–33 years) with non-occupational lead exposure. They were followed up and compared against the controls with an average age (mean age 28 years, range 25–31 years) with no history of lead exposure and with lead levels of 5.58 ± 2.02 μg/dl.

Each individual was interviewed using a standard questionnaire. Information regarding their working environment, personal protective equipments, personal hygiene, and habits and working hours/day was collected. Written informed consent was obtained from them before collecting blood sample and for publication. Blood samples were drawn by venipuncture for the estimation of lead. The patients were subjected to chelation therapy using Cuprimine (D-penicillamine, 3-mercapto D-valine) 25–35 mg/kg body weight/day.

The blood lead levels (PbB) were estimated using ESA model 3010B lead analyser (ESA, Inc., Chelmsford, MA, USA), which uses the principle of differential pulse anodic stripping voltammetry (DPASV) and zinc protoporphyrin (ZPP) using AVIV model 206 Hematofluorometer (Aviv Associates, Inc., Lakewood, NJ, USA) which works on the principle of front surface fluorometry.

The statistical analysis was carried out using unpaired Student's *t*-test, Wilcoxon test, and two way analysis of variance.

Results and Discussion

Lead can get into human body through various sources and pathways. The sources of lead exposure in the patients selected for this study is given in Table 1. The symptom of lead poisoning varies and sometimes mimics that of the other disorders. In the present study the various symptoms of the patients were compared against control group having no history of lead exposure and with lead levels of 5.58 ± 2.02 μg/dl. The statistical significance is given as $P \leq 0.001$ very highly significant; $P \leq 0.01$ highly significant; $P \leq 0.05$ significant; $P = 0.05$–0.1 possibly significant; $P > 0.1$ not significant. Systolic blood pressure (SBP), diastolic blood pressure (DBP), and levels of hemoglobin (Hb), ZPP, and PbB were measured in patient and the control groups. SBP and DBP has increased significantly in patients ($P < 0.01$) compared to control group. Several studies have been reported the increase in blood pressure with an increase in the body burden of lead. Studies conducted by Hu et al. [1] suggested that cumulative lead burden, might be a significant risk factor for hypertension. Perry et al. [2] demonstrated in rats exposed to lead in amounts comparable to the environmental lead exposure to human beings had an average elevation in systolic pressure comparable to that of human beings. Studies conducted by Nomiyama et al. [3] demonstrated that blood lead above 40 μg/dl was found to be the most potent factor for elevating systolic/diastolic blood pressure. Their data suggested that lead induced changes in lipoprotein metabolism that play an important role in the lead induced increase in blood pressure.

Table 1 Sources of lead exposure

Sources	Number ($n = 14$)	Percentage
Unbranded medicine	4	28.6
Food	3	21.4
Cooking vessel	1	7.1
Oil spill on body	1	7.1
Parental occupation	1	7.1
Bullet injury	1	7.1
Drinking water	1	7.1
Pica	2	14.3

A very high significant decrease ($P \leq 0.001$) in Hb and a very high significant increase ($P \leq 0.001$) in ZPP and PbB levels were seen in the patients compared to the controls Table 2. Studies have reported elevation in ZPP and a decrease in hemoglobin level in people exposed high amount of lead [4]. Lead is shown to inhibit enzymes δ-aminolevulinic acid dehydratase, coproporphyrinogen oxidase and ferrochelatase of the haem synthesis pathway [5]. Ferrochelatase is responsible for the incorporation of iron into protoporphyrin IX to form heme. As a result of inhibition, protoporphyrin accumulates in erythrocytes, with the majority binding to zinc and to form zinc protoporphyrin [6].

Table 3 shows the various symptoms associated with lead poisoning in the two groups. The proportion of weakness is 92.9% in patients when compared with controls (35.7%), the difference of proportion being statistically significant ($P = 0.002$). It is observed from the odds ratio with 95% confidence interval (95% CI), that weakness in patients is 23.4 times more likely compared to the control group. An increased proportion of dizziness is observed in patients (57%) compared to controls (28.6%) with $P = 0.127$. Dizziness in patients is 3.31 times more likely compared to controls with 95% confidence interval (0.71–15.53). Increased proportion of abdominal pain is observed in patients (85.7%) with odds ratio 3.33 indicating, abdominal pain in lead-exposed is 3.33 times more likely compared to controls.

Loss of appetite observed in patients is 92.9% compared to 42.9% in the control group and anxiety is 64.3% compared to 35.7% in the control group.

All the patients had elevated PbB and ZPP levels. The control group had lead levels in the range of 5.58 ± 2.02 μg/dl. In 1991 the Centers for Disease Control (CDC) has established an "elevated" blood lead level of concern is

Table 2 Effects of lead exposure

Parameters	Patients ($n = 14$)	Controls ($n = 14$)	Significance (P)
Systolic blood pressure (mm Hg)	131.0 ± 13.26	118.86 ± 6.90	0.005
Diastolic blood pressure (mm Hg)	89.07 ± 10.96	76.36 ± 6.97	0.001
Hemoglobin (gm/dl)	9.26 ± 1.79	12.64 ± 2.20	0.000
ZPP (μg/dl)	148.29 ± 88.66	33.86 ± 7.56	0.000
Pb (μg/dl)	86.46 ± 32.29	5.58 ± 2.02	0.000

Table 3 Symptoms associated with lead poisoning

Symptoms	Lead exposure in adults through various sources			
	Patients ($n = 14$)	Controls ($n = 14$)	Significance (P)	Odds ratio (patients) 95% CI
General symptoms				
Weakness	13 (92.9)	5 (35.7)	0.002	23.4 (0.30–165.20)
Dizziness	8 (57.1)	4 (28.6)	0.127	3.31 (0.71–15.53)
Abdominal pain	12 (85.7)	9 (64.3)	0.385	3.33 (0.56–19.99)
Generalized body ache	9 (64.3)	5 (35.7)	0.131	3.24 (0.71–14.76)
Loss of appetite	13 (92.9)	6 (42.9)	0.002	17.33–31.15
Anxiety	9 (64.3)	5 (35.7)	0.131	3.24 (0.71–14.76)
General physical examination				
Elevated systolic BP	3 (21.4)	0 (0.0)	0.222	3.55–5.86
Elevated diastolic BP	8 (57.1)	1 (7.1)	0.013	17.33 (2.35–124.04)
Anemia	13 (92.9)	5 (35.7)	0.002	23.4 (0.30–165.20)
Blue line on the gum	–	–	–	–
Basophilic stippling	–	–	–	–
Laboratory investigations				
Decreased hemoglobin	13 (92.9)	8 (57.1)	0.077	9.75 (1.28–73.99)
Elevated ZPP	14 (100.0)	5 (20.0)	0.001	23.40–41.73
Elevated lead	14 (100.0)	0 (0.0)	0.000	169.0–729.0

$P \leq 0.001$ very highly significant, $P \leq 0.01$ highly significant, $P \leq 0.05$ significant, $P = 0.05$–0.1 possibly significant, $P > 0.1$ not significant

10 μg/dl and above. Later studies have reported the cognitive deficits associated with blood lead levels below 10 μg/dl [7]. A threshold value below which lead has no apparent adverse developmental effect has not been identified [8]. In this study slight elevation in ZPP levels was observed in five of the controls, the elevated ZPP might be due to the anemic conditions seen in them. In case of iron deficiency instead of iron binding to the protoporphyrin ring zinc ions are incorporated into the protoporphyrin ring forming ZPP [9].

The patients were subjected to repeated course of chelation therapy using the chelator, Cuprimine (D-penicillamine, 3-mercapto-D-valine), 25–35 mg/kg body weight/day in divided doses, which was effective in reducing the total lead body burden in individuals with high blood lead levels. Chelation therapy increases the rate of excretion of lead in the short term, by 25–30 times the normal, which may otherwise take months to years. Chelating agent competitively binds lead, removing it from biologically active molecules, and the complexes formed are easily excreted from the body.

In this study, chelation therapy has resulted in a significant decrease ($P < 0.01$) in the ZPP and PbB levels in all subjects during the three courses of therapy (Table 4).

We were able to follow up only nine patients for the third chelation therapy. The third course of chelation therapy has brought down PbB and ZPP levels within acceptable levels in seven patients and in two of the patients, the levels remained high. Few patients are on follow up.

Lead poisoning though most common in lead based industrial workers, is often seen in the general population. Both occupational and environmental exposure to lead remains a serious problem all over the world. Lead can get into the body through alternative sources. It is a versatile element which has been used by mankind for over 6,000 years and is today one of the most widely distributed metals in the environment. Common sources of lead are

Table 4 Effect of chelation therapy in patients (mean ± SD)

Parameters	Before chelation therapy (14)	Chelation therapy		
		I course (14)	II course (14)	III course (9)
ZPP (μg/dl)	148.28 ± 88.7	75.78 ± 35.8[a]	52.57 ± 24.9[a]	43.13 ± 19.8[a]
Pb (μg/dl)	86.46 ± 32.3	44.86 ± 28.5[a]	40.37 ± 34.1[a]	22.13 ± 22.6[a]

[a] Wilcoxon signed rank test, significance from the values of before chelation therapy ($P < 0.01$)

lead based paint, lead contaminated air, soil, dust, drinking water got through lead soldered pipes, food stored in lead soldered cans, traditional medicines, cosmetic, and artisan ceramics.

Lead may be introduced into food inadvertently during harvesting, processing, packaging or preparation. The main sources of contamination of food are soil, industrial pollution, agricultural technology, and food processing. Surface contamination of homegrown vegetables, storage cans with lead solder seams and kitchenware are some of the sources of lead content in food. Soil in or adjacent to lead smelters, lead mines, houses painted with lead paint, and urban areas where there has been heavy automobile traffic is likely to contain high concentrations of lead [10, 11]. Fruits and herbs grown in such places contain higher amount of lead levels [12]. Milk samples obtained from cows grazing in areas adjacent to highways and industrial areas contain high lead levels [13]. Homes in close proximity to either lead smelters or industries involved in the manufacture of lead products may contain elevated concentration of lead in their surrounding soil, thus providing a potential source of lead exposure to humans [14]. Lead in drinking water, especially in the first flush water arises primarily because of contamination by lead-containing components of distribution or plumbing system rather than from source water itself [15]. Smelters, incinerators, lead based industries contribute to substantial elevations in air lead [16, 17]. Lead is used in many colored pigments, colored inks and paints because it holds pigments well. For infants, ingestion of the house dust due to leaded paint on walls in the older properties and chalking of paints from woodwork and toys becomes the major pathway to lead [18, 19].

Lead crystal glasses, ceramic and other glazed containers used for storing, cooking or serving food is a source of lead. Lead glazes are used on ceramic kitchenware, earthenware and stoneware because they allow more flexibility in the kiln temperatures for firing pottery [20]. Lead is also used in welding, soldering making bullets, ammunition and some brass and bronze products. It is also found in cosmetics like surma in Asia, Kohl in India, and Al Kohl in Saudi Arabia and Kuwait [21, 22]. Traditional remedies found to contain lead [23, 24]. Many hobbies like oil painting and art work, making stained glass, glazed pottery making, and casting molten lead for making fishing weights are also the source of lead [25]. Gunshot wounds received through bullet injury either accidentally or due to reasons of crime act as long-term sources. Retained lead bullets and pellets release lead gradually into body fluids [26].

The possibility of lead exposure in general population is therefore can occur through many sources and pathways mentioned above. Lead does not spare any organ in the body and not known to serve any necessary biological function. Some of the patients studied in this study did not show any symptoms accept weakness and loss of apatite and we were able to identify these cases only after estimating blood lead levels. Blue line on the gum and basophilic stippling was not seen in any of the patients studied. Since the symptoms of lead poisoning are often similar to other disorders, most of the lead poisoning cases go undiagnosed and untreated and many a times being treated symptomatically, without proper diagnosis. Screening and medical management of lead-exposed individuals is very important to identify and eliminate sources of lead. The treatment and management of lead-exposed individuals requires a thorough medical evaluation and environmental intervention. Chelation therapy is not a substitute for environmental remediation or preventing exposure to lead. Chelation therapy is known to reduce blood lead concentrations acutely, but the levels may rebound within weeks to months after treatment, often requiring repeated courses of treatment. Routine screening and increased awareness to lead hazards would be beneficial in reducing exposure. Lead is very useful metal, same time highly toxic. If not handled carefully, causes dangerous health effects leading to death at very high levels.

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