Lead in Blood of Albino Mice after Oral Administration of Different Doses of Lead Acetate

SHAUKAT A SHAH, SAROSH MAJEED, QAMMAR SULTANA, *SAEED A KHAN*

ABSTRACT

Objective: Correlation of lead in blood of albino mice with orally administered different doses of lead.
Material and methods: This experimental study was conducted at Postgraduate Medical institute Lahore from Fist Feb to 31st March 2004.A total of 40 adult virgin female albino mice of 6-8 weeks age weighing between 30±2 grams were divided randomly into four groups of ten each. Group I was not given lead acetate, where as group I,II and IV were given lead acetate in doses of 2,4 and 8mg/kg/day, respectively for 60 days by oral route.
Results: Blood lead levels were lowest in group I(0.16ugm/ml mean SD 0.18±2) and highest in group IV(0.62ug/ml mean SD 0.60±0.015) and revealed significant statistical differences(P<0.001) between groups I vs II,I vs III A and I vs IV. Leads levels were found to be elevated with increment in doses of lead acetate.
Conclusion: There is linear correlation between concentration of lead and its absorption and even low dosage of exposure leads to rise to toxic level especially for children.
Keywords: Blood lead levels, mice, correlation,

INTRODUCTION

Lead is xenobiotic and is toxic at any level of exposure[1]. Pathological effects can be manifested in multiple organs. Specific organ dysfunctions include central and peripheral nervous system, renal, gastrointestinal, hematological and reproductive system[2].

Lead is a toxic agent with no known beneficial role in the human body[3].Several attempts have been made to relate blood lead levels to adverse health effects[4].The concentration of lead in blood is most widely used indicator for monitoring the intensity of exposure to inorganic lead in workers employed in lead based industries[5]. There is evidence in literature that lead poisoning reduced Roman reproduction[6]. Lead damages blood brain barrier and subsequently the brain tissue. Severe exposure resulting in blood lead level>80ug/dl may cause coma, encaplopathy or death[2]. Workers with blood lead level of 40-50ug/dl may experience fatigue, irritability, insomnia, headache and evidence of mental and intellectual decline[7].Blood lead level as low as 30ug/dl decreases motor conduction[8]. Significant rise of blood lead level leads to anemia due to decrease in erythropoiesis[9]. Enviormental or occupational exposure has been associated with significant impairment of renal function. A rise in blood level of 10ug/dl is associated with creatinine clearance of 10.4ml/minutes[10].

Department of Pathology, Avicenna Medical College, Lahore
Dr Syed Shaukat Ali Shah, Assistant professor Email---shaukatshah00@hotmail.com Cell-03454756105

Lead has also been implicated in disturbance of calcium metabolism, particularly its role in modulating blood pressure through control of vascular tone[3].On gastrointestinal system lead can cause anorexia, constipation or occasionally diarrhorea[11].A lead line some time develops at gingival tooth border after high lead exposure. These symptoms may appear at blood lead level of40-80ug/dl[1].

Chronic exposure to lead in cynomologus monkeys resulted in decreased level of luteinizing hormone (LH), Follicle stimulating hormone (FSH) and prostaglandin E2.Pathological changes in the leyding cells brought about decline in the level of androgen in mice[12,13]. Lead is a known reproductive toxin and there are many evidences in literature about its toxicity both in male and female[3].

Lead enters the body through inhalation, ingestion and does not undergo biological transformation. Absorption of inorganic lead depends upon its physical and chemical form. Gastrointestinal absorption in adults is 10-20% while in children it can be up to50%[1].Lead absorption is increased during fasting and due to deficiency of calcium, zinc and iron[14]. Once in blood stream lead is distributed in blood, soft tissue and mineralized tissue. In the blood it is bound to red blood cells[11].

The main entry of lead is though ingestion by contaminated food and water. The present study was designed to see how increasing concentration of lead given by oral gavage leads to increase in blood lead levels which may reach to toxic level.

MATERIALS AND METHODS

Forty adult virgin female mice of 6-8 weeks age weighing between 30±2gm were procured from Veterinary Research Institute, Ghazi Road, Lahore. The animals were kept in animal house of Post graduate Medical Institute, Lahore. The animals were randomly divided into different groups and kept in separate cages. They were numbered and weighed at one-week acclimatization and thereafter at 60 days. Mice were maintained in standard animal house conditions and were provided with animal feed (Punjab Poultry feed no 3) and water at libitum. These animals were divided into four groups of ten animals each and were given lead (as lead acetate in deionized water) for 60 days. Group II, III & IV were given lead in dose of 2, 4 and 8mg/kg/d respectively while group I was given deionized water and only without lead at the same volume and frequency. The dose and duration schedule was based on as described by Junaid et al[15.] At the end of 60 days five sub-groups of two animals from each group were made by random selection (a, b, c, d and e). For the estimation of blood lead level, blood was collected by puncture of the heart under ether anesthesia. Blood form two animals was pooled to make a sample so five samples were obtained from each group.

Lead Estimation: Acid digestion method was used for the preparation of blood sample i.e. the blood sample was digested in nitric acid: hypochlorite (6:1) mixture and lead level was estimated using flame atomic absorption spectrophotometer[18] model Varian Spectra AA 250. Statistical significance was evaluated by calculating standard deviation (SD) followed by Student's t-test. Correlation between two sets of data (r value) was done and the significance level was ascertained at $p<0.05$.

RESULTS

Two animals died during study in group I and IV. The postmortem was performed but the cause could not be ascertained. Remainder animals were healthy with no significant change in body weight. Lead levels were found to increase with the increased in doses of lead acetate as shown in table I. In group I (control group) mean lead level was 0.18ug/ml with mean SD 0.18±.02.Highest level of lead was found in group IV which was 0.62ug/ml with SD 60±015. The 2nd group shows blood lead level of 0.46ug/ml which is almost double as in group II while group IV reveals average of 0.60ug/ml.

Table 1: Blood lead levels (ug/ml) in mice exposed to different doses of lead for 60 days.

Group	Lead Dose	Blood Levels in subgroups(ug/ml)					Mean± SD
		A	B	C	D	E	
I	0mg	0.19	0.21	0.18	0.16	-	0.18±.02*
II	2mg	0.25	0.27	0.22	0.21	0.26	0.24±.02
III	4mg	0.46	0.46	0.44	0.47	0.47	0.46±.014
IV	8mg	0.62	0.59	0.60	0.60	-	0.60±.015

*P<0.001 as compared with II, III and IV

DISCUSSION

Lead has been recognized as toxicant and injurious to health and effort has been made to reduce the use of lead in daily life[16].Many industrial activities and particularly its use in gasoline and sugar industries has led to his wide distribution so that all human have lead in their bodies. The level of lead in general population in America now averages about 2.8ug/dl[17].

Lead was recognized clinically as occupational hazard in 1939.Workers employed in mining, smelting, spray paintings, radiator repair, recycling and batteries manufacturing are exposed. Environmental sources are urban air, soil contaminated with lead paint, water supply due to lead plumbing and house dust contaminated with lead paint. Consumer may be exposed to lead glazed ceramic, lead solder in food and soft drink cans[12].Flaking lead paint in older houses and soil contamination pose major hazard to youngster and ingestion up to 200mg/day can occur[11].

Lead is a known toxic agent with no beneficial role in human body. Excessive exposure of lead over brief period of time can cause acute poisoning with classical finding as abdominal colic, constipation, fatigue and central nervous system dysfunction, encephalopathy, coma and convulsion[4]. Acute lead toxicity occurs at levels of about 120ug/dl or more in adults and 80ug/dl in children[2].A lead level of 20ug/dl can cause neuropathy and low IQ in children[18].

Toxic effects of lead are preventable by reducing its exposure to the environment and at working places where lead is used[4].Keeping in mind this study was carried out in 40 albino mice to see pattern of rising level of lead after administration of different doses of lead. The animals in group I (control group) were sacrificed after 60 days (only deionized water was given). The blood samples were taken for the

base blood lead levels for comparison with other groups of experimental animals.

The blood lead level in control groups was high. It may be due to presence of lead in the animal feed. On the other hand doubling of blood lead level between group II (2mg/kg/day) and III(4mg/kg/day) and failure to similar rise between group III (4mg/kg/day) and IV (8mg/kg/day) may be explained by fact that the relative blood levels are not linearly correlated with the dose administred[19]. It was suggested by Balttop and Khoo that the mechanism responsible for absorption of lead might be saturable if large single doses are administered. Our data of blood lead levels 0.25,0.46,0.62ug/ml in group II, III and IV) are comparable with lead levels measured in the general population 0.43ug/ml)[20], 0.25-0.30ug/ml)[21], 17.2ugm/ml)[22] and (27.2ugm/ml)[23]. All these concentration are above toxic level. Lead concentration <0.20ug/ml has been found to have deleterious effect on nervous system leading to low IQ level[18]. Hilderbrand and colleague have reported atresia of ovarian follicles of rats at blood lead level of 30ug/ml. Our study reveals that continuous exposure of even low lead concentration (2mg/kg/day) will result in rise to above toxic levels (CDC lowered the definition of toxicity from 0.25ug/ml to 0.10ug/ml)[24].

CONCLUSION

It is evident from study that continuous exposure even to low level of lead can lead to toxic blood levels. In the developed countries use of lead has been reduced but in Pakistan it is still used in plumbing, in toys, paints and other lead based industries. Many studies in Pakistan have shown blood lead level is much higher in our general population as compared to western countries[22,23,25,26,27].

REFERENCE

1. Hu H. Heavy metal poisoning: Fauci AS, Braununwalad E, Issel Backer KJ. Harrison principles of medicine 14th ed, MC GRAW HILL 1998;2564-9.
2. NIOSH. Health effects of lead exposure and occupational exposure criteria. DDHS (NIOSH) publication 1997; 98-112.
3. Schwartz J. Lead blood pressure and cardiovascular disease in men. Arch Env Health 1995; 50:317
4. Staudinger KC, Roth VS. Occupational lead poisioning. Am Fam Phy, 1995; 1-13
5. Mc Grail MP, Stewart W, Schwartz BS. Predictor of blood lead levels in organ lead manufacturing workers. JOEM 1995; 37(10):1224-9
6. Hilderbrand BC, Der R Griffin WT. Effects of Lead acetate on reproduction. Am J Obs gyne 1973;115: 1058 -1165.
7. Bogden JD, Qleske JM. Lead poisioning,one approach to a problem that would not go away. Enviorenmental Health Prospect 1997;39:426.
8. Todd AC, Wetmur JG, Mdine JM. Unrevealing the chronic toxicity of lead; an essential priority for environmental health prospect 1996;104: 141 -6.
9. US Deptt of Health and Human Services. Case studies in environmental medicine; Lead toxicity 1992; 1-23.
10. Payton M, HU H, Sparow D, Weiss ST. Low lead exposure and renal function in the normative aging study. Am J Epidemiol 1994; 140:821-9.
11. Robibns and Cotran. Environmental and nutritional pathology. In: Kumar, Abbas, fausto, Aster. Pathologic Basis of Disease 8th ed. Philadelphia W.B, Saunders 2010; 399-446.
12. Foster WG. Reproductive toxicity of chronic lead exposure in the female cynomolgous monkey. Reproductive toxicol 1992; 6:123-131.
13. 13-Godoweicz B. Toxic effects of lead on fertility of inbred strain mice. Folio Biol Krakaw 1992; 40: 73-8.
14. Chend Y, Wellot WC, Schwartz J, Sparrow D, Weiss S, Relation of nutrition to bone lead levels in middle aged to elderly men. Am J Epidemiol 1998; 147:1162-74.
15. Junaid M, Choudhuri DK, Naryan R, Shanker R. Lead induced changes in ovarian follicular development and maturation in mice.J-Toxicol-Env H 1997; 50:31-40.
16. Vermande-Van Eck, GI and Meigs, JW. Changes in ovary of rhesus monkey and chronic lead intoxication. Fertil, steril 1960 ;(11) 223-234.
17. Sokas R, Schwartz E, Wesdock DC. Occupational lead poisoning. Am Fam Phy 1998; 57:719-26.
18. Weden RP, TYA, Favata EA, Jones KW. Clinical application in vivo, tibial K-XRF for monitoring lead store. Arch Environ H 1995; 50:335-61.
19. Keller CA, Doherty RA.Effects of lead. Effects of dose on lead retention and distribution in suckling and adult female mice. Toxicol Appl Pharmacol 1980; 52:285.
20. Barltrop D, Khoo HE. Nutritional determination of lead absorption. In trace substances in environmental health IX ed. Hempbill Columbia University of Missouri press 1975; 79-93.
21. Hamillton A, Hardy HL. Industrial toxicology, Boston John Wright, 1983; 62-87.
22. Hafeez A. Blood lead levels in preschool children in Rawalpindi Pak Med Assoc 1996;46(12): 72–4
23. Farida Agha, Agha Sadaruddin, Naz Khatoon. Effect of environmental lead pollution on blood Lead levels in Traffic Police Constables in Islamabad, Pakistan. J Pak Med Assoc 2005; 55:410–3.
24. Barkowitz M. Survey of N.J schools & day care center for lead in plumbing solder.Env Res 1995;71: 55-9.
25. Kadir MM, Janjua NZ, Kristiansen S, Fatmi Z, Sathiakumar N. Status of children's blood lead levels in Pakistan: implications for research and policy. Public Health 2008; 122:708-715.
26. Tanveer Ahmad, Asim Mumtaz, Dilshad Ahmad et al, Lead exposure in children living around the automobile and battery repair workshops:/Biomedica Vol.25, Jul. – Dec. 2009/Bio-17.Doc P. 128– 132
27. Yasir Farooq, Muhammad Mazhar Hussain, Shoaib Bin Aleem. Lead intoxication: the extent of problem and its management; Pak J Physiol 2008; 4(2).