EFFECT OF LOW BLOOD LEAD LEVELS ON ANAEMIA INDICATORS AND CREATININE CLEARANCE RATE OF WORKERS OCCUPATIONALLY EXPOSED TO LEAD

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Background and Objectives: Although recognized and written about centuries, lead toxicity remains an occupational and public health problem of global dimensions. Several studies have demonstrated that clinical and sub clinical effects of lead toxicity at the blood lead levels considered as safe, i.e., below 30 µg/dl in adults and 10 µg/dl in children. Such studies have received scant attention in the case of lead occupational workers due to the presumption of high blood lead levels in accordance with occupation. In the present study, therefore an attempt was made to investigate the effect of low blood lead levels on indicators of anaemia and renal impairment. **Methods:** A cohort of 690 subjects who had been occupationally exposed to lead was studied using stratified random sampling design. The markers of anaemia included changes in Haematocrit value, Haemoglobin and Erythrocyte count where as renal health was judged from changes in creatinine clearance rate. The controls were derived from similar socioeconomic background and matched in age and sex with subjects. Blood lead levels were determined by graphite furnace atomic absorption and biochemical determinations carried out using standard procedures. **Results:** Blood lead levels in the range 10–40 µg/dl had significant effect on anaemia indicators and resulted in inverse co relationship. (Pearson's correlation coefficient r= -0.65, -0.71 and -0.58 respectively for haematocrit, erythrocyte count and haemoglobin). The creatinine clearance rate estimated after adjustment for body mass index and age factors was found to depend on blood lead level and duration of exposure of subjects. These effects were statistically significant in the subjects having age in the range 15–30 years. **Conclusion:** Low lead levels in blood have high potential of inducing lead related anaemia by disturbing the pathway of heme synthesis at either ferrochelatase stage or inhibiting the aminolevulinate dehydratase activity. Though creatinine clearance rate did not prove as reliable marker of renal health at low PbB levels but it was successfully used in the case of high PbB levels whereby it could be used to predict the PbB values and vice versa.

Keywords: Occupational workers, Anaemia, Battery recycling, Creatinine clearance, Blood lead, Anaemia indicators

INTRODUCTION

Lead is well known toxic metal for its adverse health effects in occupationally exposed workers and general population. Among the variety of its occupational sources of exposure, the uncontrolled battery recycling has been cited as potentially dangerous and fatal to workers health. Due to economical reasons, lack of strict laws and technically simple process, the uncontrolled battery recycling has also been reported as common practice in most of the developing countries including Pakistan. A few years back Pakistan introduced the relatively inexpensive compressed natural gas (CNG) as alternate fuel for petrol driven vehicles. The measure resulted in the proportional increase in number of cars, the size of battery scrape, the mushroom growth of recycling facilities and consequently the number of lead recycling workers. Although lead has been shown to cause variety of disorders such as anaemia hypertension kidney disorders reduction in IQ and various types of cancers but little is known about the role of quantitative levels of metal in physiological fluids, at which these effects occur.[1–3] Although it has been recommended that blood lead (PbB) levels below 30 µg/dl in adults and 10 µg/dl in children are safe limits but a number of studies have appeared in which these levels have also been questioned.[4–6] Since major part of PbB exists in the soluble form in erythrocytes therefore it is important to expect that its effects occur even at very low levels without showing any apparent clinical manifestations. In the present work an attempt was therefore made to study the prevalence of anaemia and renal impairment among workforce engaged in lead recycling smelters and determine the PbB levels at which effects such as changes in haemoglobin content packed cell volume (PCV) and erythrocyte count (EC) for anaemia and changes in Creatinine clearance (Crcl) rates indicative of renal health occur.

SUBJECTS AND METHODS

A random sample of 580 active battery recycling workers all males having age in the range 10–30 years consented to participate in the study. All the subjects were informed about the objectives of the research study and assured of confidentiality of the information they provided. The controls matched the subjects except in their occupations or known history of exposure to lead related activities.

Blood lead and other biochemical determinations

Five ml intravenous blood sample of each of the subjects was obtained and the lead in whole blood determined by recommended atomic absorption method and quality control program described in the literature.[7,8] Height weight and age of each subject were also recorded and a separate 5 ml blood taken for determination of serum creatinine by picric acid-sodium hydroxide method. Creatinine clearance was estimated using computer program based on Cockroft- Gault formula.[9] Haemoglobin, erythrocyte count and haematocrit level were determined by blood analyser as per manufacturer's directions.

Data analysis

The statistical analysis of data was performed by Minitab 14.10. The Mann-Whitney test, Two Sample *t*-test, ANOVA, Pearson's correlation coefficients, regression and descriptive statistics were used to characterise the data at α or *p*-values equal to 0.05.

RESULTS AND DISCUSSION

Blood lead studies

The mean blood lead levels number and other characteristics of subject is given in the Table-1. The differential analysis of anaemia indicators according to PbB ranges is given in Table-2.

Table-1: Overall values and Subject Characteristics

Total number of subjects	690
Age range (years)	12–35
Engaging range (months)	6–24
Blood lead level (µg/dl) Mean±SD	55.8±6.7
Amount of haemoglobin% Mean±SD	12.1±6.2
Hematocrit value (%)	39.5±5.2
Erythrocyte count (10^4/mm^3)	4.60±0.015

Table-2: Changes in PCV, Hb and EC contents corresponding various PbB levels

PbB Range (µg/dl)	No. of subjects (%)	PbB Mean±SD	PCV% Mean±SD	EC10^4/mm^3 Mean±SD	Hb% Mean±SD
5–14	50 (7.2)	8.31±3.1	40.19±0.321	620±36	13.6±1.3
15–24	110 (15.9)	20.4±3.5	39.52±0.412*	580±43	13.2±2.2
25–34	120 (17.4)	29.05±5.1	39.47±1.328*	560±54	12.7±2.7
35–44	135 (19.5)	41.10±2.9	38.63±2.16*	450±61	12.1±3.2
45–54	155 (22.4)	49.70±6.6	38.81±3.26**	455±53	11.9±1.4**
55–64	120 (17.4)	59.50±4.16	38.72±5.28**	420±65	11.3±2.8**

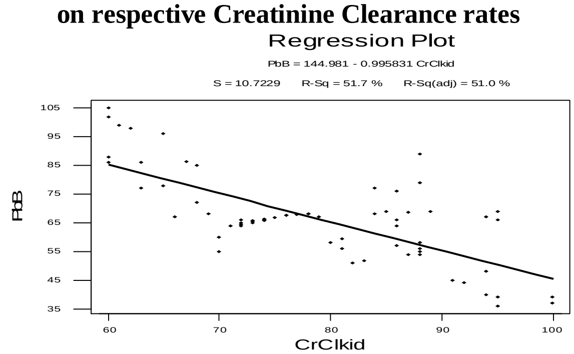
*2 tail *t*-test $p<0.01$ **2 tail *t*-test $p>0.01$

It may be noted that higher number of subjects presented with higher blood lead levels probably due to lack of on site control measures, greater durations of exposure and lack of occupational education. As result of these trends subjects with higher PbB levels had also multiple health problems complicating the study of anaemia and/or renal heath of subjects. To overcome this difficulty the random sampling of subjects was restricted to certain particular jobs of recycling which did not involve exposure to heavy concentrations of lead. The results of analysis of lead in blood and the data categorised in six ranges of values reflects the effects on packed cell volume erythrocyte count and haemoglobin level of respective groups (Table-2). It can be seen from the data that PbB range 5–14 µg/dl (Mean±SD 8.318±3.1) had highest levels of PCV EC and Hb among the ranges studied. These values in the range 2, i.e., 15–24 µg/dl (20.42±3.5) were significantly different ($p<0.001$) from those in the range 1 as well as reference population. The trend continued till the range 4, i.e., 35–44 µg/dl (41.10±2.9) after which despite higher mean values of PbB the values of PCV EC and haemoglobin were not seen decreasing in regular patterns. This result is in contrast to the earlier findings wherein mean PbB levels higher than 50 µg/dl were reported to cause anaemia, and increase the level of Aminolevulinic acid (ALA) in urine.[10] To confirm this we also measured the ALA levels in urine of the subjects and correlated with various PbB levels whereby it was found that despite of its increased levels the ALA neither correlated with respective PbB nor with any of the anaemia indicators of the subjects. These observations suggest that kinetics and mechanism of low PbB levels, i.e., below 40 µg/dl in body pools such as blood are probably some what different than those of the levels greater than 40 µg/dl of the metal. When the individual PbB ranges and the respective anaemia indicators were statistically compared by two sample *t*-test as well as Mann-Whitny tests significant differences were found among the ranges below 44 µg/dl but no significant differences were noted among the ranges higher than 44 µg/dl. These results indicate that lower PbB concentrations or more appropriately trace amounts of lead in blood have greater potential to induce anaemia. Makino et al also reported similar findings in the case of low PbB levels. In the present study the data was also examined by dividing it in two groups as 5–4 µg/dl and 45–64 µg/dl and compared by two sample *t*-test. Here also the significant differences were noted ($p<0.001$) in the values of PCV, EC and haemoglobin.

Kidney Function

The kidney function in relation to PbB has remained subject of several studies and a number of markers have been used to study the effect. It has been reported that PbB levels equal to or below 60 µg/dl do not significantly influence the creatinine clearance but may accelerate the renal failure in the presence of some chronic kidney disease.[11–14] In present study we studied these aspects by estimating the creatinine clearance from serum creatinine, body mass index and age of lead workers using cockcroft-gault formula.[9] The creatinine clearance rates thus determined indicated some abnormalities corresponding to lower PbB ranges but did not significantly differ when compared with reference subjects. The Crcl study when extended to subjects having PbB levels greater than 60 µg/dl it was found that the Crcl decreased at the rate of 0.8 ml/min for every 5 µg/dl rise in PbB value provided subject had remained exposed to lead related activities for a minimum period of two years. Since renal impairment is a chronic condition we also compared the creatinine clearance of lead exposed renal patients (n=80) with equal number of non-exposed reference patients and found its mean value significantly lower in former group. The analysis of data by simple regression of lead in blood and creatinine clearance rate resulted in to the inverse relationship between the two variables with R^2= -51.7% and correlation coefficient r= -0.719 (p<0.01) (Figure-1).

Figure-1: Regression plot showing effect of PbB on respective Creatinine Clearance rates



The regression equation thus obtained (PbB=144.98-0.995×Crcl) explained the variability to fairly good extent. Our experiments suffered from lack of availability of samples in sufficient number to further study the effects due to advanced age, sex, duration of exposure, and follow up studies of cases after receiving the treatment. However despite of these limitations the results obtained so far indicate that lead in blood or overall increase in body lead burden may become a cause of adverse effects on kidney function and result in to the end stage renal failure.

CONCLUSIONS

The results of the work demonstrate that low lead levels in blood have high potential of inducing lead related anaemia by disturbing the pathway of heme synthesis at either ferrochelatase stage or inhibiting the aminolevulinate dehydratase activity. The pattern of variations in anaemia indicators, i.e., PCV, EC and Hb corresponding to PbB levels below 44 µg/dl and those above this level clearly demonstrate the differences in the kinetics of process. In the present study though creatinine clearance rate did not prove as reliable marker of renal health at low PbB levels but it was successfully used in the case of high PbB levels whereby it could be used to predict the PbB values and *vice versa*.

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