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Effect of Lead Acetate on Spleen and Blood Parameters in Albino Rats

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Abstract: *Lead is a heavy metal widespread in the environment. This study was aimed at assessing the effects of lead acetate on the rat morphology, haematological parameters and microscopic appearance of the spleen. Forty male albino rats were randomly divided into four groups of 10 rats each. The low dose group were intubated 25mg/kg body weight of lead acetate, while the high dose and recovery groups received 50 mg/kg body weight of the lead acetate solution. The control animals were administered equivalent amount of distilled deionized water at not more than 1 ml. Intubation was by oral gavage and was conducted for 28 alternate days. The rats were sacrificed 24 hours after the last administration, except the recovery group that were left on normal feed and water for additional 14 days for the self-recovery study. Blood was drawn for determination of lead concentration and haematological analysis and the spleen was processed partly for estimation of lead deposition and partly for haematoxylin-eosin staining. Results showed that the animals had minimal mean body weight reduction but marked splenomegaly, with mean blood lead concentration of 0.10ppm. Haematological analysis showed significant ($p<0.00$) reduction in packed cell volume (PCV) but minimal change in the haemoglobin levels. The total leucocyte counts (TLC) were raised significantly ($p<0.05$) in the treated rats. Histopathological effects of lead were dose-dependent hyperplasia of the lymphoid follicles in the spleen which were reversed in the self-recovery group. In conclusion, lead acetate was observed to cause significant alterations in the PCV and TLC as well as splenomegaly in albino rats.*

Keywords: *Haematological parameters, Lead acetate, Spleen*

I. Introduction

Lead and other heavy metals are found with relatively low anthropogenic concentrations in all parts of the environment. However, human activities have added exceptionally higher concentrations of these heavy metals into the environment, particularly in areas where the metals are mined, processed and used industrially [1]. Lead is not a normal constituent of the body and causes serious damage in all human tissues [2; 3].

When lead enters the bloodstream, it is primarily distributed to blood, soft and mineralizing tissues [4]. About 5-10 % of the total body burden of lead is found in the blood; soft tissues accumulate 10-20 %, and bones contain 70-85 % of the total body burden of lead [5]. Lead toxicity often affects the erythrocyte membrane, significantly leading to decrease in the mobility of the erythrocytes [6] and alterations in other haematological parameters [7].

Environmental lead is ubiquitous and everyone has some amount of blood lead level [8; 9]. Lead presents one of the largest environmental medical problems because of the number of people being exposed and the attendant public health impact [10]. In a study that surveyed the causes of lead toxicity in Jos, Nigeria, mean blood concentration of 8.7 µg/dl with a range of 1-34 µg/dl were reported, with 34 % of the subjects having concentrations of 10 µg/dl or greater [11].

Determination of blood lead level is the most direct assessment of the body lead burden, although it represents only about 5-10% of the total body lead. Haematological profile of laboratory animals exposed to lead showed polycythemia with elevated level of haemoglobin [12; 13]. Mice treated with lead acetate showed significant decrease in the total erythrocyte and total leucocytes counts but significant reductions in the haemoglobin (Hb) content and packed cell volume [14; 15]. Similarly, it was observed that Hb level was reduced after intoxication with lead acetate at a dose of 400 mg/kg body-weight of fodders [16], an indication that lead interferes with the formation of haemoglobin [17].

Other report recorded a significant reduction in the Hb value but increase in the total leucocytes count following lead acetate administration at different doses [18]. Though significant increase in the total leucocytes count and lymphocytes were reported, reduced absolute number of monocytes and neutrophils were obtained following lead acetate administration to rats [19].

Oral administration of lead acetate can cause elevation of lead concentration in the body. The present research was therefore, conducted to observe the effect of lead on the microscopic appearance of the spleen and possible alterations in the PCV, Hb, TLC and DLC of the blood in albino rats.

II. Materials and Methods

2.1 Experimental Animals

In order to minimize variations in response, only adult male rats were used for this study. Forty albino rats, weighing between 200 and 280 grammes were obtained from the Animal House of the Department of Human Anatomy, University of Maiduguri, Nigeria. The animals were maintained on standard pellet diet and potable water ad libitum. All the animals were kept in well-ventilated cages and housing with the average humidity and temperature of 75 % and 26 ± 2 ºC, respectively, at 12 hours light and 12 hours dark cycle.

2.2 Experimental Design

The animals were randomly divided into four groups of ten rats each. Group I received low dose (25 mg/kg body weight) of lead acetate solution while group II were administered high dose (50 mg/kg body weight) of the lead acetate. The chosen doses fell within the range of doses applied in previous studies [14; 19]. The animals in groups I and II were administered the lead acetate for 28 alternating days. Group III animals received high dose of lead acetate (50 mg/kg body weight) for duration of 28 days, then the administration was withdrawn for two weeks before the animals were sacrificed. This group III was designated as recovery group. Group IV received only distilled deionized water. The route of administration was by oral gavages and the maximum volume of the solution did not exceed 1 ml to all the animals.

At the end of 28 days all the animals were sacrificed after 24 hours of the last dosage except the animals in the recovery group which were sacrificed two weeks after cessation of oral gavages.

2.3 Morphological and Histological Examinations

The whole spleen was procured and cleared from adjoining supporting, connective tissues. The organ was gently blotted with filter paper and weighed. Thereafter, each spleen was bisected and one half was processed for elemental analysis. The lead concentration was estimated using a Single Beam Spectrophotometer [20]. The values obtained were recorded in parts per million (ppm). The second portion of the spleen was immediately immersed in 10% formalin solution to be processed for haematoxylin and eosin staining and light microscopic studies.

2.4 Haematological Parameters

The blood samples were collected from the heart ventricle of the rats through a sterilized syringe into heparinised bottles, for determination of lead concentration, the red cell count (RBC), packed cell volume (PCV) and haemoglobin concentration (Hb) using Automated Haematological System (Diatrioe), Abacus Junior Haematological Analyser. Erythrocyte indices were calculated from values obtained.

2.5 Statistical Analysis

The data obtained from the morphological studies, metal concentrations in the blood and spleen, and haematological parameters were calculated and subjected to statistical analysis. The results were expressed as means ± standard deviation and the levels of significance were determined using Duncan's Multiple Comparison Test. Analyses of data were carried out with the aid of the SPSS computer software, version 11. All statements of differences were based on significance at $p < 0.05$.

III. Results

3.1 Morphological Changes

There was no significant change in the body weight of the treated rats compared to the non-treated rats. While the mean spleen weight in the recovery group (0.64±0.11 g) that received high dose of lead acetate (50 mg/kg) appeared to be restored, the spleen from those animals that were treated with the same high dose of lead acetate but not passed through recovery had mean weight (0.85±0.17 g) that was significantly higher at p 0.03 (Table 1). The average blood lead concentration ranged between 0.07 ± 0.05 to 0.10 ± 0.13 ppm (Table 2).

3.2 Histological Evaluation of the Spleen

In both low and high dose treated rats there were visible and widespread hyperplasia of the lymphoid follicles in the white pulp. There was also evidence of haemolysis and congestion of blood vessels which overshadowed the red pulp. These reactions were more prominent in the rats that received the high dose of lead acetate (Fig. 5). On the other hand, the recovery group showed more prominent red pulp, an indication of reduction of the hyperplastic lymphoid reaction (Fig. 6).

3.3 Analysis of the Haematological Parameters

The results of haematological analysis are presented in Table 3. Estimate of the packed cell volume (PCV), which is the percentage volume of the blood, occupied by the red blood cells, revealed very significant

($p < 0.000$) changes between the experimental groups. There was a significant reduction in the PCV (38.10 ± 1.52 ml %) of the 25 mg/kg lead acetate-treated rats and a significant increase of PCV (44.60 ± 3.37 ml %) in the 50 mg/kg treated animals when compared with the control group with a PCV value of 43.5±3.41 ml%. However, minimal decreases were observed in the haemoglobin concentration within the three treated groups.

The total leucocytes counts or white blood cells (WBC) were significantly ($p < 0.000$) increased by lead acetate administration in all the treated groups. The increases in the TLC counts were mainly attributed to the increased relative percentage of neutrophils in the differential leucocytes count. The mean percentage portions of lymphocytes for the three treated groups and the non–treated control did not differ significantly ($p < 0.331$). The amount of eosinophils was significantly ($p < 0.000$) reduced (4.3 ± 0.95 %) in the high dosed treated animals.

Table 1: Effect of Lead Acetate on the Weight of Rat Spleen.

	Doses Administered (mg/kg)				p value
	Control 00	Low Dose 25	High Dose 50	Recovery Group 50	
Weight of Spleen	0.68±0.14[b]	0.66±0.21[b]	0.85±0.17[a]	0.64±0.11[b]	0.030*

Unit: g; Values are Mean ± SD.
*Indicates significant difference between the mean values of the experimental groups at $p < 0.05$.
The mean spleen weights having different superscripts are significantly different at 5 % by the Duncan Multiple Comparison Test (DMCT).

Table 2: Mean Lead Concentrations in Blood and Spleen of Rat under Normal Conditions and After Oral Administration of Lead Acetate

Tissue	Doses Administered (mg/kg)			
	Control 00	Low Dose 25	High Dose 50	Recovery Group 50
Blood	0.10±0.06[a]	0.07±0.05[a]	0.10±0.13[a]	0.08±0.10[a]
Spleen	BDL	0.10±0.06[a]	0.10±0.01[a]	BDL

Units: Parts per million, ppm (mg/kg), and values are Mean ± SD of 6 rats in each group.
If values in the same row have different superscripts they are significantly different at 5 % by DMCT.
BDL: Below detectable level.

Table 3: Comparison of Blood Parameters of Lead Acetate Treated Male Rats and Non-Treated Controls. Values are Mean ± SD.

Blood Parameter	Doses Administered (mg/kg)				p value
	Control 00	Low Dose 25	High Dose 50	Recovery Group 50	
PCV (ml%)	43.5±3.41[ab]	38.1±1.52[c]	44.6±3.37[a]	41.1±1.91[b]	0.000*
Hb (g/dL)	11.09±1.03[a]	10.30±0.14[b]	11.04±0.76[a]	10.22±0.06[b]	0.010*
TLC ($x10^3/mm^3$)	8420±262[d]	11600±300[b]	9900±510[c]	12770±951[a]	0.000*
Neutrophils (%)	34.80±1.23[b]	35.10±1.20[b]	36.50±1.08[a]	36.70±1.06[a]	0.001*
Lymphocytes (%)	48.9±1.29[a]	49.3±0.82[a]	49.8±1.23[a]	49.1±1.10[a]	0.331
Monocytes (%)	8.8±1.03[a]	8.9±0.88[a]	9.1±0.88[a]	7.7±0.48[b]	0.003*
Eosinophils (%)	6.7±0.68[a]	6.5±0.71[a]	4.3±0.95[b]	6.5±0.71[a]	0.000*

* Indicates significant difference between the mean values of the experimental groups at $p<0.05$.
The mean values in the same row having different superscripts are significantly different at 5 % by DMCT.

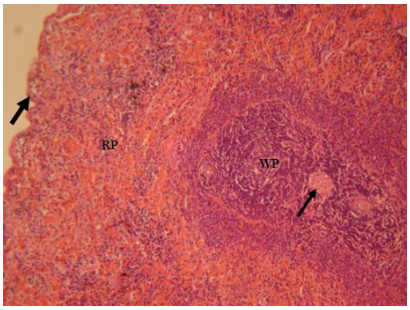

Figure 1: Photomicrograph of a representative section of spleen from control rat (RP). The capsule (thick arrow) of the spleen is intact. H & E stains. x 200.

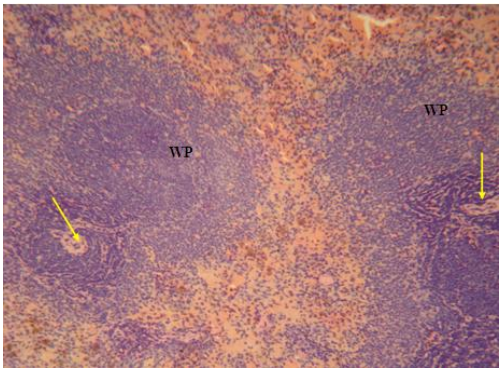

Figure 2: Photomicrograph of a representative section of spleen from 25 mg/kg body-weight (Low Dose) lead acetate-treated rat showing wide-spread hyperplasia of lymphoid follicles and eccentric arterioles (arrows) in the white pulp (WP). Haemosiderin-laden macrophages are shown in the red pulp. H & E stains. x200.

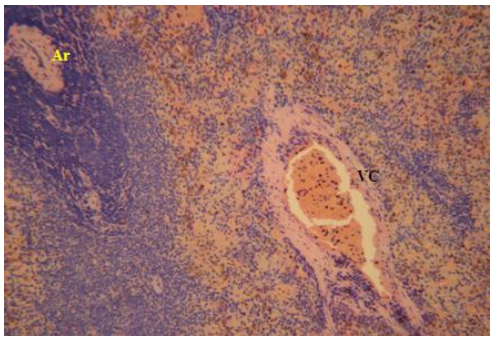

Figure 3: Photomicrograph of a representative section of spleen from 25 mg/kg body-weight (Low Dose) lead acetate-treated rat, showing slightly dilated and congested vascular channel (VC), aggregation of lymphocytes around the sheathed arterioles (Ar). H & E stains. x200.

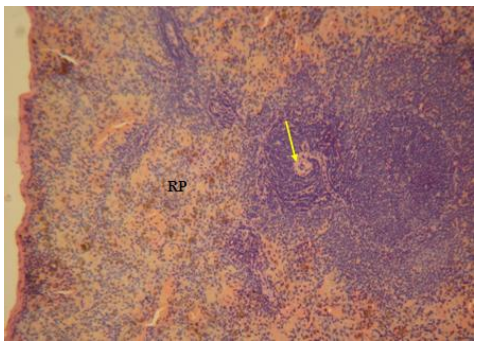

Figure 4: Photomicrograph of a representative section of spleen from 50 mg/kg body-weight (High Dose) lead acetate-treated rat, showing marked hyperplastic lymphoid follicle in the white pulp with eccentric arteriole (arrow). There are mild haemosiderin-laden macrophages in the red pulp (RP). H & E stains. x 200.

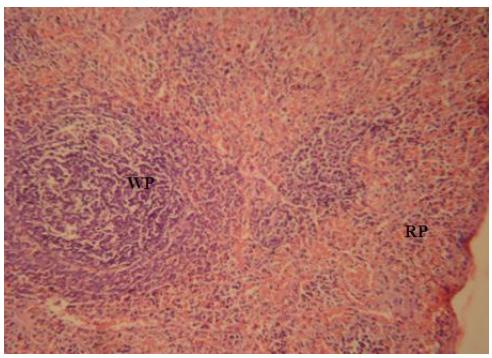

Figure 5: Photomicrograph of a representative section of rat spleen pre-treated with 50 mg/kg body-weight of lead acetate (Recovery Group) showing white pulp (WP) and red pulp (RP) returning to normal proportions. H & E stains. x200.

IV. Discussion

The rats with the high dose of lead acetate in this study had the heaviest mean spleen weight compared to the other experimental groups and non-dosed controls. In a United States Agency Report [21] the varied effect on the mean weight of organs from different species of birds following lead exposure were documented. The document reported smaller–than-average liver, kidney and spleen in water-fowls exposed to lead poisoning in contrast to enlarged liver found in swans that died from lead poisoning from mine wastes and enlarged kidney, spleen, and liver in wild lead-poisoned Canada geese and ducks. The marked enlargement of the spleen in the present investigation might be a result of the reactive hyperplasia of the white pulp and increased content of the fibrous tissue in the organ, following lead exposure.

The concentration of lead in the blood and spleen of the rats were determined to show the measure of exposure levels in these tissues. The blood lead level is a convenient and direct indicator of the metal toxicity [22]. In the present experiment the lead concentration in the blood from all groups of animals were moderately elevated within the range of 0.07 ppm to 0.10ppm. Similar results were obtained when chronic administration of lead (1g % lead acetate) was given through drinking water. Even when the lead exposure was prolonged for 9 months, the mean blood lead levels remained at almost the same value of 100 µg/dl [23].

Varied and contrasting results have been reported by previous researchers. Oral exposure of rabbits to 12.50 mg/kg bwt of lead acetate for 15 days caused significant increase in the blood lead concentration (173.40 ± 13.56 µg/dl) compared with the control (10.30 ± 0.56 µg/dl). Even after stoppage of the lead administration and the animals allowed for self-recovery for another 15 days the blood lead concentration was still elevated (121.00 ± 7.45 µg/dl) compared with the controls [22]. The variations in these results are comparable to the mean blood lead levels in the high dosed animals (0.10 ppm) and in the self–recovery group (0.08 ppm) in the present study.

Exposure to heavy metals can cause alterations and damage to the haematological profile and haematopoietic system in man and animals [24; 25]. In this study, the PCV was significantly decreased in the rats administered the low dose of lead acetate, while the results for the other experimental groups were raised in the amount of their PCV. These results indicated that increased doses of lead acetate did not have direct adverse effect on the percentage volume of blood occupied by the red blood cells or caused significant damage to the RBCs. Probably the rats exposed to higher doses of lead acetate only experienced polycythemia vera. Increase in the PCV values following the treatment of rats with lead acetate were reported [26]. The increased RBC counts might have been due to stimulation of erythropoietin by the elevated demands for oxygen and carbon dioxide transport as a result of increased metabolic activity or the destruction of the respiratory membranes causing faulty gaseous exchange [12; 13].

In this study, lead acetate exposed rats in the high dose group recorded minimal amounts of haemoglobin (Hb) contents, a normal range in rats being 11–17 g/ml with a mean of 14.2 g/ml [27]. At the low dose and from the recovery group, the amounts of Hb were moderately reduced compared to the other groups of animals. Attention should be drawn to the blood lead concentrations in the low dose treated group and in the group that were left for self–recovery (recovery group), which were decreased compared to the control and high dose groups. The passive explanation for these mixed results is that the effect of lead on Hb could be more on the quality of the Hb rather than the amount in the circulating blood. High alterations in the biophysical parameters of haemoglobin in terms of shape and size at the levels of one molecule had been observed [22]. These changes were complementary to the oxidative stress caused by lead poisoning because the affected Hb was not able to carry out its normal function. This function disability could result in reduction in the molecular oxygen supply to tissues, thereby multiplying the oxidative stress of lead [22].

Generally, when the Hb content drops below the normal values (like in the low dose and recovery groups in the present work) and the PCV also drops below the normal values (like in the low dose group) the resultant medical condition is anaemia. Lead compounds have effects on the haem synthesis in the blood and liver in both animals and humans [28; 29]. Lead-induced anaemia could be caused by the reduction in the life-span of circulatory erythrocytes and the inhibition of Hb synthesis [30].

The reduction in the Hb content in rats was also reported to be due to the decrease in the value of the total erythrocyte count [31]. Furthermore, the possible reasons for the results could be the adverse effects of lead acetate on the haematopoietic system and on the absorption of essential vitamins and minerals from the intestines as well as the destruction of the red blood cells in the body of the animal. These adverse effects of lead were also demonstrated in some of the histopathological results in the present study.

Lead acetate administration to rats in the present study caused significant increase in the total leucocytes count (TLC) values over the non-treated control, with highest elevation seen in the recovery group. These increments were mainly contributed by the increase in the amount of neutrophils in the case of high dose and recovery groups. The amounts of monocytes were similar in all experimental groups while eosinophils were significantly reduced in the high dosed rats. The leucocytosis was probably a result of the adverse effect of lead

in these animals, in terms of proliferative response of the granule cells which are the chief phagocytic cells in the blood to the denatured Hb and damaged red blood cells.

Increases were not observed in the amounts of lymphocytes in the treatment groups relative to the value of lymphocytes of the control group in this study. Results of other work showed that the administration of lead acetate to rats caused a significant increase in the amount of lymphocytes [18]. Functionally, monocytes are large phagocytic leucocytes with basophilic cytoplasm while eosinophils modulate allergic inflammatory reactions and destroy antigen–antibody complexes [18]. Contrary to the increased TLC values, few authors reported significant decrease of the TLC values after lead acetate administration [14; 17].

Lead-induced oxidative stress contributes to the pathogenesis of lead poisoning [32]. Thus, low to high doses of lead exposure could cause different responses of oxidative stress in various target sites including blood vessels, liver, brain, testes and lungs [33]. With increase in the environmental exposure to lead, the toxic effects of lead on various organ systems in the body have serious public health implications [30].

Lead could cause splenomegaly, damage to the other haemotopoietic system and the central nervous system [34]. The microscopic changes from the sections of the spleen of the lead treated rats were also dose-dependent, but in this case there were signs of recovery on two weeks withdrawal of treatment. The rats treated with low dose lead acetate exhibited widespread hyperplasia in the white pulp and distinct haemosiderosis of erythrocytes in the red pulp. The blood vessels were also congested. These splenic alterations were accentuated in the high dosed group, particularly the hyperplastic lymphoid follicles in the white pulp. In the recovery group the hyperplasia was reduced and the red pulp became visible with only scanty haemosiderin–laden cells. Haemorrhages in the spleen were also reported in lead-poisoned dogs [35]. Samples of the spleen from lead acetate treated rats were also reported to show basophilic granular degeneration of erythrocytes, necrosis and perivascular cuffing by fibrous tissue. These pathological lesions were increased in magnitude with increase in the dose of the lead compound [18].

The microscopic changes in the spleen of the lead treated rats suggested immune alterations and splenic damage. The histomorphological alterations in the spleen of rats exposed to lead acetate, suggested that exposure of the animals to lead, particularly high doses, stimulated the spleen to become reactive. Thus, the impact on human and animal health from the immune perspective, following environmental lead exposure, is of great health implications.

V. Conclusions

The results of the present study suggest that lead acetate at environmentally comparable concentrations could induce haematological changes leading to significant reduction in PCV and HB in the rats. The total leukocyte counts were elevated significantly, with the increase contributed mainly by the percentage of neutrophils in the differential leukocyte counts. The major histopathological alterations brought upon the spleen by the lead were hyperplasia of the lymphoid follicles and haemosiderosis in the red pulp.

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