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Effect Of Sub-acute Administration of Lead Acetate on Blood Pressure, Pulse Rate And Histology of The Heart in Wister Rat.

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ABSTRACT

This study was carried out to determine the effects of sub-acute administration of lead acetate on the cardiovascular system and rat heart histology. Sixteen male Wister rats were used for the study which were weighed and grouped after acclimatization into two groups; group A: control group and group B: Experimental group. Rats in group B were given 10mg/ml of lead acetate everyday for 28 days. Their weight, blood pressure, pulse rate and heart weight were measured and their hearts prepared for histopathological analysis. The results showed that the weights of the rats increased. Although the increase was more in control than in the lead-treated group, the P-value showed that there was no significant difference at P=0.05. There was an increase in systolic blood pressure in the lead group as compared to control. The mean systolic pressure in the lead treated group was not significantly different from the diastolic blood pressure and pulse rate. From the histopathological analysis, it was shown that 100% of the control rats had normal heart muscles while in the lead-treated group 90% had normal heart muscles and 10% had inflammation of the heart muscles. From the studies, it is shown that sub-acute administration of lead acetate has little or no effect on rat heart histology, but could elevate systolic blood pressure.

Key Words: Sub-acute, Lead, Cardiovascular, histopathological

Lead is a soft, malleable, silvery white or bluish-grey heavy metal in Group IVa of the periodic table. It is a poor conductor of electricity, highly durable and resistant to corrosion. Lead is usually found in ore with zinc, silver and (most abundantly) copper and is extracted together with these metals. It is presents in several minerals; but all are of minor significance except the sulfide, PbS (galena), which contains 86.6% of lead and is the major source of lead production throughout the world.

Lead is used in the manufacture of batteries, paints, pottery glazing, and lead-glazed ceramics. It is used for linings for corrosive pipes, conduits and structures for the transportation, processing of corrosive substances, coverings for electric cables placed in the ground or underwater, ammunition. Lead sheets are also used in walls to block the transmission of sounds and vibrations. Because lead effectively absorbs electromagnetic radiation of short wavelength, it is used as a protective shield around nuclear reactors, X-ray equipment and containers used for transporting and storing radioactive materials.

Lead is widely distributed in water, soil, air and food. As a result, the potential of exposure to significant lead levels is high (means et al, 2009). Inhalation is the second major pathway of exposure, especially for workers in lead-related occupations. Occupational exposure may occur in the manufacture of batteries, painting, pottery glazing, lead smelting processes, manufacture of ammunition and devices to shield X-rays etc. Lead may impair development and have harmful health effects even at lower levels and there is no known safe exposure level.

The environmental significance of lead as a chemical species exhibiting various forms of toxicity in humans has well been documented. Although lead poisoning is one of the oldest known environmental hazards, the modern understanding of the small amount of lead necessary to cause harm did not come about until the latter half of the twentieth century (Gate et al, 2009). Lead poisoning may be acute or chronic, but the latter is much more common.

Lead is not useful to the body. Lead perturbs the function of enzymes and proteins of varied classes. Studies have shown that lead exerts its influence physiologically and biochemically as a mimetic agent substituting for essential elements participating in metabolism such as calcium, iron and zinc (Bento et al., 2002). Lead binds to different kinds of transport proteins including matallothionein, transferin, calmodulin and calcium ATPase. By associating with these proteins, it is transported to specific tissues

where it causes damage (Means et al, 2009).

Lead interferes with a variety of body processes and is toxic to many tissues, organs and systems. Some adverse conditions associated with lead poisoning include: DNA damage, neurological impairment, abnormal heart function, osteoporosis, among others. Classic symptoms of lead poisoning include: abdominal pain, constipation, fatigue and tremors.

Premenstrual depression (PMT-D) is also linked to lead toxicity. A type of gout can result from lead toxicity because lead decreases uric acid excretion. Lead pollution has been linked to increased numbers of stillbirths and to cancer. Moderate lead poisoning causes kidney damage and suppresses the immune system, thus increasing the susceptibility to many diseases. It can be a contributory cause of hypertension (high blood pressure). Severe lead poisoning causes disability, senility and death.

Good nutrition provides a successful antidote to lead poisoning. Most nutrients work by blocking the absorption of lead, while others work by reducing tissue build-up by blocking its detrimental effects on enzymes. Like many toxins, lead is fat-soluble which makes it difficult for the body to excrete them.

Several studies have documented increased systolic blood pressure with the administration of increasing doses of lead (Gates et al, (2009), Victory, W (1988) ; Perry M (1899). Reza et al, (2008) studied the effects of low-level lead exposure on blood pressure and the function of the rat isolated heart. In this study, the blood pressure in the 8-week and 12-week lead-exposed groups was significantly increased with the heart rate and contractility significantly higher but not in the 4-week group. No significant changes were observed in coronary flow.

Noori et al, (2003) studied the effects of chronic lead acetate intoxication on blood indices of male adult rats. Results showed that lead concentration in the treated group was significantly higher than the control group and basophilic stippling, Howell-Jolly bodies, decreased RBC count, increased leukocyte court, monocytosis, eosinopenia, neutrophilia and thrombocytosis were observed in the test group.

Wolf et al, (2007) studied the effects of lead on blood pressure in occupationally non-exposed men. Demographic and clinical data of a group of 507 males without any occupational exposure to lead were analyzed in a retrospective study. A significant effect of lead was found only for diastolic blood pressure; they found that found that lead ranks after age and weight.

Bagchi and Press (2005) studied the effects of acute and chronic oral exposure of lead on blood pressure (BP) and bone mineral density (BMD) in rats. The early ingestion and accumulation of lead was associated with an increased Systolic BP acutely returned to control levels with continuing challenge and later rose above control months later after lead challenge had been halted. Early accumulation of lead over a short period was also associated with decreased (BMD) at the end of one year.

Odigie et al, (2004) studied the effects of chronic exposure of lead on renal function and renal ultrastructure in Sprague-Dawley rats. Treated rats had elevated blood pressures. There was no significant difference in renal blood flow. Glomerular filtration rate (GFR) was comparable in the two groups. No significant difference in serum creatinine was observed. Renal histology showed minimal interstitial change in the experimental group. Significant sodium, potassium, and chloride retention were observed in the lead treated rats. Elevation in blood pressure occurred at a stage when low-level lead exposure did not alter renal parameters appreciably.

Rationale of Study: Lead is widely distributed in the environment. Since lead is not useful to the body, the research will help identify some of the effects of sub-acute dose of lead especially on the cardiovascular system.

Aim and Objectives:

1. To determine the effects of sub-acute administration of lead acetate on blood pressure and pulse rate in Wistar rats.
2. To determine the effects of sub-acute administration of lead acute on the histology of the heart.

MATERIALS AND METHOD

16 albino Wister rats were kept in cages in the Animal House of the University of Port Harcourt for two weeks for acclimatization. During this period, the rats were fed *ad libitum*. The rats were weighed and grouped according to their weights into two groups: Control group and lead (Experimental) group.

A lead solution made up of 10mg of lead acetate in 1 ml of the solution was administered orally to each rat in the test group daily for 28days.

The blood pressures of the rats were measured daily after the administration of lead acetate, using a 58500 blood pressure recorder manufactured by Ugo Basile. After the 28 days of lead administration, the heart was removed by surgical dissection following chloroform anesthesia and fixed in a bottle containing 10% formalin for 3 days. The tissue was then processed for paraffin wax sections and studied and photographed with a photomicroscope (Olympus E330M1). Histological features between the Control slides and Experimental slides were then compared.

Statistical analysis was done using SPSS version 17.0. This program was used to determine the mean, standard deviation, T-value, P-value, and mean difference of each of the variables.

RESULTS

A total of sixteen rats were used for this study of which 6 were control and 10 were in lead group. Below is a table showing the mean of the initial weight, final weight, diastolic and systolic blood pressures.

Table 1: Mean Morphometric and Cardiovascular Parameters

Variables	Control Group N=6 (mean ± SD)	Lead Group n=10 (mean ± SD)
Initial weigh	203.3 3 ± 29.40	210.00 ± 10.54
Final weight (g)	245.83 ± 51.00	230.00 ± 34.96
Weight of heart(g)	0.64 ± 0.11	0.66 ± 0.73
Systolic blood pressure (mmHg)	120 ± 1.73	131-80 ± 20.17
Diastolic blood pressure (mmHg)	79.33 ± 1.16	79.60 ± 0. 52
Pulse rate (beats/min)	389.20 ± 61.35	

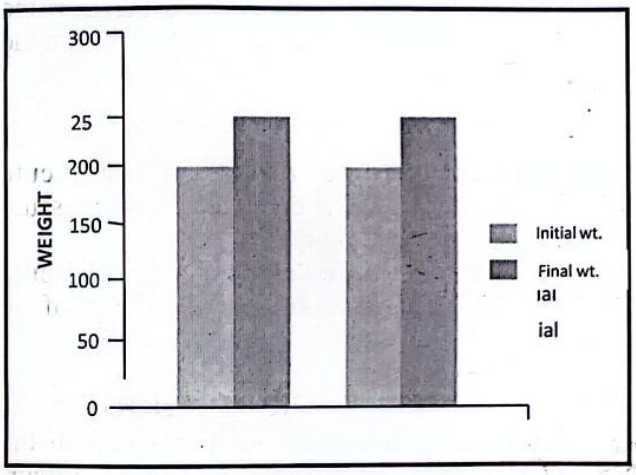


Figure 3.1: Mean Initial and Final Weights of the Groups

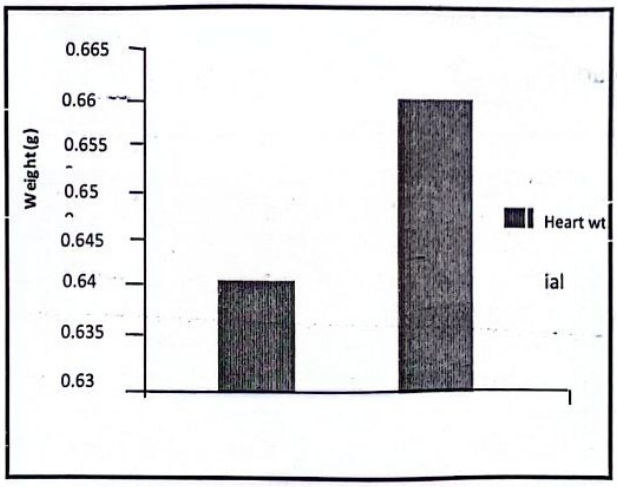


Figure 3.2: Mean Heart Weights of the Groups

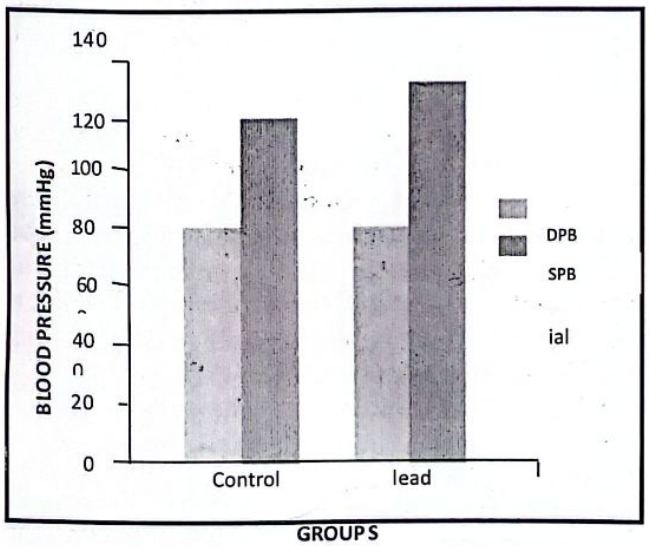


Figure 3.3: Mean Diastolic and Systolic Blood Pressures of Groups

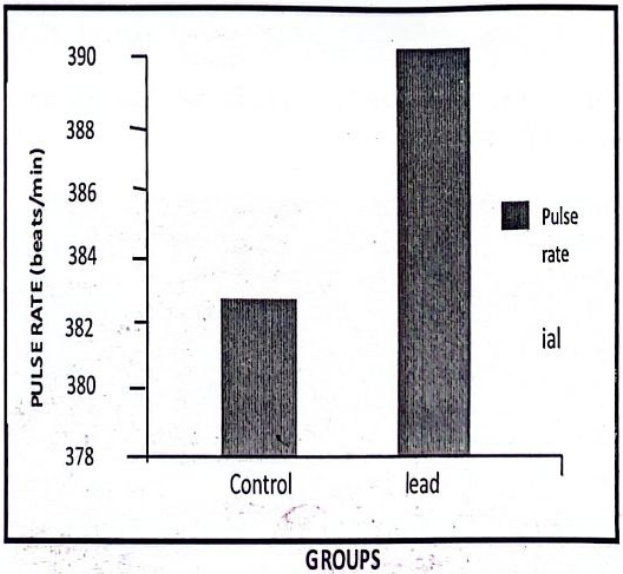


Figure 3.4: Mean Pulse Rates of the Group

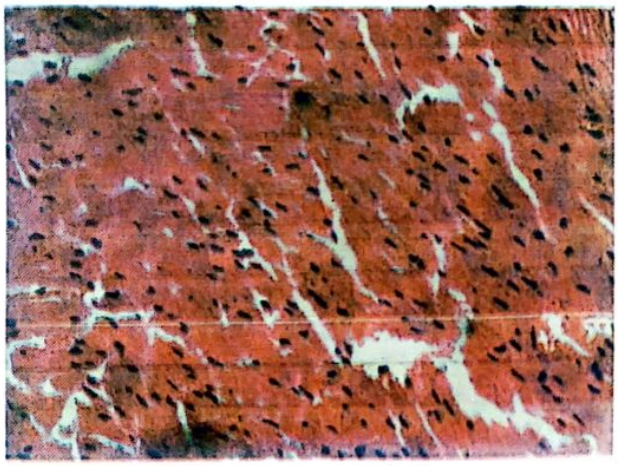
Table 2: Comparison of Morphometric and Cardiovascular Parameters between Test Group and Control Group

VARIABLES	MEAN DIFFERENCE	T-VALUE	P-VALUE (2-TAILED)	INFERENCE
Initial weight (g)	-6.67	-0.54	0.61	Not significant
Final weight (g)	15.83	0.67	0.52	Not significant
Heart weight (g)	-0.02	-.036	0.73	Not significant
Pulse rate (beats/min)	24.8	0.65	0.56	Not significant
Diastolic blood pressure (mmHg)	-0.27	-0.39	0.73	Not significant
Systolic blood pressure (mmHg)	-11.8	-1.83	0.09	Tending towards significance

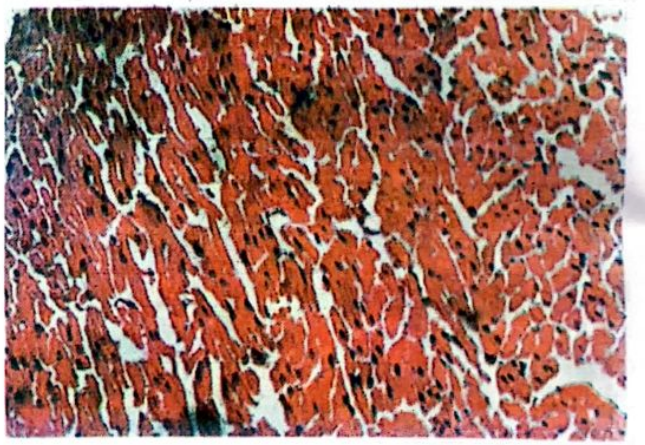
Slides that were obtained from cardiac tissue preparation were viewed and the following observations were made:

Table 3: Histopathological Features of the Cardiac Tissue

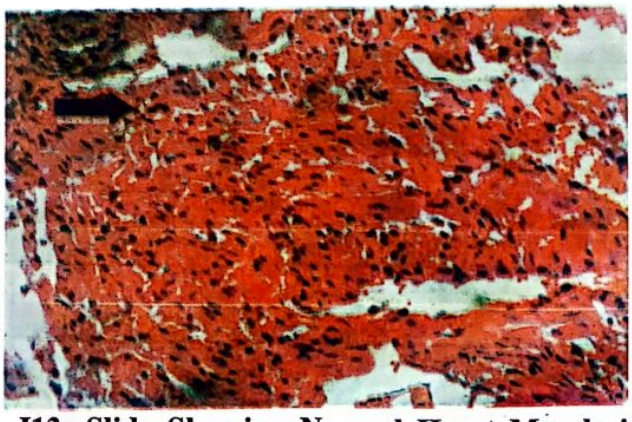
HISTOPATHOLOGICAL FEATURES	CONTROL GROUP		LEAD GROUP	
Normal heart muscle	6	100%	9	9%
Inflammation of heart muscle	0	0%	1	10%



J6A: Slide Showing Normal Heart Muscle in a Control Rat



J13: Slide showing Inflammation of Heart Muscle in Lead Group



J13: Slide Showing Normal Heart Muscle in Lead Treated Rat

RESULT & DISCUSSION

As shown in Figure 3.1, there is an increase in the mean final weight of control (245g) and lead (230g) groups as compared to their mean initial weights of 203g and 210g respectively (Table1). But the mean final weight of the control group was higher than that of the lead group. This could be as a result of lead having a depressive effect on growth. From this result, it can be suggested that lead has a toxic effect on growth as it was found to reduce the level of growth in rats fed with lead as compared to the normal growth observed in the control rats.

The mean heart weight of the control group (0.64g) was seen to be slightly lower than that of the lead group (0.66g) as shown in figure 3.2. But, the heart weight of the lead group was not significantly different from that of the control group. This result could be due to the fact that lead has no significant effect on the heart.

Diastolic pressure was not significantly different in both groups, but the systolic pressure tends towards significance with p-value of 0.09. This is partially in support with the study carried out by Badalzedeh *et al.,* (2008) on the effect of low-level lead exposure on blood pressure and the function of the rat isolated heart. They reported that there was a significant increase in the blood pressure of rats chronically fed low-levels of lead. This result also correlates with the study carried out by Victory *et al.,* (1988) on the increase in the blood pressure of rats chronically fed low-levels of lead.

There was no significant difference in histological features in both groups. 100% of the rats control had normal heart histology and 90% of the rats in the lead-treated group had normal heart histology while only 10% had inflammation of the cardiac muscle. This could be as a result of the dose of lead given to the rats or the duration of administration.

CONCLUSION

Sub-acute intake of lead acetate has no significant effect on the cardiovascular system although there was increase in systolic blood pressure that tended towards significance.

RECOMMENDATION

Further studies should be carried out on dose-dependent effect of lead acetate and also on the effects of chronic administration of lead on the cardiovascular system especially of the histology of the heart and great vessels.

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