Structural Characterization of the Kidney Following Lactational Lead Intoxication in Sprague Dawley Rats

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Abstract: This study was designed to examine the effect of lactational lead intoxication in the kidney of Sprague-Dawley rats. 12 female rats were used in the experiment. These rats mated with male rats to reproduce 23 offspring for the analysis of lactational lead intoxication. The offspring were divided into four groups. Groups B, C and D were administered 10 mg/dL, 30 mg/dL and 70 mg/dL of lead acetate respectively while group A was control. The animal was firstly sedated using a chloroform-damped cotton wool in a vacuum (air-tight chamber). The sedated animal was weighed on a weighing balance and figure recorded. The animal was then perfused to clear blood from the organs before the organs were harvested. The kidneys were removed, weighed and fixed by immersion in 4% formal saline for further histological processing. The result showed the total body weight appeared to be significantly (p<0.05) lower in groups B, C and D when compared to the control group (29.00±2.31g) and is significantly (p < 0.05) higher in groups B and C when compared to the control. Also, total body length, right and left kidneys showed a significant (p<0.05) increased in group B when compared to the control group in both male and female. Abnormalities in the functional components of the kidney were observed with a rise in the administered dose, with the condition being most severe in the group treated with 70mg administration. It is concluded that high levels of lactational lead is very toxic to rat pups causing histoarchitectural pathologies in the kidney.

Keywords: Lactational, Lead, Intoxication, Kidney

1. Introduction

Lead is a stable, silver-gray, ubiquitous heavy metal and is detectable in all phases of the inert environment (e.g., air, water, and soil) as well as in most biological systems [1]. Unique properties of lead, like softness, high malleability, ductility, low melting point and resistance to corrosion, have resulted in its widespread usage in different industries like automobiles, paint, ceramics, plastics, etc. [2]. This in turn has led to a manifold rise in the occurrence of free lead in biological systems and the inert environment. Human exposure to lead occurs through various sources like leaded gasoline, and industrial processes such as lead smelting [2]. Lead is a persistent metal that is still present in the environment water, brass plumbing fixtures, paints, soil, dust and imported products manufactured with lead [3]. Research in humans and animals have shown that lead has toxicological effect on the liver, bone, blood, kidney, lung, heart, brain and testis, [4-10].

Lead nephrotoxicity is characterized by proximal tubular nephropathy, glomerular sclerosis and interstitial fibrosis [11-13]. Functional deficits in humans that have been associated with excessive lead exposure include enzymuria, low- and high-molecular weight proteinuria, impaired...
transport of organic anions and glucose and depressed glomerular filtration rate. A few studies have revealed histopathological features of renal injury in humans, including intranuclear inclusion bodies and cellular necrosis in the proximal tubule and interstitial fibrosis [14, 15]. In rats, proximal tubular injury involves the convoluted and straight portions of the tubule [16-18] with greater severity, at least initially, in the straight (S3) segment [19]. There is no uniformity on the direction of change of renal function parameters in chronic lead poisoning. Some studies reported a stimulatory effect of lead on renal hypertrophy and glomerular filtration rate (GFR) during lead exposure [20] while others reported a significantly reduced glomerular filtration rate, adjusted for age [21]. In animal studies, acute low-dose lead-treatment caused no significant pathological changes in rats [20].

The disparity in the onset of renal function abnormalities reported in laboratory animals appear to be related to the duration and dose of lead administration. Exposure beyond 6 months led to severe tubulointerstitial disease which resulted in significantly decreased GFR with attendant increase in serum creatinine and urea nitrogen [20]. Most studies on the effect of lead on renal function parameters investigated high doses of lead [21]. This study characterized the histoarchitecture of the kidney following lactational lead intoxication in Sprague Dawley rats.

2. Materials and Methods

A total of 12 female rats, assessed and presumably healthy, having unlimited access to standard rat feed and distilled water was kept under standard laboratory conditions at a constant 12 hour light/dark cycle to acclimatize for 1 week. The sexually matured female Sprague Dawley rats were mated at a proportion of 3 females to 1 male. After child birth, mothers and their pups were randomly divided into 4 equal groups of 8 pups each: 1 control group and 3 treatment groups that received 10, 30, and 70 mg/dL of lead acetate in their drinking water dam from day 1 (day of birth) to day 21 of the lactational period.

2.1. Lead Acetate (Dosage and Preparation)

200mg, 600mg, and 14000mg of Lead acetate powder were weighed with a Metler Toledo sensitive weighing balance and prepared in 2000ml of distilled water each, giving a final solution of 10mg/dL, 30mg/dL and 70mg/dL respectively. The solutions were administered through their water dams ad libitum.

2.2. Sacrifice of Animals

The animal was firstly sedated using a chloroform-damped cotton wool in a vacuum (air-tight chamber). The sedated animal was weighed on a weighing balance and figure recorded. Thoraco-abdominal incision was made and blood was collected through cardiac puncture using a 2ml needle into heparinized bottles. The animal was then perfused to clear blood from the organs before the organs were harvested. The kidneys were removed, weighed and fixed by immersion in 4% formal saline (dispensed in correctly labeled specimen bottles) for further histological processing. Blood samples from each group were collected in heparinized bottles (male and female apart). Collected blood samples were centrifuged; the plasma was then decanted from the blood into another sample bottle and kept in the freezer.

2.3. Histological Techniques

The excised kidneys tissues were fixed 10% formal saline for 48 hours, and processed using paraffin wax embedding method. Sections of 5 µm thickness were cut from the paraffin embedded tissues and stained with haematoxylin and eosin stain to demonstrate the general histoarchitecture of the kidney.

2.4. Photomicrography

Stained sections were viewed under a Leica DM750 microscope (Leica Microsystems, Heerbrugg, Switzerland) with digital camera attached (Leica ICC50) and digital photomicrographs were taken at various magnifications.

2.5. Statistical Analysis

One-way ANOVA was used to analyze data, followed by Tukey test for multiple comparisons. Statistically significant difference was set at p<0.05.

3. Result

Statistical analysis of the results obtained reveals from the table above show the effects of lead treatment on total body weight, total body length, weight of right and left kidney in both male and female Sprague-Dawley rats.

In male Sprague-Dawley rats, the total body weight appeared to be significantly (p<0.05) lower in groups B (19.75±0.75g), C (22.50±0.50g) and D (15.33±1.21g) when compared to the control group (29.00±2.31g) (Figure 1). Also, the results of the total body length showed a significant (p<0.05) increase in group B (25.00±2.00cm) when compared to the control group (18.50±0.87cm). Groups C (15.68±0.45cm) and D (19.67±1.86cm) appear to be insignificantly (p>0.05) different from the control group (18.50±0.87cm) (Figure 2). However, the analysis of the weight of the right kidney in the rats showed a significant (p<0.05) increase in group B (157.33±9.84mg) when compared to the control group. On the other hand, groups C (147.50±24.50mg) and D (112.67±9.02mg) appeared to be insignificantly different from the control group (98.00±14.57mg) (Figure 3). The weight of the left kidney appeared to be significantly (p>0.05) higher in group B (205.50±16.50mg) and lower in group D (105.33±10.40mg) when compared to the control group (163.33±5.90mg). However, group C (132.50±2.50mg) was not significantly (p>0.05) different from the control group (163.33±5.90mg) (Figure 4).
In female Sprague-Dawley rats, the analysis of the total body weight showed significant \( p<0.05 \) increase in groups B \((18.07\pm0.07g)\) and C \((21.50\pm0.96g)\) when compared to the control group \((12.00\pm2.00g)\). Group D \((12.67\pm2.67g)\) was not significantly \( p>0.05 \) different from the control group \((12.00\pm2.00g)\) (Figure 5). Also, the results of the analysis to total body length showed a significant \( p<0.05 \) increase in groups B \((24.67\pm0.33cm)\) and C \((15.68\pm0.45cm)\) when compared to the control group \((19.67\pm0.93cm)\). Group D \((19.67\pm1.86cm)\) however was not significantly \( p>0.05 \) different from the control group \((19.67\pm0.93cm)\) (Figure 6).

Analysis of the weight of the right kidney in the rats showed significant \( p<0.05 \) increase in group B \((198.00\pm2.52mg)\) when compared to the control group \((98.00\pm14.57mg)\). However there was no significant \( p<0.05 \) difference in groups C \((138.50\pm4.05mg)\) and D \((98.00\pm14.57mg)\) when compared to the control group \((98.00\pm14.57mg)\) (Figure 7). The result of left kidney in the rats showed significant \( p<0.05 \) difference in group B \((234.67\pm26.91mg)\) compared to the control group \((102.00\pm9.29mg)\). On the other hand, groups C \((133.50\pm11.09mg)\) and D \((91.00\pm18.34mg)\) is not significantly \( p>0.05 \) different from the control group \((102.00\pm9.29mg)\) (Figure 8).

![Figure 1. Bar chart showing total body weight in male sprague-dawley rats.](image1)

![Figure 2. Bar chart showing total body length in male sprague-dawley rats.](image2)
Figure 3. Bar chart showing weight of right kidney in male sprague-dawley rats.

Figure 4. Bar chart showing the weight of the left kidney in male sprague-dawley rats.

Figure 5. Bar chart showing the total body weight of female sprague-dawley rats.
Figure 6. Bar chart showing the total body length in female Sprague-Dawley rats.

Figure 7. Bar chart showing weight of right kidney in female Sprague-Dawley rats.

Figure 8. Bar chart showing the weight of left kidney in female Sprague-Dawley rats.
4. Discussion

The obtained results of total body weight are in agreement with the findings in previous studies such as that of Nabil [22]. The observed decrease in body weight that occurred following the lead treatment may be associated with several factors, one of which is imbalance in body metabolism produced by lead-induced impairment of zinc status in zinc-dependent enzymes which are necessary for many metabolic processes [22].

In the group that was treated with 10mg/dL of lead acetate, there was a significant (p<0.05) increase in the weight of the right and left kidneys when compared to control group. The detected elevation in the organ weight may be attributed to the fact that lead ingestion causes a significant accumulation of lipids in the kidney cells [23]. However at a higher dose of 70mg/dL, a significant decrease in the kidney weight was observed when compared to the control. This corresponds with the findings of Wright [24], that the effect of lead on the kidney weight is dose-dependent.

With respect to the total body length, a significant increase was observed in the groups treated with 10mg of lead acetate, when compared to the control group. However, at doses of 30 and 70mg/dL, statistically insignificant (p>0.05) increases were observed. The findings of Pounds [25], suggested that lead has direct suppressive effect on osteoblast function. This however only occurs following treatment with high doses of lead, which may explain the decrease in body length observed with administration of 70mg/dL of lead, in contrast to the increase observed following treatment with 10mg/dL.

The histological evidence from this study indicated the occurrence of a progressive degeneration of the renal (kidney) tissues with exposure to lead acetate in all the treated groups. This is similar to the observation of Fowler [26]. It also indicated abnormalities in the functional components of the kidney such as glomerulosclerosis, which occurred in association with renal arteriosclerosis, necrosis (pathologic cell death), haemorrhage and severe tubulorhexis (rupture of renal tubules). These observations correlate with the findings of Loghman-Adham [27]. The severity of the damage appeared to increase with a rise in the administered dose, with the condition being most severe in the group treated with 70mg of lead acetate [28].

The pathological changes may be attributed to damage caused by lead, since it is well known that lead is a nephrotoxic element that causes damage to tubular cells by necrosis and apoptosis. The damage to kidney tissues may also be due to lead-induced oxidative stress with subsequent lipid peroxidation produced by reactive oxygen species (ROS) [29].

5. Conclusion

Based on results obtained from this study, it can be concluded that lead is a nephrotoxic and its administration has a dose-dependent toxic effect on the kidneys. It is capable of causing both histoarchitectural disruption and dysfunction.
According to the study above, high levels of lactational lead is very toxic to rat pups causing histological pathologies in the kidney. Lead intake from leaded water pipes, canned foods, cutleries and other sources of lead should be avoided, especially during pregnancy.

**Conflict of Interest**

The authors declare that they have no competing interests.

**References**


