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Effects of High dose Lead Toxication on Liver, Kidneys, Heart, Brain and Blood in Rabbits: An Experimental Study

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Abstract

The aim of the study was to investigate effects of high dose lead (Pb) exposure on heart, blood, kidney, liver and brain in rabbits using clinical, electrocardiographical (ECG), ultrasonographical, haematological, biochemical and pathological methods. The experiments were performed on 15 male New Zealand rabbits, divided into three equal groups and were orally given 80 ppm or 160 ppm Pb for 15 days and the other group was used as control. Administration of 80 or 160 ppm lead significantly increased the activities of serum aspartate aminotransferase (AST), alanin aminotransferase (ALT), lactate dehydrogenase (LDH), creatine phosphokinase (CPK) and alkaline phosphatase (ALP). Hemoglobin (HB) and hematocrit (HCT) values were significantly lower in 80 and 160 ppm Pb-treated animals compared to the control animals ($p<0.001$). QRS complexes were wider and amplitudes of T wave were larger in treatment groups compared to contro group ($p<0.05$). Severe hydropic and vacuoler degenerations were seen in hepatocytes and vacuolation and degeneration of proximal tubular epithelial cells in cortex in the treatment groups histopathologically. Some neurons were severely degenerated, and severe neuron necroses were seen in cornu ammonis of both of the treatment groups. Severe mononuclear cell infiltrations were observed in Wirchow-Robin spaces. In conclusion, deleterious effects observed in liver, kidney and blood in high doses of lead administration with some similarities to chronic oral administration of low doses.

Key words: Lead toxication, Haematology, Biochemistry, ECG, Histopathology, Ultrasonography

INTRODUCTION

Lead is an environmental toxin with multisystemic effects. Exposure to lead has been shown to affect a number of different biochemical and physiological process, cell types, tissues and organ systems in animals [1, 2]. The lead levels of some target tissues and organs such as kidneys, livers, lungs and bones can reflect short-term or long-term exposure to lead [3-5]. Exposure to lead presents a major concern because of its toxic effect on the urinary, nervous, hematopoetic, reproductive and gastrointestinal systems [3, 4, 6, 7]. There have been many studies on tissue distribution of lead in rats [8-11], beagles [12], monkeys [13] and other small rodents. Because of its broad industrial usage in the manufacture of batteries, fuel additives, pipes, paint pigments, solders, shielding, etc., lead is a common occupational and environmental hazard [1, 14].

The purpose of this study was to investigate effects of high dose lead exposure for 15 days on heart, blood, kidney, liver and brain in rabbits using clinical, electrocardiographical, ultrasonographical, haematological, biochemical and pathological examinations.

MATERIALS AND METHODS

Animals

The experiments were performed on 15 male New Zealand rabbits weighing 2-3 kg and of 10-14 months age. The animals were fed ad libitum pelleted standard rabbit ration and free access to water. Animals were divided into three equal groups and were given the following treatments orally with catheter daily for 15 days; treatment groups (80 ppm Pb-treated and 160 ppm Pb-treated groups) received Pb as Pb acetate at doses of 80 and 160 mg kg^{-1} body weight respectively in isotonic saline (1 ml kg^{-1} body weight), and control group received equal volumes of istonic saline.

Physical examination

Genarel physical examinations including apatite, behaviour, and appearances of mucosal mebrans, teeth and giniva were performed.

Haematology and Biochemistry

Blood samples were collected from ear veins of rabbits on the days 15^{th} for the haematology and biochemistry. Haematologic parameters including RBC (red blood cell),

WBC (white blood cell), HB, HCT, MCV (mean corpuscular volume), PLT (platelet), neutrophil, lymphocyte, monocyte, eosinophil and basophil were examined by manual methods. The activities of ALT, AST, LDH, CPK and ALP and the concentrations of urea, creatinine, total bilirubin and albumin were spectrophotometrically determined on an autoanalyzer using commercial diagnostic kits (AMS, Italy).

Electrocardiography recordings

ECG recordings were performed on the days 0, 7th and 15th. The ECGs were recorded in sternal position without sedation and with minimum restrain. Recordings were made on a direct writing on a channel electrocardiograph (Cardiofax, Nihon Kohden Co, Japan) with the calibration at 1 mV=20 mm deflection and paper speed of 50 mm sec^{-1}.

Ultrasonographic examination

Ultrasonographic evaluation of the liver, kidneys and heart was performed using a scanner 100 LC Vet ultrasound machine (Pie Medical Equipment B.V., The Netherlands).

Histopathological examination

At the end of the experimental period, the rabbits were killed with intravenous sodium pentobarbital and subjected to a complete necropsy. Representative samples of all organs, including livers, kidneys, hearts and the whole brain, were fixed in 10 % neutral buffered formalin for routine histopathology. Sections were cut in 5 µm and stained with haematoxylin and eosin (H&E).

Digestion of tissue samples for lead analysis

Liver, brain and heart muscle samples were collected. Visible fat, blood and connective tissues were removed from all tissue samples. One g of tissue samples were weighed in glass digestion tubes and dried in an oven at 85°C for about 15 h to a constant weight. The dried samples were then cold digested in 2 ml of concentrated high purity nitric acid (Suprapure grade, Merck) overnight. Then each sample was incubated at 120°C until all the organic matter was digested. Two ml of hydrogen peroxide (30% w/v) was then added to finalize the organic matter digestion. The digest was allowed to cool down and subsequently diluted to 20 ml (liver and bone), 15 ml (kidney) or 10 ml (brain, heart muscle and skeletal muscle) of final volume with ultrapure water and stored in glass tubes until analyzes. Two ml of serum were treated with 8 ml of 1N nitric acid and then briefly centrifuged. The supernatant was used for the measurement of lead.

Determination of lead concentrations in tissue digests and serum

The determination of lead in tissue digests and serum was carried out in an inductively coupled plasma-atomic emission spectrometry (ICP-AES, Liberty Series-II Varian, USA). All specimens were analyzed 3 times, and the averages were taken when the relative standard deviation was less than 5%. The wavelength used was 283.306 nm. Calibration standard series were prepared by appropriate dilutions from 1000 mg/L stock lead solution (Merck, Darmstadt, Germany) and the acidity of standards were matched to that of the sample solutions.

Statistical analyis

Comparisons of the data between groups were made with Student's-t test and group means of each parameter compared by one-way analysis of variance followed by Duncan's test (Windows version of SPSS 13.0).

RESULTS

Clinical signs

The classical "lead line", a dark bluish discoloration of the teeth where gingival mucosa joins the teeth, was cearly observed in 160 ppm lead-treatment group compared to control animal. Lead-related behavioral disturbances were observed in both treatment groups including irritability, fatigue, myalgia and neurologic symptoms such as pica, exaggerated deep reflexes and postural tremor. Furthermore, stiff-legged gait, weakness, painful kidneys on palpation, less urine production and pale mucous membranes were also observed in the animals of both treatment groups. Obvious distentions were observed on the right side of animals in 160 ppm Pb-treated group on day 15th.

Haematology and Biochemistry findings

Haematological findings are given in Table 1. Hemoglobin and hematocrit values were significantly lower on the day 15th in 80 and 160-ppm Pb-treated animals than those of the control animals ($p<0.001$). However, there was no significant difference between 80 and 160 ppm Pb-treatment groups in terms of hemoglobin and hematocrit concentrations. In addition, RBC counts were significantly less in 160 ppm Pb-treated animals (2.78±0.44 /ml) than that in the control group (5.79±0.14 /ml) ($p<0.001$). Differential WBC counts revealed that peripheral neutrophil counts did not change in 80 ppm Pb-treated animals, but significantly increased in 160 ppm Pb-treated animals on day 15th than that in the control group. On the other hand, lymphocyte count was significantly less in 160-ppm Pb-treated animals on day 15th than that in the control group. Administration of 80 or 160 ppm lead significantly increased the activities of serum AST, ALT, LDH, CPK and ALP compared to the control values on day 15th ($p<0.05$). The concentations of urea and total bilirubin in serum significantly increased in the 160 ppm group compared to control group. The concentations of creatinine, total bilirubin LDH, CPK, and ALP were found statistically different in both treatmet groups (Table 2).

Table 1. Some haematologic findings in 80 ppm and 160 ppm Pb-treated animals compared to the control animals on the day 15th.

Parameter	Control Group (n=5)	80 ppm Pb (n=5)	160 ppm Pb (n=5)
	Mean±SE	Mean±SE	Mean±SE
WBC ($X10^6$/ml)	8.88±0.72[a]	14.86±4.87[a]	32.30±13.38[b]
RBC ($X10^3$/ml)	5.79±0.14[a]	3.93±0.54[a]	2.78±0.44[b]
HB (g/dl)	11.78±0.28[a]	7.40±1.02[b]	5.06±0.76[c]
HCT (%)	38.13±0.82[a]	24.30±2.99[b]	17.56±2.21[c]
MCV (fL)	66.01±1.05[a]	62.54±2.86[a]	64.86±3.40[a]
PLT ($X10^3$/ml)	514.46±39.33[a]	472.20±108.21[a]	583.40±149.68[a]

[a-c] Means within a column with no common superscript differ significantly ($p<0.05$)

Table 2. Effects of lead exposures 80- ppm and 160-ppm on serum parameters of rabbits on the day 15th.

	Albumin (g/dl)	Urea (mg/dl)	Creatinine (mg/dl)	T.Bilirubin (mg/dl)	AST (IU/L)	ALT (IU/L)	LDH (IU/L)	CPK (IU/L)	ALP (IU/L)
	Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE
Control Group (n=5)	3.10±0.003[a]	25.80±0.37[a]	2.81±0.13[a]	0.08±0.02[a]	203.20±29.2[a]	14.60±2.50[a]	141.60±15.5[a]	357.20±17.5[a]	2.53±0.08[a]
80 ppm Pb (n=5)	3.06±0.11[a]	32.00±2.34[a]	3.27±0.35[a]	0.13±0.03[a]	984.20±217.7[b]	22.20±2.40[b]	637.50±18.3[b]	1465.00±173.8[b]	3.85±0.03[b]
160 ppm Pb (n=5)	2.93±0.09[a]	42.00±2.69[b]	3.52±0.24[a]	0.48±0.08[b]	773.00±158.9[b]	22.17±0.87[b]	895.80±50.4[c]	3843.80±299.2[c]	5.67±0.11[c]

[a-c] Means within a column with no common superscript differ significantly ($p<0.05$)

Electrocardiography findings

Atrial arrhythmias were detected electrocardiographically in both treatment groups. Heart rates were significantly high in treatment groups compared to control group ($p<0.05$). QRS complexes were significantly wider in the animals of the treatment groups than those of the animals of control group ($p<0.05$), and the amplitudes of T wave were significantly larger and inverted in the animals of the treatment groups than those of the animals of control group ($p<0.05$). However, there was no significant difference between 80 and 160 ppm Pb-treatment groups on electrocardiografic findings (Table 3).

Table 3. ECG findings of 80- ppm and 160-ppm Pb-treatment groups and control

Parameter		Day 0	7th day	15th day
		Mean±SE	Mean±SE	Mean±SE
P-wave duration (s)				
	Control Group	0.031± 0.0026	0.028±0.0026	0.027±0.0027
	80 ppm Pb	0.028±0.0030	0.031±0.0030	0.028±0.0037
	160 ppm Pb	0.038±0.0066	0.028±0.0049	0.025±0.0028
PR interval (s)				
	Control Group	0.065±0.0033	0.058±0.0038	0.066±0.0037
	80 ppm Pb	0.065±0.0034	0.070±0.0081	0.077±0.0143
	160 ppm Pb	0.068±0.0058	0.060±0.0044	0.055±0.0086
QRS complex duration (s)				
	Control Group	0.044±0.0024	0.051±0.0077	0.042±0.0022a
	80 ppm Pb	0.043±0.0021	0.125±0.075	0.056±0.0024[b]
	160 ppm Pb	0.044±0.0040	0.050±0.0054	0.052±0.0037[b]
R amplitude (mV)				
	Control Group	0.42±0.05	0.45±0.10	0.42±0.05
	80 ppm Pb	0.45±0.07	0.48±0.15	0.69±0.14
	160 ppm Pb	0.44±0.06	0.5300±0.05	0.48±0.16
T-wave duration (s)				
	Control Group	0.087±0.0054	0.086±0.005	0.095±0.0053[a]
	80 ppm Pb	0.088±0.0054	0.170±0.086	0.062±0.0091[b]
	160 ppm Pb	0.10±0.007	0.090±0.013	0.064±0.0067[b*]
QT interval (s)				
	Control Group	0.144±0.0041	0.15±0.0028	0.150±0.0028
	80 ppm Pb	0.150±0.0036	0.15±0.0044	0.144±0.0040
	160 ppm Pb	0.146±0.0040	0.16±0.0130	0.144±0.019
ST segment (s)				
	Control Group	0.028±0.014	0.014±0.0017	0.032±0.014
	80 ppm Pb	0.038±0.018	0.020±0.0081	0.038±0.016
	160 ppm Pb	0.012±0.0025	0.020±0.0054	0.014±0.0024
Heart rate (minute)				
	Control Group	98.88±4.77	99.66±5.03	93.88±4.15[a]
	80 ppm Pb	94.16±6.11	104.16±8.70	122.0±3.391[b*]
	160 ppm Pb	106.0±8.27	104.40±10.06	133.0±4.06[b]

* : significant at the level of $p<0.05$ compared to the day 0

[a,b]: means within a column with no common superscript differ significantly ($p<0.05$)

Ultrasonographic findings

On ultrasonographic examination, diffuse increases in echogenicity were detected in kidneys of the animals in both treatment groups. In addition, partial loss of distinction between cortex and medulla, pelvic dilatation and echogenicity in kidneys with enlarged and irregular architecture were the major findings. Either focal or diffuse parenchymal hyperechogenicity in liver were also determined in both of the treatment groups, whereas no characteristic changes were noted in heart.

Necropsy and Histopathological findings

No gross pathological changes were seen in the liver, kidney, heart and brain of the control rabbits either. In macroscopical examination of the Pb-treated animals, livers were pale and swollen and pale pink to grayish. Gall bladders were distended with increased gall fluid. Kidneys were also pale and swollen with indented outer surface. Myocardial muscle appeared macroscopically normal except in some pale area. Brains of the Pb-treated animals were normal in the gross pathological examination. A variety of histopathological lesions was observed when compared with control animals. On H&E-stained sections from heart, kidney, liver and brain of the 80 and 160-ppm Pb-treated rabbits and blood and/or periferic smear of blood, lead associated lesions were observed with no appreciable difference in the severity between two treatment groups. No histopathological changes were seen in control animals of the liver (Figure a). In liver histopathology, severe hydropic and vacuoler degenerations were seen in hepatocytes, mainly perifery of the centrolobuler zone in both of the treatment groups. In these areas, hepatocytes were swollen and picnotic. Sinusoids were fiiled with erytrocytes and a few mononuclear cell infiltrations were seen in the portal areas (Figure b). No histopathlogical changes were seen in control animals of the kidney (Figure c). In kidneys, moderate to severe cytoplasmic vacuolation and degeneration of proximal tubular epithelial cells in cortex were found in both of the treatment groups. In some areas, there were mild mononuclear cell infiltrations in the interstitium of cortex. No histopathological lesions were found in the medulla of kidneys (Figure d). In cornu ammonis histopathology, some neurons were severely degenerated and severe neuron necroses were seen in both of the treatment groups (Figure e). In addition, neuronophagia and glial cell proliferations were detected in cornu ammonis. Severe mononuclear cell infiltrations were observed in Wirchow-Robin spaces. Intramyelinic edema was present in same areas in all the treatment animals (Figure f). In the histopathological examination of myocardial muscle, moderate degenerations of myofibrilles were found. Cytoplasms of the myocardial fibers were stained dark pink to reddish. Mild mononuclear cell infiltrations were seen in the interstitium of myocardial muscle in all the treatment animals (Figure h) compared to the control animals (Figure g).

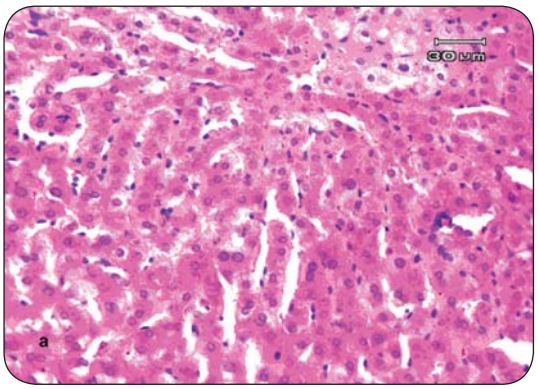

Figure a. Light micrograph of rabbit liver section from a control animal.

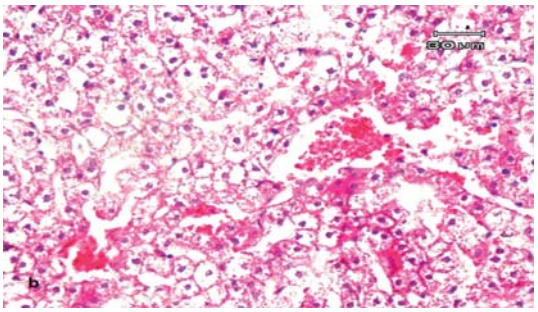

Figure b. A light micrograph of rabbit liver section from the 80 ppm lead-treatment group. Severe hydropic degenerations and hyperemia in hepatosites are seen.

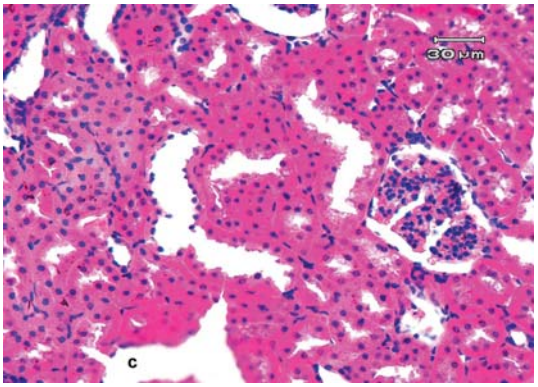

Figure c. A light micrograph of rabbit kidney section from a control animal.

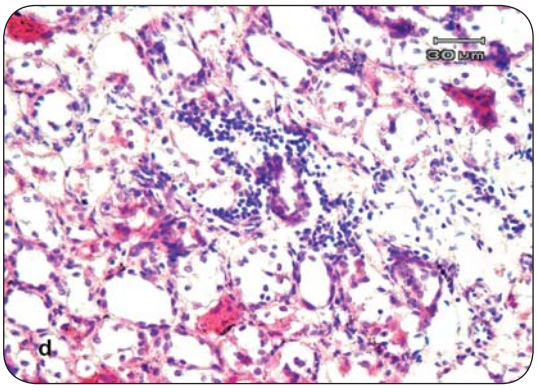

Figure d. A light micrograph of rabbit kidney section

from a 80 ppm lead-treatment animal. Note that a severe degeneration in epithelium of proximal tubulus and mild mononuclear cell infiltration and hyperemia in intersititium are clearly seen.

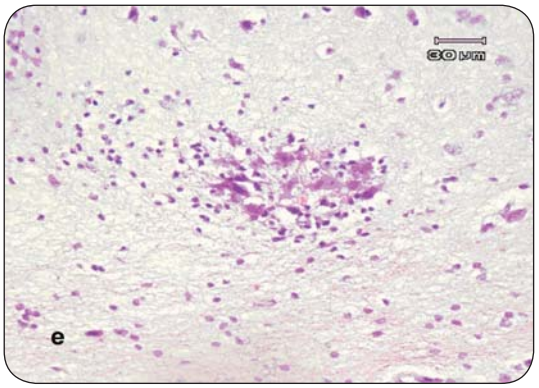

Figure e. Light micrograph of rabbit cornu ammonis section from a 80 ppm lead-treatment animal. The arrow shows necrozis of neurons and focal glial cell proliferation.

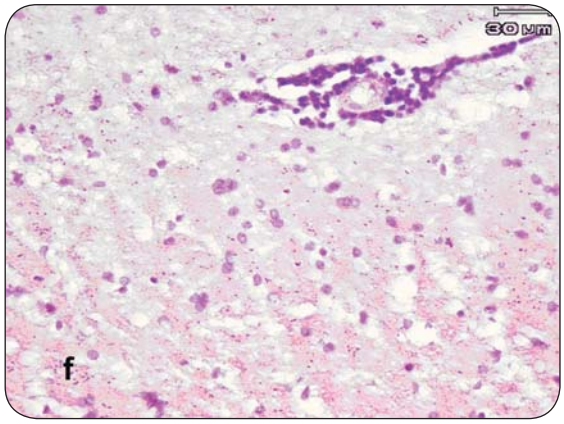

Figure f. Light micrograph of rabbit cornu ammonis section from a 80 ppm lead-treatment animal. Note that there is a mononuclear cell infiltration in Virchow-Robin space.

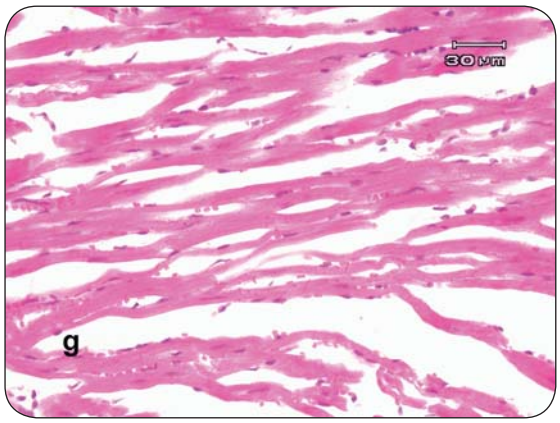

Figure g. Light micrograph of rabbit myocard section from a control animal.

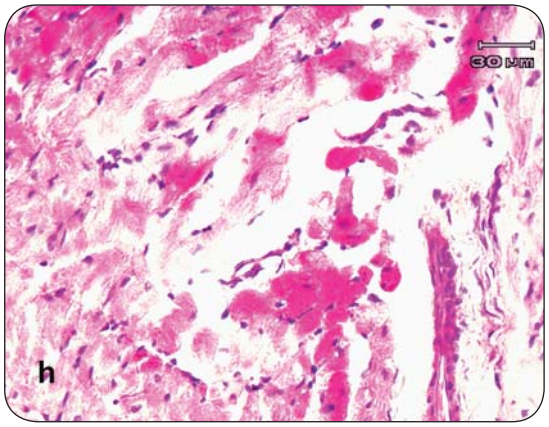

Figure h. Light micrograph of rabbit myocard section from a 80 ppm lead-treatment animal.

Finding of lead concentrations in tissue and serum

In both lead treated groups, lead accumulated preferentialy in kidneys, liver and to a less extend brain. In heart muscle, a significant accumulation of lead occurred only in 160 ppm Pb-treated animals, but not in 80 ppm Pb-treated animals at the end of the experimental period compared to the control animals. The lead concentration in serum in animals of both treatment groups did not significantly differ compared to the control animals (Table 4).

Table 4. Concentrations of lead (ppm) in tissues (µg/g WW) and serum (µg/dl) of 80- ppm and 160-ppm lead dosed rabbits.

	Liver	*Kidney*	*Brain*	*Heart muscle*	*Blood Serum*
	Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE
Control Group (n=5)	0.20±0.05^{a}	0.20±0.01^{a}	0.13±0.006^{a}	0.16±0.005^{a}	29±2.0^{a}
80 ppm Pb (n=5)	2.99±0.27^{b}	8.47±1.03^{b}	0.33±0.03^{b}	0.27±0.04^{ab}	28±2.0^{a}
160 ppm Pb (n=5)	3.32±0.16^{b}	23.50±1.76^{c}	0.42±0.06^{b}	0.34±0.08^{b}	29±1.0^{a}

$^{a-c}$ Means within a column with no common superscript differ significantly ($p<0.05$)

DISCUSSION

Lead is one of the most common toxic metals. The most common route of exposure is by ingestion of lead-containing substances such as certain folk remedies, or by consuming foods prepared or served in containers made with lead solder, glaze, or crystal. This was the first extensive study with very high doses lead exposure (80-160 ppm kg^{-1} body weight) in rabbits.

The study showed that the overt toxic effects of lead in the rabbits especially nervous system involvement were present after the 15 days of lead exposure, but the features of acute lead poisoning such as severe abdominal pain and diarrhea were not seen in either treatment groups. It is reported that clinical effects of lead poisoning in dogs were variable, but the signs of gastrointestinal and nervous system involvement were predominant [12]. In the current study, absence of gastrointestinal signs in rabbits may be due to the differences in duration of lead toxication or species. In the nervous system, lead causes segmental demyelination of motor axons [15, 16]. In the present study, the most prominent effects were noted in the radial and peroneal nerves, presenting as wrist drop and foot drop. In the central nervous system, lead toxicity has deleterious effects on the behaviors of both treatment animals. It is reported that the most dramatic consequence of central nervous system toxicity is lead encephalopathy, which can result in cerebral edema, seizures, and death [15, 16]. Nevertheless, in the present study acute lead encephalopathy findings were not clearly observed. It is conceivable that the findings reported above might be disorders of end-stage lead toxicity.

The hematopoietic system is also known to be highly sensitive [6]. Excessive lead exposure inhibits heme synthesis, leading to anemia and erythrocytes degeneration [15, 16] as observed in the present study. Lead is toxic to the proximal tubules of kidneys, causing interstitial changes, which possibly culminated anemia in the present study. Experimental group's lower hemoglobin level reached statistical significance when compared to control group. Dose dependent reducing in hemoglobin levels were also detected in treatment gropus. This lower hemoglobin is possibly attributable to direct disturbances of cellular function by lead as reported previously [3, 4, 17, 18]. We believe that the low hemoglobin concentration is very important for the differential diagnosis of experimental lead toxicities of rabbit as seen in this study.

The biological mechanisms through which lead may impair conduction in the cardiac system are not well-understood. However, there are reports suggesting that lead may act directly on myocardial cells and damage cellular functions, resulting in impaired myocardial conduction and contractility as observed ECG findings, since the myocardial degeneration and necrosis are common finding in lead-intoxicated animals. In the present study, the degeneration of cardiac musculature, mononuclear cell infiltration was evident signs of lead toxicity, which were manifested in ECG as depressed conduction, inverted T waves. The results of the present study are consistent with the data from previous studies [1, 19, 20].

In the present study, increases in serum enzyme activities are attributed to their release from the cells and this may be related to the tissue injury induced by lead. Halliwell (1994) has reported that lead-associated tissue injuries are mediated by oxidative stress in organs. The increases in the activities of AST and especially ALT in blood are associated with liver damage and an increase in the activity of AST together with that in CPK may also be related to cardiac or skeletal muscle damage. Detection of degeneration of cardiac musculature and mononuclear cell infiltration in histophatology of heart with increasing in serum AST and CPK levels might have explained the lead causing heart degeneration. Nehru and Kaushal (1993) reported that administration of 50 mg of lead acetate for 15 days in rats resulted in an initial decrease in ALP and an increase in lead concentration to 0.07 ppm in the liver. Furthermore, prolonged administration of lead for 2-3 months resulted in increased activities of succinic dehydrogenase, the acid and ALP and concentration of lead in liver. In this study, two high doses of lead administrations resulted in accumulation of lead in the liver at 2.99 and 3.32 ppm levels respectively. All the enzyme activities measured in the serum were significantly higher from those in control group and were in proportion to the lead residues in liver, kidney and heart muscle in animals of both treatment groups. In the current study, the activities of CPK in both treatment groups increased in a dose dependent manner as reported Altintas et al., (2001). Chronic lead toxication results in progressive renal deficiency with hyperuremia and hypercreatinemia [24]. The increased concentrations of urea ($p<0.001$) and creatinine (insignificantly, especially the 160 ppm group) in serum indicated a nephropathy possibly induced by lead. The accumulation of lead in tissues occurred with a rank order of kidney, liver, brain and heart muscle.

The most common and constant findings in liver was a moderate fatty infiltrative change throughout the parenchyma of hepatic lobules and a loss of normal architecture of the hepatocytes. The brain revealed dilatations and congestions of vessels, both in meningeal and brain substance. There were focal degenerative changes in the hippocampus. Similar histopathological lesions have been reported in experimental lead toxicity with different species [8-13] in low level of lead administration. We believe that the lead-related behavioral disturbances seen in both treatment groups may be due to the degenerative changes of the hippocampus. In the liver histopathology of the present study, liver hepatocytes parenchyma with severe hydropic and vacuoler degeneration was the major findings. Riera de Martinez Villa (1993) reported that low doses of lead acetate administered to rats resulted in a great amount of constant macrophages infiltration in liver by light and electron microscopy. But we observed a few mononuclear cell infiltrations in the portal areas in the current study of high doses (80-160 mg kg^{-1} body weight) in rabbits. It seems that low doses of lead might induce macrophage activity leading to protective function of liver in the mentioned study above. Lead exposure causes renal injury through several pathways. Lead appears to act as a direct tubular toxin. Light microscopy of kidney revealed morphological changes mainly in the epithelial cells of the proximal tubules as reported previously [8-10, 26]. These morphological changes could be a protective mechanism of the epithelial cells to protect them from the toxic effects of lead.

In the present study, the administration of very high doses of lead to the animals from both of the treatment groups resulted

in the highest lead accumulation in the kidneys, but moderate increases were detected in liver, brain and heart muscle (Table 4). It is reported that chronic oral administration of low doses of lead results in accumulation particularly in bone, kidney and skeletal muscle in most animal species [27]. The results presented in here did not show a dose-response correlation since serum lead level did not change during and after lead treatment. This might imply that the concentration of ionized lead in serum did not increase following lead treatment in animals of both treatment groups or the ionized lead level did not exceed the capacity that the erythrocytes could hold. An increase in the concentration of free or ionized lead only occurs when the binding capacities of erythrocytes and plasma proteins are exceeded after exposure to a relatively large amount of lead [28]. Furthermore, according to the Dally et al (1980) blood lead reflects the instantaneous state of equilibrium between the absorbed lead and the lead fixed into the tissues. Therefore, the lead concentration in blood did not appear to be proportional to the level of lead toxication in the present study.

In conclusion, some deleterious effects observed in liver, kidney and blood in very high doses of lead administration with some similarities to chronic oral administration of low doses of lead. It is reported that rabbits and humans share many similarities in the effects of lead intoxication on hemesynthesis [3, 4, 6, 21, 30]. The luminal lead load of renal tubular cells may be very similar in humans and rabbits; therefore, rabbit may be an acceptable model of human lead intoxication. Futher investigation of this aspect can be helpful in exploring the exact mechanism of lead intoxication.

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