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ORIGINAL ARTICLE

Effects of Lead Nitrate Induced Histological Changes in Liver of Male Sprague Dawley Rats

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ABSTRACT

Lead is a highly toxic agent and a potent risk factor for various diseases as its quantity in an environment is increasing day by day.
Aim: To observe and analyze the lead nitrate induced histomorphological changes in the liver of Sprague Dawley rats.
Study Design: Experimental Study.
Methodology: Animals of group A (control) were fed on normal diet but the animals of group B were given 50mg/kg of lead nitrate dissolved in 10ml of distilled water through oral gavage for 14 days daily. SPSS version 22 was used for data analysis. All the quantitative data was expressed as means ± SD. One Way ANOVA followed by Post Hoc Tukey test was applied.
Results: Degenerative effects were noted. The number of Inflammatory and Kupfffer cells is increased with decreased in the body weight. Steatosis and central vein congestion were also present. **Conclusion**: It was concluded that degenerative effects histologically may be due to oxidative stress produced by formation of free radicals and denaturation of proteins by lead nitrate.
Keywords: Lead, Liver, Central Vein Congestion, Oxidative Stress and Free Radicals.

INTRODUCTION

Lead (Pb) is a white sand like meta[1,2]. Presence of lead due to rapid urbanization and industrialization has posed a major public health crisis[3]. It can enter into the body either through ingestion or inhalation and out of these two routes, ingestion is more common than inhalation and there is no feedback system which limits its absorption[4,5]. Lead has been used in countless industrial applications like water pipes, batteries, paints, agrochemicals, construction materials, glass and cosmetics[6,7]. Lead is also present in gasoline which is another significant route of inhalational exposure[5]. Its exposure is the oldest known occupational health hazard[8]. Every year 143,000 people die because of lead poisoning and the main contributor for it is lead paint. Though many countries have prohibited lead paint for more than a decade but it is still used for ornamental purpose[9]. According to WHO lead poisoning has catastrophic health effects and they account for 0.6 percent of the worldwide ailments.

Primary target of lead are enzymes like, glucose 6 phosphate dehydrogenase, glutathione peroxidase and catalase. It alters the activity of enzyme and also targets the antioxidant which contain thiol and glutathione[10,11]. This glutathione plays an important role in qualling free radicals[12]. Oxidative stress induced by lead, results from two pathways which act simultaneously; first there is a production of ROS and the second pathway is depletion of antioxidants. This oxidative stress plays a vital role in the pathogenesis of certain diseases and it results from the imbalance between the production of ROS and the defensive response of antioxidant[12-14]. It is also used in the formation of pigments and mordants for purpose of printing and dyeing cotton material[15-17].

Detrimental effects of lead depends upon the route of administration because 20-70% of the lead will enter into the blood stream taken through ingestion and 100% will enter into the circulatory system, taken through inhalation[18].

Lead affects hematological, cardiovascular, reproductive, gastrointestinal, renal and neurological system[18]. Excessive exposure of lead contributes in cancers of stomach, small and large intestine, kidney and leukemia[19]. Lead impairs the process of digestion, causes colicky abdominal pain and diarrhea. It also shifts the physiology and histology of a liver tissue by altering liver enzymes because liver is a vital organ responsible for detoxification[20].

The objective of the study was to observe and analyze the lead nitrate induced histomorphological changes in the liver of Sprague Dawley rats.

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METHODOLOGY

It was done at the department of Anatomy, Islamabad regional centre, College of Physicians and Surgeons, Pakistan. 60 adult male Sprague Dawley rats were purchased. The rats were divided into two groups (control group A and experimental group B) each group contain 30 rats. Experimental group B received 50mg/kg of lead nitrate is dissolved in 10ml of distilled water and given to rats by oral gavage daily for 14 days[1]. Rats were fed with a standard pellet diet (purchased from the National Institute of Health Sciences, Islamabad) and water ad libitum. Six rats were housed per cage. They were acclimatized for about 1 week before the start of the experiment. They were kept at 26±2 ^{0}C with 12 hour light dark cycle[8]. The humidity was maintained at 55%. Mice had free access to food and water.
Statistical analysis: The data was analyzed statistically with the SSPSS version 22. All the quantitative data was expressed as means±SD. One Way ANOVA followed by Post Hoc Tukey test was applied to quantitative variables to detect any significant differences between experimental and control groups. Qualitative data was expressed in percentages and Chi square test was applied. The *p*-value of 0.05 or less was considered statistically significant.

RESULTS

Different parameters like central vein congestion and steatosis were studied in both groups and were shown in table-1 as percentages.

Table 1: Central vein congestion and steatosis in Control group and Experimental group

Groups	Central vein Congestion	Steatosis
Group A	0%	0%
Group B	86.6%	67%

Weight of an animal in both groups were shown in table-2 and 3 respectively as mean ± SD with their p-values. Parameters like

number of Inflammatory and Kupfffer cells in both groups were shown in table-3 as mean ± SD with their p-values.

Table-2: Body weight (gms) in Control group and Experimental group

Groups	Initial body Weight	Final body Weight	P value
	Mean ± S.D	Mean ± S.D	
Group A	246.6 ± 9.2	263 ± 7.1	0.04*
Group B	250.6 ± 10.4	208.6 ± 21.2	0.03*
P value	0.27	0.00*	

Table 3: Number of inflammatory & kupffer cells in Both Groups

Parameters	Group-A	Group-B	S. significance between group B vs A	*P-value*
	Mean ± SD	Mean ± SD		
Number of inflammatory cells	0.00 ± 0.00	5.09± 0.929	5.091	0.00*
Number of Kupffer cells	4.47 ± 0.78	6.71±1.60	2.241	0.00*

Fig-1: Photomicrograph of liver at 40X, control group A showing central vein, hepatocytes.

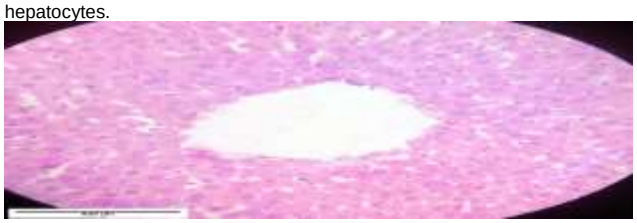

Fig.2: Experimental group B showing hepatocytes, Obliterated sinusoids, inflammatory & kupffer cells.

DISCUSSION

Lead is recognized as a noxious agent in animal models and clinical cases. The mean body weight of experimental group B was significantly decreased in comparison with the control group A with a *p*-value of 0.03. The result of this study are in accordance with the study done in 2013, 2004 and 2012 in which animals were exposed to lead and have undergone the weight reduction[21-23]. Mechanism behind the weight reduction due to lead exposure is most probably due to anorexia and vomiting accompanied by metal toxicity. This metal toxicity is produced by oxidative stress which leads to muscle wasting[21]. In contrast, result of aforementioned variable disagree the weight loss caused by lead. Proposed mechanism behind increase in body weight bring about by lead is due to DNA methylation and type II diabetes mellitus. In other words Pb causes abnormal DNA methylation which is involved in lipid and glucose metabolism[24].

The mean number of inflammatory cells per unit area of group B was significantly increased in comparison with the group A. Results of this study is in accordance with the previous study in which lead acetate trihydrate was given[25]. The observation in the current study is in harmony with the study done on a renal tissue in which lead acetate was given for a period of 6 weeks[26]. Pb is responsible to play a negative role on immune system by releasing chemical mediators such as leukotrienes, platelet activating factors and cytokines such as IL-1,IL-2, IL-6 and TNF-α which in turn release reactive oxygen species; responsible for physiological and morphological damage to cells[27] .

The mean number of kupffer cells per unit area of group B was significantly increased in comparison with the group A. Result of the present study is in accordance with the study done in 2012 and in 2009[25,28].

In the current study, none of the rats in group A showed central vein congestion, whereas in group B, 86.6% showed congestion. The result of this study was consistent with the previous work[28-30]. In group A, none of the rats showed hepatic steatosis, whereas in group B, 67% showed steatosis. Results of the current study is in agreement with the work[29].

Limitations: Limitations included limited time frame, resources and financial constrains.

CONCLUSION

It was concluded that lead has detrimental effects by disrupting normal histology of rat liver. There was a change in the liver weight and number of kupffer cells. Inflammatory cells, central vein congestion and steatosis were also present.

Author's contribution: SA&MA: Conceptualized the study, analyzed the data, and formulated the initial draft, **KA&AM:** Contributed to the histomorphological evaluation, **AI&HAB:** Contributed to the proofreading the manuscript for intellectual content.

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