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Effect of different dosage from lead acetate administrated on the liver enzymes and histopathilogical of liver in white male rats

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Abstract

Lead acetate is a toxic compound and causing cancer. In this study the effect of different dosage of lead acetate on the liver enzyme and histological structure of liver. Eighteen male rats are used in this experiment and it's divided into three groups and used six animals for each group. Group I was given a normal saline 0.9% NaCl injected intra peritoneal, group II was given lead acetate intra peritoneal injection at a dose (120) mg/Kg, group III administration through intra peritoneal injection at dose (160) mg/Kg for 7 weeks. At the end of experiment blood samples were collected from cardiac puncture and estimated for Alanine transaminase (ALT) and Aspartate transaminase (AST), in this study a significant increase in the level of ALT and AST in serum the cause of this result toxicity of lead acetate caused damage of hepatocyte lead to leakage of these enzyme to blood stream. An elevation in cholesterol and bilirubin caused by dead of hepatocytes caused this elevation. Histopathological studies of liver was shown increase in necrosis and hypertrophy of hepatocyte and hemorrhage and congestion in liver section. These effects caused by damage or dead of hepatocytes by lead acetate.

Key words: Lead acetate, liver enzyme, histopathology, male rats

INTRODUCTION

Lead is naturally occurring bluish grey heavy metal found in earth's crust. Lead have a useful in paints and protective coatings, pigments to glaze ceramics, water pipes, storage batteries and gasoline additives (1,2). Because increasing of using and its' compound, also poisoning by lead varying by the forms of this chemical (lead).

Lead acetate is a strongly soluble and poisonous compared to another shape of lead such as lead oxide or solid lead sheeting. During the last decades tetraethyl lead from gasoline cause the pollution in the environment and increasing the content of CO_2 in the atmosphere and caused greenhouse effects (3).

The main source of lead contaminated to human life from food, water and air. The poisonous in farm animal mostly in cattle by lead poisonous (3). The mainly source of this poisonous to suckling lead paints or contaminated drinking water by petroleum activity. A considerable source of loam contamination by combustion of waste and used of some pesticides such as arsenate pesticides (4).

Pollutant concentrated in different animal's tissue depend on the pathway of common and time of exposure to these pollutant, where the injection or inspiration of these pollutant and consumed in food for long time (4). In this case when: living think consumed and enter to digestive system lead concentrate and deposited in skeleton system and in different organs such as liver, kidney, testis , ovary, nerve cell and depopsite on the red blood cell causing leukemia, when this pollutant concentrate and deposite in this organs causing reflect in their function (5, 6, 7). The symptoms to lead poisonous refer to headache, vomiting, anemia, loss of body weight and losses of Appettite (7). The poisoning with heavy metal caused oxidative stress and increasing of free radical such as oxygen species (8, 9), when free radical increasing damage of target tissue and reflect in their function and decreased of antioxidant and concentrated in some soft tissue such as liver and alteration of their enzyme and hormones (9).

Although lead is a non-essential trace element. It's a toxic heavy metal it's mostly used in some industries and this compound when enter to human body disturbance of many minerals and metabolism and function of antioxidant by producing of reactive oxygen species (ROS) (10, 11). Acute and chronic toxicity of lead promote damage in oxidative stress, DNA, lipid and protein synthesis (12). The generation of superoxide dismutase (SOD), It's used to protect tissue from (ROS). The substrate of superoxide dismutase (SOD) is a superoxide radical anion (O_2^-) which producing by transfer of one electron to molecular oxygen and it's a responsible for the direct damage of biological macromolecules and generating the reactive oxygen species (SOD) and maintains the concentration of superoxide radical at low concentration and play an important role in the defense of different tissue from oxidative stress (13).

MATERIALS AND METHODS

Laboratory Animals

Adults mate rats weight from 220gm to 240 gm were adapted in animal house located in the university of Babylon research center. These animals housed in a temperature (25±1) °C and moisture approximately 49% on 12:12 h light: dark and take feed *ad lebetum*. These animals are divided into three groups and used 6 rats in each group. Lead acetate given to two groups by intra-peritoneal injection (120) mg/Kg from lead acetate for seven weeks and second group were given intraperitoneal injection with (160) mg/Kg from lead acetate for seven weeks and third group were given a normal saline 0.9% NaCl intraperitoneal injection for seven weeks all of them housed at the same conditions.

Serum ALT, ASP, cholesterol, bilirubin

At the end of experiment the cardiac puncture was used to obtain the blood samples of rats in experimental groups after anaesthetizing. Them with diethyl ether. The blood samples were located in a gel tube and put in the ice bag and spun in a desk top centrifuge at 2500 rpm for 10 minutes and samples of serum were examined for ALT, ASP, cholesterol, bilirubin applying the enzyme by reflotron.

Histopathological studies

After rats scarified liver were put in the Boun's solution overnight and then put in alcohol 70% for used in the histological section and stained with hematoxylin and eosin (14). Staining and examined with a light microscope. The procedure of slide preparing used methods of Bancrof and Steven (15). The morphological structure of liver was pale to yellow and very soft it's a signs for toxicity of lead acetate.

Statistical analysis

Data obtained from this experiment were given as mean± standard error. A significant differences between groups were finished with SPSS. The one way analysis (ANOVA) was used for data analysis.

RESULTS

The present study was designed to investigate the effects of lead acetate on the some biochemical parameters and histopathological study on the male rats.

In this study used a different doses from lead acetate and injected through intraperitoneal for 7 weeks causing an elevation of the serum Alanine transaminase (ALT) and serum Aspartate transaminase (AST) (figure. 1) refer to increasing value from 27.98 to 59.68 at 120 mg/Kg.

Moreover, lead acetate caused increase of ALT to 67 at 160 mg/Kg (fig.2) refer to the administration of different doses of lead acetate caused a marked elevation of ASP as compared to control group (fig.3) refer to effects of different doses from lead acetate on the level of cholesterol. This results refer to an increasing on the level of cholesterol from 147.5 to 184.83 and 193.17 at 120 and 160 mg/Kg respectively. However, treatment of animal with lead acetate refer to increase in the concentration of bilirubin from 0.27 to 1.08 and 1.83 at 120 and 160 mg/Kg from lead acetate respectively (fig.4).

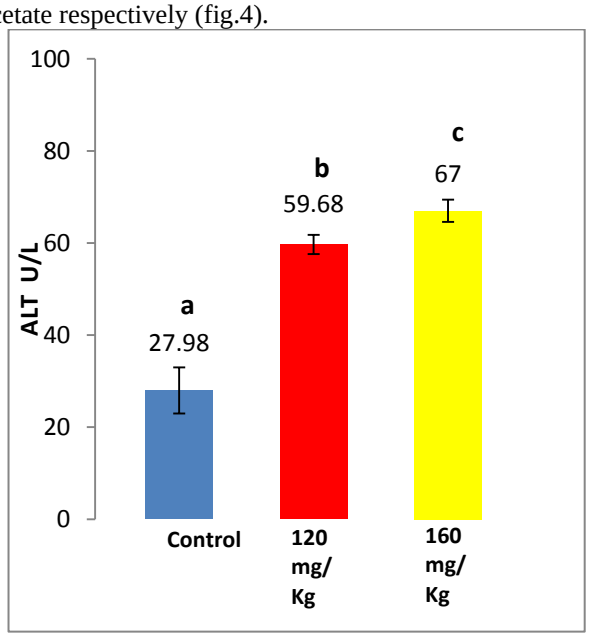

Figure (1): Administration of lead acetate at a dose 120 and 160 mg/Kg for 7 weeks on the level of Alalanin transaminase U/L.
*N= 6 animal *P<0.05

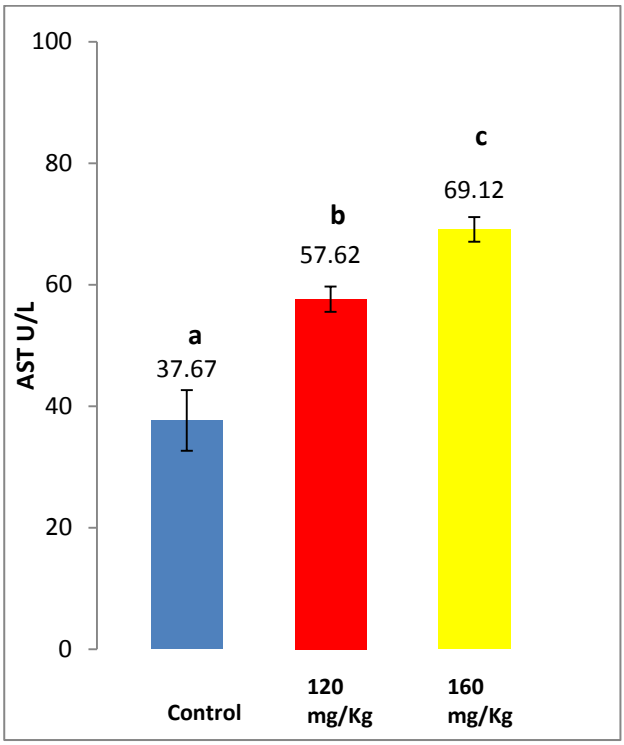

Figure (2): Administration of lead acetate at a dose 120 and 160 mg/Kg for 7 weeks on the level of Aspartate transaminase U/L on the male rats.
*N= 6 animal *P<0.05

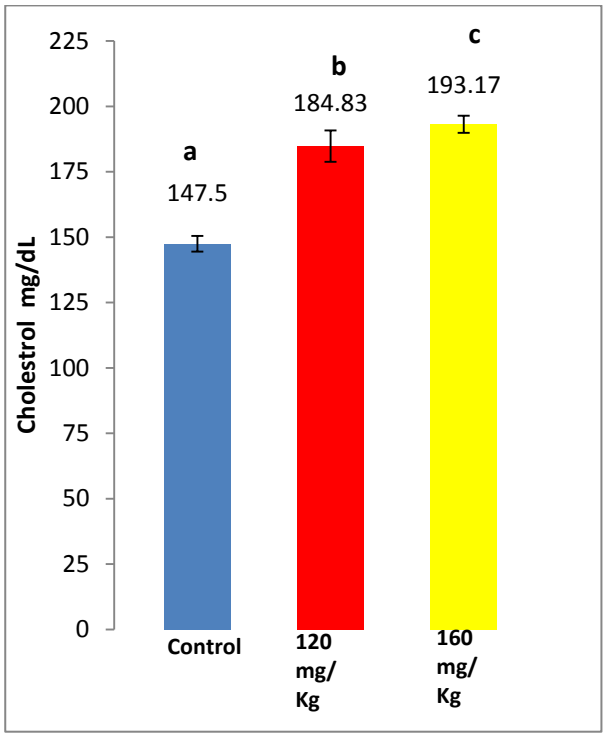

Figure (3): Administration of lead acetate on the level of cholestrol mg/dL on the male rats at a dose 120 and 160 mg/Kg for 7 weeks .
*N= 6 animal *P<0.05

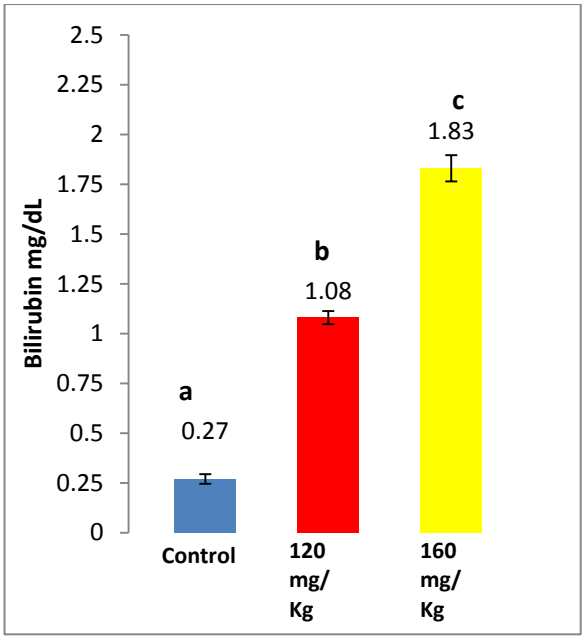

Figure (4): Administration of lead acetate at a dose 120 and 160 mg/Kg for 7 weeks on the level of bilirubin mg/dL on the male rats.
*N= 6 animal *P<0.05

Histopathological study

In this study when examine the soft tissue liver to investigate different changing in liver section from experimental animals treated group shown increasing in the Kupffer cells activation and found as clusters, and increasing in the cell of hepatocyte hypertrophy (fig. 5b) and a degeneration of hepatocytes (fig. 5b,c) and a different dosage of lead acetate can caused a vascular congestion and hemorrhage were observed (fig. 5b,c). So the treatment with lead acetate refer o markedly necrosis of hepatocytes and mostly bleeding and lysis in hepatocytes (fig.5c) as compared to control group.

DISCUSSION

Heavy metals becomes poisonous when they are not consumed and useful for human body and accumulated in different soft tissue. The major target organ liver, these elements can enter to human life from food chain (nutrition), attachment with this compound, drinking water and through inhalation (20). Lead acetate it's a toxic compound, there for the present study was designed to investigate the harmful effects of lead acetate on the liver enzyme and histopathological study on the liver for different doses during 7 weeks.

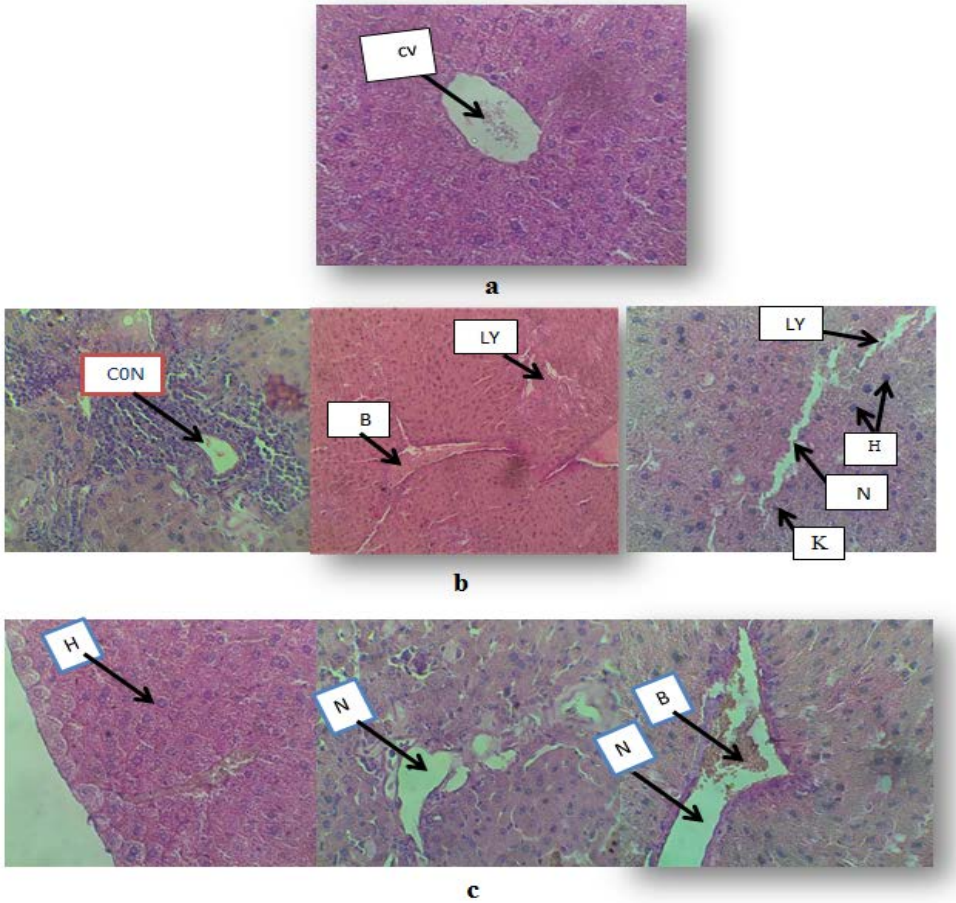

Figure (5): a. Cross section from liver control group in white male rats shown a central vein, normal shape of hepatocyte (c.v.) 40x.b. Cross section from liver administrated with 120 mg/Kg from lead acetate shown c. Cross section from liver administrated with 160 mg/Kg from lead acetate shown

The present study shown a significant elevation in serum Alanine transaminase (ALT) and Aspartate transaminase (AST). For treated groups with lead acetate with (120 and 160) mg/Kg, this enzyme produced in hepatocyte in liver, any damage or toxicity in liver with lead acetate induce oxidative stress and I suggest the main source of this elevation, this tests used to estimate liver function. The concentration of ALT and AST increased may be by damage of hepatocytes or dead. When this cell damaged the content of ALT and AST infiltration into blood stream. The elevation in this enzyme can caused in some cases such as death of hepatocytes this caused by shock. Toxicity by environmental pollutant or by some drugs can caused this shock (23).

In this study was shown a significant increasing in cholesterol caused by a loss of membrane propriety (28). This result a similarly to Wilhem *et al*. (29) improve exposure to lead acetate may be accumulate in liver and dysfunction unbalance metabolism of lipid and cause the elevation in cholesterol. When hepatocytes loss their viability that's caused the elevation in liver enzyme and bill duct pigment and caused jaundice because of failure of liver (7,19). Toxicity by environmental pollutant such as Aluminum and lead acetate induce free radical and shock DNA in hepatocytes and another fatty acid in phospholipid in target, organs such as liver, kidney, nervous system and reproductive system (8, 20). Lipid hydro peroxides are form as a result of oxidation of lipid and cholesterol consist of cellular molecules such as phospholipid in cell membrane, lipoproteins and glycolipids (6).

Lipid peroxidation can caused inhibit of some antioxidant enzyme such as superoxide dismutase (SOD) and catalase (CAT).

In this study we noticed a significant increase in the bilirubin the reason about it because toxicity of lead acetate induced damaged cell membrane by causing hepatocellular lesion and destruction of bill duct that's lead to increase in liver enzyme and destruction in hepatocytes (21) and release of liver enzyme and bilirubin from hepatocyte to blood stream. Toxicity by lead acetate caused oxidation stress and caused damaged or deaying cell. There for oxidation stress increase reactive oxygen species (ROS) that's caused this damaged and cause cancer by causing hepatocellular necrosis this caused by toxicity with environmental pollutant or malignant infiltration or liver cirrhosis. This lead to leak out this enzyme from destruction of hepatocytes and came to blood stream. The another reason about this elevation in ALT and AST toxicity of lead acetate increase the ability of liver to produce some proteins such as metalothionin and enzyme transaminase (22).

In this study chronic exposure to lead acetate can caused histopathological effects in liver such as necrosis, hepatocellular degeneration and hepatocyte hypertrophy caused by toxicity of lead acetate on liver (20). Another symptom of hepatotoxicity causing bleeding and congestion. The main source about it oxidative stress increase in ROS in liver and this caused death of hepatocyte and caused cancer in liver (23, 24) at the same time toxicity of lead acetate increasing in Kupffer cell cluster and it's play a markers of hepatotoxicity and liver injury. This result increased with increasing of concentration of lead acetate (22). Liver play an important role in the filtration of harmful molecules from blood. When human exposed to poisoning or toxicity of drugs hepatocyte damaged or dead and release their enzyme to blood (16, 25).

CONCLUSION

The exposure for long time to lead acetate can caused some biochemical and histopathological effects in target organ liver. This changes observed by causing bleeding and congestion in hepatocytes in liver and degeneration and necrosis in liver texture.

REFERENCES

1. Hurst, H.E. and Martin, M.D. Toxicology in Yagiela, J.A.; Dowd, F.J. and Neidle, E.A. Pharmacology and Therapeutic for Dentistry, 5th edn. Mosby, USA, 2004, P: 829.
2. Mudipalli, A. Lead hepatotoxicity and potential health effects. Ind. J. Med. Res., 2007,126. P: 518-527.
3. Baars, A.J.; Spierenburg, I.J. and Graff, G.J. Chrome, lead and Cadmium poisoning in farm animals. 2nd annual Conference on trace substances in environment health. St. touis. Missouri,1988, 23-25 May.
4. National Academy of Sciences . Lead air borne lead in perspective committee on biologic effect of atmospheric pollutants, Division of Medical Sciences. National Academy of Science, Washington, D.C , 1972.
5. Jarrar, B.M. Histological and histochemical alteration in kidney induced by lead. Ann. Saudi. Med.2003, 23 (1-2) P: 5-10.
6. Hsu, C.P. and Guo, L.Y. Antioxidant nutrient and lead toxicity. Toxicol.2002, 180: 33-44.
7. Taib, N.T.; Jarrar, B.M. and Mubarak, M. Ultrastructural alteration in hepatic tissue of white rats (*Rattus norvegicus*) induced by lead experimental toxicity. Saudi. J. Biol. Sci., 2004, 11 (1): 11-20.
8. Upasani, C.D.; Khera, A. and Balaraman, R. (2001). Effect of lead with vitamin E, C or spirulina on malondialdehyde conjugated dienes and droperoxides in rats. Ind. J. Exp. Biol. 2001, 39: 70-74.
9. Sharma, V.; Sharma, A. and Kansal, L. The oral administration of *Allium sativum* extract on lead nitrate induced toxicity in male mice. Food Chem. Toxicol., 2010,48: 928-936.
10. Koller, L.D. (1990). The immunotoxic effects of lead exposed laboratory animals. Ann. N.Y.Acad.Sci., 1990, 587: 160-167.
11. Gurer, H. and Ercal, N. Can antioxidants be beneficial in treatment of lead poisoning. Free Radic. Biol. Med. 2000, 29:927-945.
12. Adonaylo, V.N. and Oteiza, P.I. Lead in toxication: Antioxidant defences and oxidative damage in rat brain toxicology,1999, 135: 77-85.
13. Fridovi, CH, I. Superoxide anion radical (O_2^-), superoxide dismutase and related matters. J. Biol.Chem., 1997, 272: 18515-18517.
14. Humans, G.L. Animal tissue technique, WHO. Freeman Company; San Francisco 1978.
15. Bancroft, J.D. and Steven, A.F.. Theory and practice of histological techniques: 2nd ed., Churchill Living Stone. Endinburgh, London,1982, pp. 622-630.
16. Robert, J. R. Metal toxicity in children in training manual on pediatric Environmental Health. Putting it into practice 1999.
17. Rana, S.V.; Rekha, S. and Seema, V. Protective effects of few antioxidants on liver function in rats treated with cadmium and mercury. Indian J. Exp. Biol., 1996, 34: 177-185.
18. Sarin, S.; Cupta, V. and Gill, K.D. Alteration in lipid composition and neural injury in primate following chronic Alumnium exposure. Biol. Trace Elem. Res.,1997, 59: 113-143.
19. Wihelm, M.; Jacger, D.E.; Schull-Cablitz, H.; Hafner, D. and Idel, H. (1996). Hepatic clearnance and retention of Aluminum. Studies in the isolated perfused rat liver. Toxicol. Lett., 1996, 89: 257-263.
20. Raja, M.; AlFtal, A.; Ali, M.; Afzal, M.; Hassan, R.A.; Menon, M. and Dhami, M.S. Modification of liver and serum enzyme by paraquat treatment in rabbits. Drug Metab. Drug Int., 1992, 10: 279-291.

21. Kadhum, Sh. Ab. H. Toxicity of Aluminum chloride on the biochemical factors and histopathological liver in white male rats. Biochem. Cel. Arch., 2018, 18 (1): 85-89.
22. Ogunkey, O.O. and Roluga, A.I. Serum cholinesterase activity helps to distinguish between liver disease and non-liver disease aberration in liver function tests. Pathophysiology,2000, 13:91-93.
23. Loumbardis, N. S. and Danscher, G. Autometallographic tracing of Mercury in frog liver. Environ. Pollut., 2004, 129: 299-304.
24. Ribarov, S.R. and Bochev, P.G. Lead hemoglobin interaction as possible source of reactive oxygen species-achemiluminescent study. Arch. Biochem. Biophy., 1982, 213: 288-292.
25. Kadhum, Sh. Ab. H. Effects of Aluminum chloride on the some blood parameters and histological spleen in white male rats. Journal of university of Babylon, Pure and Applied Sciences, 2017, 5 (25): 1886-1895.