Histopathological Changes in the Liver and Kidney of Albino Mice on Exposure to Zinc Toxicity

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Abstract

Background: Zinc is one of an essential trace element, it has an important role in many enzymes of the body. It is less harmless in comparison with several other metal ions. Acute zinc intoxication occurs only if there is an exposure to high doses of zinc. Zinc poisoning may be mostly from dietary supplements, including multivitamins, or results from an accidental ingestion of zinc-containing household products.

Aim: The present study was designed to evaluate the histopathological changes of zinc toxicity in liver and kidney of albino mice.

Materials and Methods: Fourty-eight male Albino mice divided into four similar groups, the first three groups exposed during 15 days to different zinc concentrations in the form $ZnSO_4$ (60 mg/kg, 80 mg/kg and 100 mg/kg) intraperitoneally. Fourth group set as a control group, treated with saline (0.9%) for the same period of intraperitoneal injection. Sections of liver and kidney were stained with hematoxylin-eosin and examined by light microscopy.

Results: Several changes in the liver and kidneys sections like cell necrosis, congestion, swelling, disappearing of cell borders and others was observed during histopatological examination. It appears from the results that the intensity of tissues defects increased with increasing of zinc toxic concentration.

Conclusion: Results of study suggest that zinc may be toxic for use in mice and cause many toxicological changes in the liver and kidney.

Keywords: zinc sulfate, toxicity, mice, liver, kidney

Inroduction

Zinc is an essential micronutrient that almost found in all tissues of the body and is important for DNA synthesis, growth and differentiation of cell, in addition, zinc is essential for the immune system[1,2,3], protein metabolism so, it has an indispensable role for human health[4]. Zinc is less harmless in comparison with several other metal ions. Acute zinc intoxication occurs only if there is an exposure to

high doses of Zinc[5]. It has recognized zinc deficiency for many years, but currently, there are limited toxicological data available for zinc[5]. In eukaryotic cells, the physiologically Zn^{2+} concentration is about 10 ng/L but if the level of zinc below 0.06 ng/L lead to trigger of apoptosis and when level rises above 60 ng/L toxicity can ensure[6]. Excessive zinc can cause as many problems in the body as the deficiency. The first signs of zinc toxicity include reduced feed intake, reduced weight gain, bone resorption[7], vomiting, nausea, epigastric pain, fatigue and anemia[6] and excessive Zn may reduce the absorption of calcium or phosphorus [8]. Recent studies improved that free ionic zinc (Zn^{2+}) is a powerful killer of neurons, glia and other cell types[6]. In a study to Servet et al.[9] on 119 autopsy cases to determine the levels of toxic metals (cadmium and lead) and trace elements (zinc and copper) in the liver tissues, they found the average liver levels of metals and trace elements were found 29.5 µg/g, 216 µg/g, 0.39 µg/g and 4.38 µg/g dry weight for copper, zinc, lead and cadmium, respectively. In other study about zinc toxicity, Nilukshana et al.[10] improved that when a person attached directly for any cause with zinc phosphide which is a rodenticide caused severe acute kidney injury, abnormal liver profile, pancreatitis and possible myocarditis. The renal biopsy revealed.

As the animal receives higher levels of zinc or toxic amount for long periods of time, the animal will suffer from diarrhea, internal hemorrhage and even death[7]. The more remarkable pathological lesions of zinc poisoning in liver and kidney were focal mononuclear degeneration, necrosis and derangement of liver and kidney[6]. Liobet et al.[11] studied the effect of subchronic oral administration of zinc in Sprague-Dawley rats. Forty female rate were exposed to 0, 160, 320, and 640 mg/kg-day zinc acetate hydrate in drinking water for twelve weeks. The described renal lesions included flattened epithelial cells in the Bowmans capsule, desquamation of the proximal convoluted tabulated tubule and pyknotic nuclei in the 640 mg/kg-day. Intraperitoneal administration of zinc may result an increase in liver mass due to hypertrophy of the hepatocytes[12],[13]. In other study of the effect of zinc toxicity on the liver and kidney of rats for Emmanuel et al.[14]the results were hepatic cells degeneration especially at the portal areas of the livers and glomerular degeneration, mononuclear cells infiltration into the interstices of the tubules and tubular necrosis of the rats kidneys[15].

Aims of this study are:

1. To look at the importance of poisoning of the zinc element and its impact on human and animal health.

2. Study of histopathological changes in liver and kidneys because of zinc toxicity.

Materials and methods

All procedures conducted in this experiment were approved by the local authorities (Faculty of Veterinary Medicine, Basrah University, Iraq).

Experimental animals

Forty-eight adult male albino mice, 12 weeks old and 20-25 g body weight. They were obtained from the animal house of the Animal House of the Veterinary medicine College, Basrah, Iraq. They were housed in the Animal Room of the Veterinary medicine College, Basrah, Iraq, for 2 weeks before the

commencement of the experiment which lasted for 2 weeks. The mice fed appropriately using standard mice chow and water provided ad libitum. All procedures conducted in this experiment approved by the local authorities (Faculty of Veterinary Medicine, Basrah University, Iraq).

Design of the study

Forty-eight adult male albino mice used for the study divided into four groups with 12 mice in each. The first three groups were daily dosed via intraperitonial injection with 60, 80 and 100 mg/kg zinc in the form $ZnSO_4$ for 15 days. An equivalent volume of saline (0.9% NS) administered to the fourth group which set as the control group.

Histopathological examination

We took the sections of liver and kidneys for histopathological preparation and examination. The samples collected and fixed in 10% buffered formalin. Each tissue trimmed to the thickness of 5mm in size, fixed and dehydrated in a series of alcohol concentration, and embedded in paraffin by using an automatic tissue processor. Then the tissue sectioned to a thickness of 5mm micrometer on a microtome. After that, the liver and kidney tissues mounted on the glass slide, de waxed and stained with hematoxylin and eosin (EH). Finally, we examined the liver and kidney tissues using 4x, 10x, and 40x objectives for histological changes, depend on Hair-Bejo et al.[13].

Results

Figure (1) presents the liver section of the control group in which the mice exposed to 0.9% NS only. Note no observable microscopic lesions in the hepatic cells and the central vein of the liver. Figures (2-3) shows changes of liver sections against zinc toxicity. The results show that there were different stages of necrosis in the hepatic cell nuclei, swelling of hepatic cells, congestion of the central vein, and there is a disappearance feature of some hepatic cells. So The results explained that the worse histopathological changes were direct proportion with increasing doses of zinc.

Figures (4) is a section of the kidney of mice set as control croup which exposed to 0.9% NS, shows a normal glomerulus in the Bowmamńs capsule with normal tubules. While the Figures (5-6) present the results for changes of kidney sections against zinc toxicity. They show that there were different stages of swelling in tubular cells that lead to narrowing of the tubular lumen, presence of a proteinous material in the lumen of proximal and distal tubules, and also the pictures show unclearance of the cell borders especially in T3 group which treated with (100 mg/kg zinc).

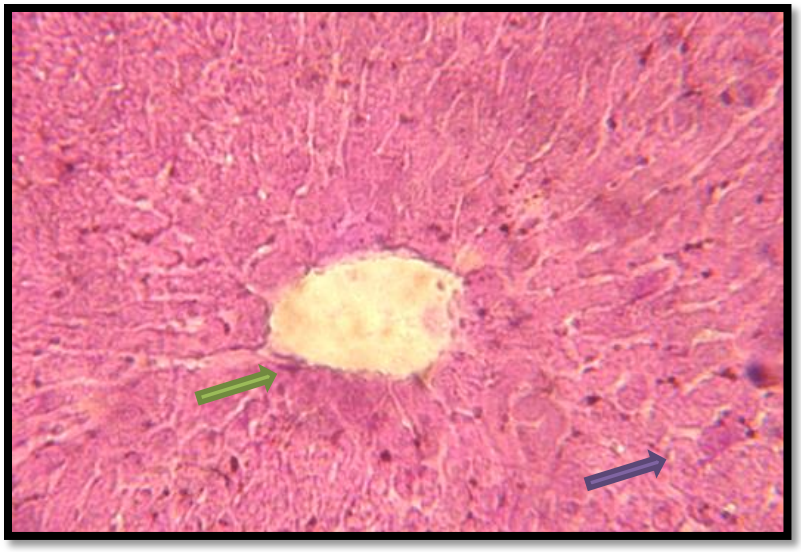

Fig.**1**: liver section of control group (0.9 N.S). H&E 400X.
Normal central vein ( ) and normal hepatic cell ( ).

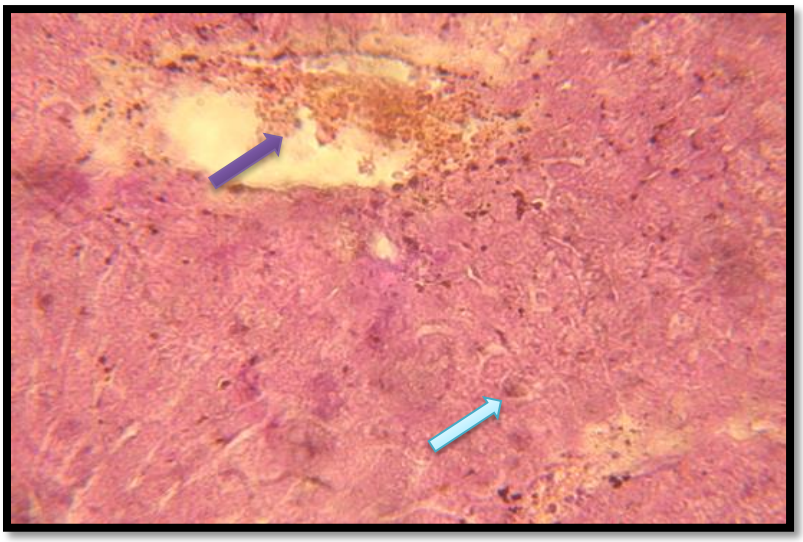

Fig. **2** : liver section of T1 treatment after 15 days (60 mg/kg zinc). H&E 400X.
Swelling hepatic cell ( ) and congestion central vein ( )

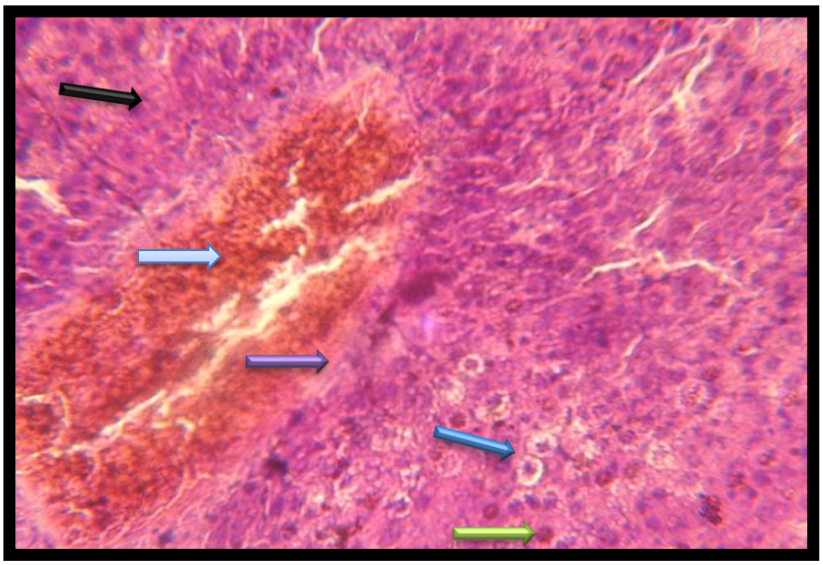

Fig. 3: liver section of T3 treatment after 15 days (100 mg/kg zinc). H&E 400X.

Congestion central vein ( ); inflammatory edge ( ); swelling hepatic cell ( ); necrosis hepatic cell ( ), and disappearing the features of hepatic cells ( ).

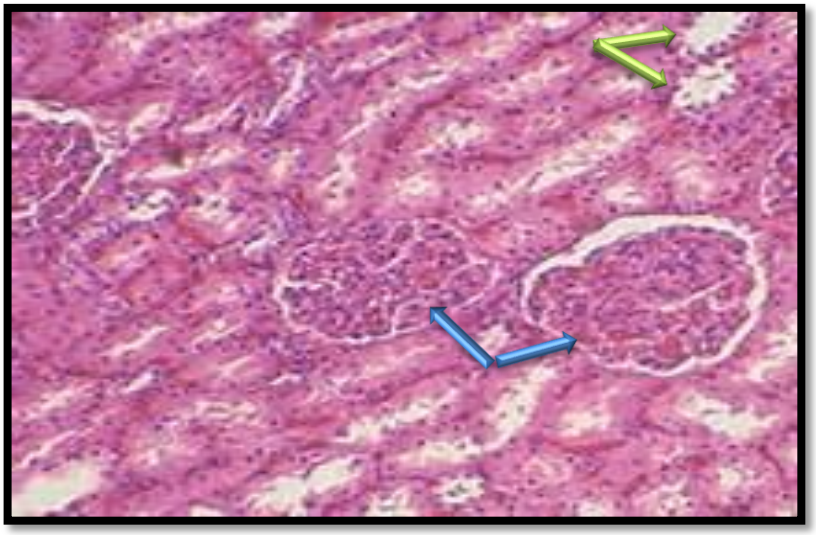

Fig. 4: kidney section of control group (0.9% N.S). H&E 400X.

Normal glumerulus ( ) and normal tubule ( ).

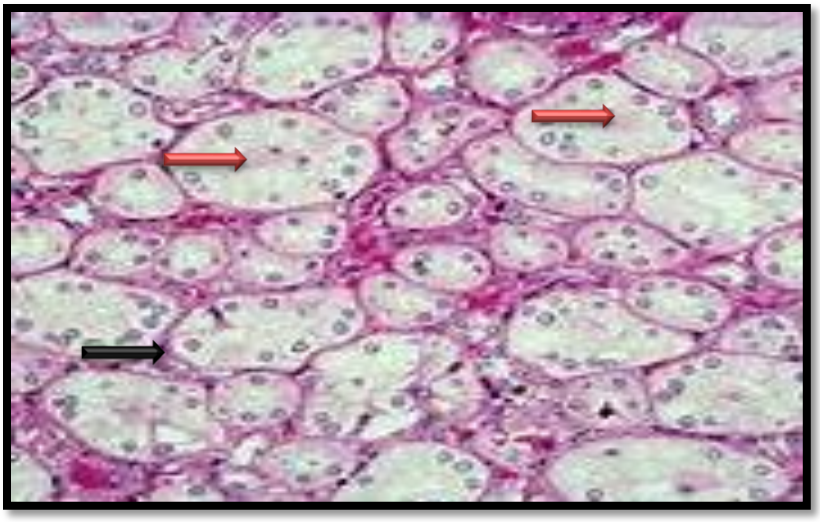

Fig. **5:** kidney section of T1 treatment after 15 days (60 mg/kg zinc). H&E 400X.

Swelling tubule ( ) and proteinous materials ( ).

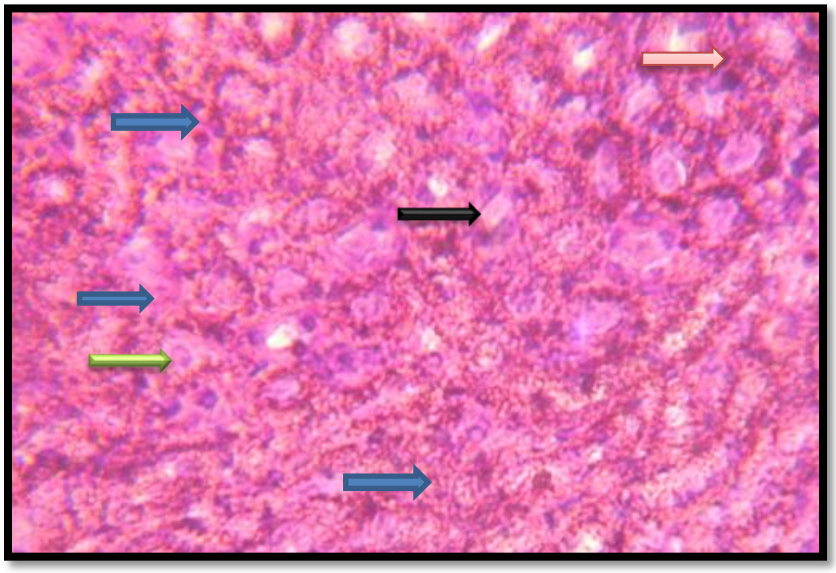

Fig. **6:** kidney section of T3 treatment after 15 days (100 mg/kg zinc). H&E 400X .

Swelling tubule ( ), proteinous materials ( ), congestion area ( ) and unclearance of cell borders ( ).

DISCUSSION

The histo-pathological changes of the liver and kidneys showed a vascular congestion. The result showed also a swelling of the cells with cell necrosis represented by condensation, division and analysis of the nucleus. It may result from the effect of zinc toxicity on the thyroid gland causing hypothyroidism[17] that leads to a decrease of the metabolism rate and then appearance of hepatic changes, or due to a decrease of the blood stream because of anemia, secondary to hypocupremia from zinc toxicity, which the commonest symptom of the zinc toxicity[18]. The administration of the gradual concentrations of zinc toxicity lead to the swelling of the tubular cells, appearance of the cells without the nucleus, which may be because of the accumulation of zinc-metallothionein complex[19] after its reabsorption by the tubules in the kidney, and this complex analysis by lysosome enzymes liberating the zinc ion which is related again with the kidney's metallothionein[19].

The intensity of the toxicity increases with increasing of the zinc dosed, and this leads to an increase in the accumulation of the zinc ions in large quantities till they become more than the ability of the kidney to form the metallothionein synthesis in the kidney is less than in the liver[19].

Conclusion:

The present study highlights significant of hepatic and kidney injury after acute zinc sulfate toxicity. We can conclude that the zinc toxicity cause histopathological changes in the liver and kidneys, exacerbated by increased zinc concentration within the body.

Conflict of interest:

The researchers declares that there is no conflict of interests with any other party.

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Ethical Clearance

According to Scientific Research Ethical Committee.
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References

1. Christa F., Philip H. Low risk of adverse effects from zinc supplementation. The USAID Micronutrient Program, 2005.
2. ÓDell B.L. History and status of zinc in nutrition. Federation Proc.1984;43: 2821-2822.
3. Kincaid Z., DEMİR N., Abdennour C., BOUZERNA N. Effect of low dietary intake and experimental diabetes on the zinc and carbohydrate metabolism in rats. Turk J Med Sci. 2002;32: 101-105.
4. Plum L.M., Rink L., Haase H. The Essential Toxin: Impact of Zinc on Human Health. Int. J. Environ. Res. Public Health. 2010; 7:1342-1365.
5. Fosmire G.J. Zinc toxicity. The American Journal of Clinical Nutrition 1990;51: 225–227.
6. Jerome N. Zinc Toxicity in Humans. School of Public Health, University of Michigan. 2007.

7. Kincaid R.L., Chew P.B., Cronrath D.j. Zinc oxide and amino acids as sources of dietary zinc for calves: effects on uptake and immunity. J. Dairy Sci.1997; 80: 1381-1388.
8. Najafzadeh H., Ghoreishi S.M., Mohammadian B., Rahimi E., Afzalzadeh M.R., Kazemivarnamkhasti M., Ganjealidarani H. Serum biochemical and histopathological changes in liver and kidney in lambs after zinc oxide nanoparticles administration. vetworld.2013; 534-537.
9. Iritas S.B., Dinc A.H., Dip A., Unal B.M., Ertan B., Soylemezoglu T. Levels of toxic metals and trace elements in autopsy liver tissue samples. Medicine Science.2017;6(2): 242-8 .
10. Yogendranathan N., Sivasundaram T., Constantine R., Kulatunga A. A case report of zinc phosphide poisoning: complicated by acute renal failure and tubulo interstitial nephritis. BMC Pharmacology and Toxicology. 2017;18: 37.
11. Liobet J.M., Domingo J.L., Colomina M.T. Subchronnic oral toxicity of zinc in rats. Bull environ contam toxicol. 1988;41 :36-43.
12. Smalinskiene A., Gaileviciute L.R., Sadauskiene I., Abdrakmanov O., Ivanov L. Effect of cadmium and zinc ions on mitotic activity and protein synthesis in mouse liver. Medicina (Kaunas).2005;41(6).
13. Hair-Bejo M., Saline S., Haifiza H., Julaida, A. Inovo vaccination against infectious bursal disease on broiler chickens. J. Vet. Malaysia. 2000;12: 63-69.
14. Tizhe E.V., Ibrahim N.D., Fatihu M.Y., Onyebuchi I.I, George B.D.J., Ambali S.F., Shallangwa J.M. Influence of zinc supplementation on histopathological changes in the stomach, liver, kidney, brain, pancreas and spleen during subchronic exposure of Wistar rats to glyphosate. Comparative Clinical Pathology. 2014; 5:1535–1543.
15. Shilpa G., Rama N., Reddy A. Toxicological studies of zinc oxide nanomaterials in rats. Journal. Toxicological & Environmental Chemistry. 2012; 94:9.
16. Dean C.E., Hargis B.M., Hargis P.S. Effects of zinc toxicity on thyroid function and histology in broiler chicks. Toxicology Letters. 1991;57(3): 309-318.
17. Johnsrud J., Abdallah A., Schichman S.A., Xiang Z. Image Diagnosis: Zinc-Induced Copper Deficiency Causing Pancytopenia Recognized on Bone Marrow Examination.. Perm J.2017; 21: 16-077.
18. Palmiter D.R. Protection against zinc toxicity by metallothioneine and zinc transport. PNAS. 2004; 101 (14): 4918-4923.
19. Hempe J.M., Cousins R.J. Cysteine–rich intestinal protein and intestinal metallothionein: An inverse relationship as a conceptual model for zinc absorption in rats. J Nutr. 1992; 122: 89-95.