EFFECTS OF ALTERED DIETARY ZINC INTAKE ON SOME GROWTH AND HEMATOLOGICAL PARAMETERS IN RATS

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ABSTRACT

The current work was carried out to study the effect of zinc deficient and zinc overdose on some blood parameters, growth hormone bioassay and its bioaccumulation in various body organs. Therefore, 36 weaned female Albino rats was induced divided randomly into 3groups: Zinc deficient (ZD) and overdose (ZO) as well as zinc adequate group as control (ZA) (12/group) by feeding them a diet containing 0.7, 7500 and 35mg Zn/kg respectively, for 8 weeks. The results showed highly significant differences in RBC count, Hb content, HCT%, MCV and MCHC ZA group as compared with ZD and ZO, while WBC count in both ZD and ZO were significantly higher as compared with ZA. Growth hormone level in ZA was significantly higher as compared with both ZD and ZO.

ZA, ZO and ZD rats exhibited highest, moderate and lowest daily food intake, respectively. The highest weekly body weight gain was observed in ZA rats as compared with ZO and ZD rats. The ZA showed highly significantly higher relative organs weight to body weight in thymus, ovary, uterus, liver and spleen as compared to ZD and ZO groups. On the other hand, ZO showed significantly higher relative brain and kidney to body weights as compared with ZA. However, no significant relative heart and lung to body weight was observed between ZA, ZD and ZO groups.

The mode of Zn bioaccumulation varied organs and treatment dose. Thus, ZD rats showed reduced Zn levels in bone, liver, uterus, skin, spleen, brain, heart and lung as compared with ZA rats. On the other hand, ZO group showed significantly higher Zn level in bone, liver, kidney, skin uterus and lung as compared with ZA group.

From the results, it can be concluded that, zinc deficient and zinc overdose induced a negative effect on RBC count, HCT%, Hb, MCV, MCH, and MCHC. Zinc deficiency and overdose induced a negative effect on serum growth hormone level, food intake, body weight gain, food efficiency ratio, body length and various body organs weight. Zinc overdose induced accumulation in bone, liver, kidney, uterus, skin and lung. The zinc deficiency produced a drop of zinc content in most organs examined such as bone, liver, heart, uterus, spleen, lung, brain and skin.

Keywords: Zn, growth hormone, body weight, bioaccumulation, rat

INTRODUCTION

Zinc is very important from biological point of view since it is involved in a wide variety of cellular processes, estimated to be required for normal functioning of over 1000 proteins, including different enzymes and transcription factors (Maret and Krezel, 2007). In addition, it is considered to be the most abundant trace element distributed throughout all body tissues at different levels (Jackson, 1989). Body has the capacity to retain constant zinc content from a wide range of dietary zinc intake and crossing this range causes a negative zinc balance (King et al., 2000). Dependent on these produce facts. could serious zinc pathophysiological conditions if taken in doses lower or higher than Recommended Daily Allowances (RDAs).

Zinc deficiency in humans is common and more prevalent in areas where the population subsists on cereal proteins (Prasad, 1996). Low consumption of foods rich in Fe and Zn such as meat, particularly red meat, and high consumption of foods rich in inhibitors of Fe and Zn absorption, such as phytate, certain dietary fibers and Ca, lead to the development of Fe and Zn deficiencies (Sandstead, 2000). Zinc deficiency can be due to inadequate dietary intake, decreased absorption, increased requirements, increased loss, or genetic disease (Sandstead 1995).

The condition of zinc excess is less common than deficiencies and it is more prevalent in areas having galvanized plumbing in their residences (Sharrett *et al.*, 1982), People that intentionally consume large doses of zinc as a dietary supplement (Hiller *et al.*, 1995), the use of zinc lozenges to treat cold symptoms for over six weeks (Blake, 2008), and smoking cause overdose symptoms (Jenkins 1986).

The objectives of the present work were to study the effect of zinc deficiency and excess on some hematological parameters, body organs Zn distribution and their effect on growth hormone and growth efficiency.

Material and methods

Materials Animals

36 young female Albino rats (two weeks old), weighed 33-35 grams were used during the present study. Animals were kept in animal house, allowed with free access to diet and water. After acclimation of the experimental animals to the laboratory conditions for one week, they were divided into Zinc deficient group (ZD) fed on a zinc deficient diet (containing 0.7mg Zn/1 kg diet), Control group (ZA) fed on diet containing adequate amount of zinc (35mg Zn/1 kg diet) (Reeves, 1997) and Zinc excess group (ZO) fed on diet containing excess zinc (7500 mg Zn /1 kg diet) (Kang *et al.*, 1977).

The composition of the diet used during the present work was formulated according to Reeves (1997) recommendation (AIN-93G purified diet).

Special care was taken to avoid zinc contamination by housing the rats in stainless steel wire-mesh cages, fed in stainless-steel feeder and distilled water in plastic bottles with stainless-steel sipper tubes (Hosea *et al.*, 2004). The rats were maintained at 23-25°C, at a relative humidity of 50-60% and exposed to a photoperiod of 12 hrs light followed by 12 hrs of darkness using automatic timer.

Food intake was determined daily and body weight was measured weekly using sensitive electrical balance (Voyager, Switzerland). The experiments were performed with least possible pains or discomforts to rats.

Methods

Sample collection

At the end of the experiment, animals were anesthetized intraperitoneally with ketamin (1ml/kg) and xyllacin 1% (50mg/kg body weight); their total body and head to tail lengths were measured before sacrificing the animals Blood (Szczurek, 2000). samples were withdrawn by heart puncture into heparinized tubes, analyzed within one hour for the determination of some hematological parameter such as RBC, WBC, Hb, HCT, MCV, MCH, MCHC using automatic computerized Coulter Counter (aSwelab, Sweden).

Serum from non heparinize blood samples were used for immunoradiometric assays for growth hormone" sandwich-type assay ". The kit utilizes mouse monoclonal antibodies directed against two different epitopes of the molecule (growth hormone) and hence not competing. Samples or calibrators (standards) were incubated in tubes, coated with the first monoclonal antibody in the present of the second ¹²⁵l-labled monoclonal antibody. The liquid content of the tubes were rinsed after incubation and bound radioactivity was measured. Values were calculated by interpolation from the standard curve. The radioactivity bound was directly proportional to its concentration in the sample.

Heart, lung, liver, spleen, decapsulated kidneys, uterus, brain, femur bone, hairless skin and muscle samples were isolated and washed 3 times with deionized water to remove the surrounding blood. The organs then dried by blotting with filter paper and weighed by sensitive balance. Then each of these organs was kept separately in a polyethylene bags. The organs were stored at -80C° in deep freezer until further analysis.

For the determination of zinc concentration in various body organs, 0.1g of the desired tissue sample was digested with 2ml of acid mixture (1:1 HNO3:H2SO4) except bone samples which were digested with 1:1 Nitric acid :Perchloric acid mixture (Al-Habbib *et al.*, 1990). The samples were left at room temperature for 24hr. for complete digestion, incubated at 70°C for 10hrs, filtered using Millipore filter (0.45 μ m), and diluted to a final volume of 10 ml using deionized water.

The zinc content of the samples was determined using Atomic Absorption Spectrometer (Perkin Elmer AA200, USA) at a wave length of 214nm.

All glass wares used in the analysis were soaked in 50% nitric acid for at least 16hr and thoroughly rinsed with deionized distilled water to avoid trace element contamination. (Sherman, A. *et al.*, 1985)

Statistical analyses

Experimental data were presented as means±standard error of the mean (SE). Data were tested using one-way analysis of variance (ANOVA). These analyses were carried out using SPSS computer software (version 15). Differences were determined using Fisher's Least Significant and considered significant at P >0.05.

Results

Effect of zinc on some hematological parameter:

Table (1) shows the effect of diet with adequate zinc content, zinc deficient and zinc overdose on some blood parameters. As the results indicate, WBC counts were significantly increased (P>0.05) in zinc deficient and zinc overdose rats as compared with zinc adequate rats. On the other hand, RBC counts were significantly decreased (P>0.05) in zinc deficient and zinc overdose rats as compared with zinc adequate rats. Parallel to RBC count, the hemoglobin

content, haematocrite percentage (HCT%), mean cell volume (MCV), mean cell hemoglobin (MCH) and mean cell hemoglobin content (MCHC) were also significantly (P>0.05) decreased in rats supplies with zinc deficient and zinc overdose groups as compared with adequate zinc(Table1).

 Table (1): some hematological parameters in zinc adequate, zinc deficient and zinc overdose rats.

Hematological	Mean ±SE						
Parameters	Zinc Deficient	Zinc Adequate	Zinc Overdose				
WBC $\times 10^{9}/L$	8.6 ±0.38694	4.925 ±0.27759	8.416 ±0.27739				
RBC $\times 10^{12}/L$	5.148 ±0.12272	6.897 ± 0.09595	5.726 ±0.20723				
HGB g/L	133 ±1.95078	147.875 ± 1.96793	121 ±6.71317				
HCT %	41.633 ±0.29954	47.3 ±0.19548	38.016 ± 1.63226				
MCV fL	60.355 ± 0.28825	67.162 ±0.3727	50.9 ±2.40069				
MCH pg	17.622 ± 0.20261	21.55 ±0.38452	14.633 ±0.28829				
MCHC g/L	318.555 ±1.65924	341 ±6.06512	315.5 ±6.90290				

Effect of zinc on growth hormone

The level of growth hormone in rats fed on diet with adequate zinc content was much greater (7.458 ng/ml) as compared with its level in zinc deficient and overdose rats, in which the levels of growth hormone were only 0.238 and 0.176 ng/ml, respectively

Effect of zinc on food intake

The results of the effect of adequate zinc supply, zinc deficiency and overdose on food

intake are shown in the Figure (1). As it is evident from the results, highest food intake was exhibited by rats supplied with adequate zinc where as lower food intake was observed in zinc deficient group. However, in zinc overdose rats, the food intake was intermediate. Statistical analysis of the results using ANOVA showed the presence of significant differences between both studied groups (P>0.05).



Figure (1): Food intake in ZA, ZD and ZO groups.

Effect of zinc on body weight gain

The rate of body weight gain was affected by zinc supply (Figure 2). Highest rate of weight gain was observed in rats supplied with adequate quantity of zinc. On the other hand, the rate of the body weight gain was significantly lower in zinc deficient and overdose rats (P>0.05). However, no significant difference in rate of body weight gain was observed between zinc deficient and overdose groups (P>0.05).



Figure (2) Effect of zinc on body weight gain in ZA, ZD and ZO rats

Body length

The head to tail and total body lengths were significantly higher (P>0.05) in rats supplied with adequate zinc as compared with zinc

deficient and overdose rats(table 2). On the other hand, no significant difference was observed between zinc deficient and zinc overdose groups (P>0.05).

Table (2) Effect of zinc on head to tail and total body lengths of ZA, ZD and ZO rats.

Mean ±SE							
Length	Zinc Deficient	Zinc Adequate	Zinc Overdose				
Head to tail	14.5 ± 0.58374	18.25±0.58374	15.1±0.58374				
Total length	27.5±0.83573	34.95±0.83573	28.625±0.83573				

Effect of zinc on food Efficiency Ratio:

Food efficiency ratio is a good indicator for the conversion of food intake to body tissue. Animals supplied with adequate quantity of zinc showed higher food efficiency ratio whereas the zinc deficient group showed a lower rate (Figure 3). However, the food efficiency ratio in zinc overdose rats was in between the zinc adequate and deficient groups. Statistical analysis of the results showed the presence of the significant differences between zinc adequate group and zinc deficient and zinc overdose groups (P>0.05). However, no significant difference was observed between zinc deficient and zinc overdose groups (P>0.05).



Figure (3) Feed efficiency ratio in ZA, ZD and ZO rats.

The effect of zinc on organ: body weight ratios

The effect of zinc on organ: body weight ratios are shown in Table (3). As the results indicate, the response to variation in zinc level was not the same for different organs. However, in most of the organs, the organ : body weight ratio of thymus, ovaries, uterus, liver and spleen was reduced in both zinc deficient and overdose as compared with zinc adequate group. On the other hand, in both brain and kidney the response was quite different, since the ratio of organ to body weight was decreased and non significantly in zinc deficient and increased significantly in zinc overdose group as compared with zinc adequate group.

However, heart: body weight and lung: body weight ratios were not influenced neither by zinc deficient nor zinc overdose as compared with zinc adequate.

 Table (3): Means organ: body weight of different organs in zinc deficient, zinc adequate and zinc overdose groups.

	Mean of organ: body weight ratio ±SE					
Organs	ZD	ZA	ZO			
Thymus	0.001317±0.00006	0.002458±0.00004516	0.2267±0.00006			
Ovaries	0.00043 ± 0.00003	0.000925 ± 0.00004626	0.000458 ± 0.00003			
Heart	0.0039 ± 0.00003	0.0038 ± 0.00003786	0.0039 ± 0.00006			
Uterus	0.001558 ± 0.00005	0.0023 ± 0.00004606	0.000992 ± 0.00007			
Brain	0.010358 ± 0.00024	0.010267 ± 0.0003043	0.012542 ± 0.00055			
Kidney	0.007033±0.00012	0.007167±0.0001606	0.008942 ± 0.00024			
Liver	0.035892 ± 0.00017	0.03975 ± 0.0008757	0.031508±0.00102			
Spleen	0.004758±0.00020	0.006667±0.0002031	0.004592±0.00019			
Lung	0.006925±0.00022	0.0069±0.0001796	0.006917±0.00021			

Thymus: body weight was significantly decreased in zinc deficient and zinc overdose group by 54% and 92%, respectively as compared with zinc adequate group. Similarly, ovaries to body weight ratio was decreased by 47% and 50%, uterus to body weight ratio was reduced by 68% and 43%, liver :body weight ratio by 90% and 72%, and spleen : body weight ratio by 71% and 69%, respectively as compared with zinc adequate group.

On the other hand, brain : body weight ratio and kidney: body weight ratio were increased in zinc overdose by 122% and 125%, respectively as compared with zinc adequate group.

Bioaccumulation of zinc in body organs

Bioaccumulation of zinc in various organs of rats supplied with adequate zinc as well as in zinc deficient and overdose rats are shown in Table (4). Normal zinc distribution in various body organs in rats supplied with adequate zinc diet are shown in table (4) and figure (4). As it is obvious from the results, the highest zinc content (89.416 μ g/g) was observed in the bone. This was followed by the liver (23.325 μ g/g). On the other hand, low zinc content was observed in brain, muscle and skin, and varied between 10.041 to 11.941 μ g/g. The zinc content in the remaining organs, namely kidney, spleen, heart, uterus and lung was intermediate and ranged from 12.300 to 14.766 μ g/g figure(4).

Table (4): Mean values of zinc concentration in various body organs. N=12.

	Zinc Concentration µg/g wet weight							
Organs	Zinc deficient(ZD)	Zinc adequate(ZA)	Zinc overdose(ZO)					
Liver	15.158±0.3331	23.325±0.2980	102.683±0.1344					
Bone	59.141±0.9428	89.416±0.7879	733.25±0.9029					
Kidneys	10.758±0.3011	14.766±0.2890	54.475±0.2770					
Brain	9.041±0.5310	11.941±0.5367	11.983±0.6308					
Uterus	9.325±0.2894	12.3±0.2640	14.45±0.2775					
Spleen	10.933±0.5225	14.091±0.5339	15.308±0.7401					
Muscle	9.608±0.2463	10.041±0.2965	10.875±0.4877					
Skin	7.008±0.1768	10.158 ± 0.4006	11.941±0.4668					
Heart	10.4 ± 0.6585	14.501 ± 0.4731	15.925±0.6609					
Lung	11.05±0.3250	12.416±0.4206	14.583±0.4201					



Figure (4) Mean zinc concentration (µg/g wet weight) in various organs of Zinc Adequate group

In rats supplied with adequate zinc, zinc deficient and zinc overdose rats, the higher rate of zinc bioaccumulation was observed in bone followed by liver(figure 4). However, zinc bioaccumulation in the bone of zinc deficient rats was significantly lower (P>0.05) as compared with the control. On the other hand, zinc bioaccumulation in bone of overdose rats was much greater as compared with zinc content in the bone of zinc adequate rates (figure 5). Zinc content of the liver also showed more or less similar pattern of bioaccumulation, since it

was decreased to 15.158 μ g/g wet weight in zinc deficient rats, while the zinc content in liverwas significantly increased (P<0.01) to 102.683 μ g/g wet weight in zinc overdose rats (figure 6). The zinc level of the kidney was comparatively lower in zinc adequate rats and the extent of the reduction was less but it was statistically significant (P>0.05) as compared with bone and liver. On the other hand, zinc bioaccumulation in the kidney of zinc overdose rats was much greater and highly significant as compared to the control (P>0.05).



Figure (5): Zinc concentration (μ g/g wet weight) in bone of ZA, ZD and ZO groups.



Figure (6): Zinc concentration ($\mu g/g$ wet weight) in liver and kidney of ZA, ZD and ZO groups.

The zinc content of the remaining organs (brain, uterus, spleen, muscle, skin, heart and lung) in rats supplied with adequate quantity of zinc, was low and varies between 10.158 to 14.09 μ g/gwet weight. In zinc deficient rats, the zinc concentration was significantly reduced (P>0.05) in all mentioned organs except the skeletal muscle in which the zinc level was non

significantly reduced (P>0.05). In rats supplied with overdose diet, the zinc content was significantly increased in uterus, skin and lung (P>0.05). On the other hand, zinc content in brain, muscle, spleen and heart were slightly changed which was statistically not significant (P>0.05)(figure 7).



Figure (7): Zinc concentration ($\mu g/g$ wet weight) in brain, uterus, spleen, muscle, skin, heart, and lung of the ZA, ZD and ZO groups.

Table (5) Z	inc concentration	in	percentage,	for	zinc	deficient	and	overdose	groups,	as	compared	with	zinc
adequate gro	oup.												

Organs	Means of Zinc concentration µg/g	Percentage of zinc concentration as compared with zinc adequate (%)			
	Zinc adequate	Zinc deficient	Zinc overdose		
Bone	89.416	66%	820%		
Kidney	14.766	N.S.	369%		
Liver	23.325	65%	440%		
Brain	11.941	76%	N.S.		
Spleen	14.091	78%	N.S.		
Skin	10.158	69%	118%		
Lung	12.416	89%	117%		
Uterus	12.3	76%	117%		
Heart	10.4	66%	N.S.		

Zinc concentration in percent of ZD group in liver 65%, bone 66%, kidney 73% as compared with ZA group for each relative organ (table 5). On the other hand, zinc concentration in percent of ZO group in liver 440%, bone 820% and kidney 369% as compared with ZA group for each relative organ.

Zinc concentration in percent of ZD rats in brain 76%, spleen % 78, skin 69%, heart 66 % lung 89% and uterus 76% of ZA group for each relative organ, as shown in (table 5). On the other hand, zinc concentration in ZO group of uterus 117%, skin 118% and lung 117% as compared with ZA group for each relative organ.

Discussion

The current work was undertaken to evaluate the importance of zinc for normal body function and the harmful effect of both zinc deficiency and overdose on the function of various body tissue and organs.

Effect of zinc on some blood parameters

Significant decline in Hb content, RBC count, HCT%, MCV, MCH, MCHC was observed in female rats fed on zinc deficient and overdose diet. This reduction in RBC count and Hb content may be used as an indicator for development of mild to moderate anemia. Reduction in Hb content may be attributed to increased rate of disruption of erythrocyte formation in zinc deficient rats (El Hendy *et al.*, 2001). Furthermore, they added that reduced RBC count in groups fed on zinc deficient diet, supports this concept. Moreover, they reported that decrease HCT% was obviously reflecting the reduction that occurs in blood cell count. Kraus *et al.*, (1997) reported that dietary Zn deficiency in rats increased osmotic fragility of their erythrocytes and resulted oxidative damage was responsible for the impaired erythrocyte stability. Shakoori *et al.*, (1994) suggested that reduction in RBC and Hb content of rabbits could be probably due to the blockage of protein synthesis and histogenesis. Interaction between folate and zinc metabolism emphasized that zinc deficiency impairs folate intestinal absorption, and subsequent Hb synthesis (Forges *et al.*, 2007).

It has been documented that excess dietary zinc in rats produces an antagonist effect on iron, copper, calcium, magnesium, and various enzymes (Lönnerdal, 2000). It has been suggested that zinc affects iron metabolism by impairing the incorporation of iron into or release from ferritin, which would influence iron absorption and storage. Furthermore, it may shorten the life span of erythrocytes, and cause a faster turnover of iron (Settlemire and Matrone, 1967).

It has been also postulated that zinc alters copper metabolism by impairing its absorption as mediated primarily via the direct effect of zinc in intestine, since copper is known to be involved in some way in red blood cell formation (Van Campen, 1967). Furthermore, he added that zinc at high dietary levels interfere with normal copper metabolism resulting in an abnormal red blood cell synthesis.

Excess intake of zinc has been shown in humans to induce sideroblastic anemia, during which by unknown mechanism ferric ion accumulates in mitochondria of erythrocytes. One hypothesis is that the symptoms of anemia result from zinc-induced copper deficiency (Walsh *et al.*, 1994).

Since Zn is essential for integrity of the immune system, its deficiency results in reduced immunocompetence and decreased resistance to infections (Prasad, 1993). Our results showed a significant increase (P>0.05) in WBC of female rats fed on low and overdose levels of Zn. Zinc deficiency affects proliferation and maturity of lymphocytes adversely (Prasad, 1996). This increase in leukocyte counts may indicate an activation of the animal's defense mechanism and immune system (El Hendy *et al.*, 2001). Ajayi, (2008) reported that there was no significant difference (P < 0.05) in the packed cell volume (PCV) whereas white blood cell count (WBC) of the zinc deficient rats was

significantly increased (P < 0.05) as compared to the control.

Growth rate and efficiency

Food intake:

The present study revealed a significant decrease in the food intake of both ZD and ZO rats as compared with ZA group. Zinc deficiency is invariably accompanied by alterations in smell and taste followed by anorexia and weight loss. Zinc may also control the appetite by acting directly on the appetite center in the brain. The growth inhibition caused by zinc deficiency may be partially responsible for the changes in smell, taste and appetite, which in turn reduce food consumption and utilization (Brandao-Neto *et al.*, 1995).

Zinc deficiency activates the hypothalamuspituitary-adrenocortical (HPA) axis and induces profound increases in glucocorticoid synthesis, and this may explain the role for corticosterone in reducing protein synthesis and cyclic food intake (Evans, 2003).

Maita *et al.*, (1981) reported that food intake of rats and mice fed on excess zinc diet reduced food intake and this agree with results of the current work. However, feeding chick with zinc overdose diet for 3 weeks causes significant reduction in food intake with growth retardation (Sandoval *et al.*, 1998). Reduced food intake in rats fed on zinc deficient diet was reported by several workers (Fosmire *et al.*, 1975 and Wallwork *et al.*, 1983; Evans, 2003).

Kang *et al.*, (1977) showed that FER (food efficiency ratio) of ZD was significantly lower than control whereas ZO and control were not differed due to the use of comparatively much lower concentration as compared with concentration used on this study.

Total body and organ weight:

Total body weight (TBW) and length were significantly higher in zinc adequate as compared with both ZO and ZD groups. Adequate zinc level plays an important role in body growth, gene expression and induction of enzymes linked to DNA synthesis before cells enter the S phase of the cell cycle, as well as the induction of new proteins during cell differentiation (Chesters, 1989). Furthermore, he added that zinc deficiency in experimental animals caused considerable changes in the differentiation of chondrocytes, osteoblasts and fibroblasts, thus impairing bone maturation which is resulted from its interference with DNA synthesis and osteoblast or fibroblast proliferation. Moreover, it has been reported that

zinc is present in appreciable amounts in cell nuclei, nucleoli, chromosomes, ribosomes, and secretory granules. Zinc is intimately linked to DNA and RNA structure, synthesis and degradation, thus playing an important role in the control of cellular replication and transcription (Salgueiro *et al.*, 2002).

The current results agree with that reported by Stewart and Magee, (1963) and Maita *et al.*, (1981), they indicated a significant decrease in the BW of young rat feeding a diet with excess zinc. Also it has been reported that zinc deficiency decreased the final body weight of the rats as compared to the control (Fraker *et al.*, 1978; Evans, 2003 and Ajayi, 2008). Kang *et al.*, (1977) reported that weight gain and food efficiency ratio in ZD rats were lower than control whereas ZO remain unaffected due to the use of comparatively much lower concentration as compared with concentration used on this study.

Relative organ to body weight in ZD group of thymus, ovaries, uterus, liver and spleen were significantly lower than that of ZA group where as organs such as lung, kidney, brain and heart were showed no significantly difference from those of ZA group (P>0.05). Thus, it seems that such tissues may have a minimal need for Zn that, if not met, limits their growth (Bentley and Grubb, 1991).

Relative organ weight to body in ZO group of thymus, ovaries, uterus, liver and spleen were significantly lower than that of ZA group. Brain and kidneys were significantly higher than that of ZA group but there were no significant differences in the relative weight of heart and lung for both ZO and ZA groups.

A similar lack of response of lung to body weight was observed in both ZD and ZO rats as well as heart of ZO group (Kang *et al.*, 1977). Furthermore, an elevated kidney to body weight rate was observed in ZO group. Body length, tail length, femur dry weight, Liver, and kidney weights of the ZD rats were dramatically reduced as compared with the control group (Szczurek, 2000). Relative weight of brain in male rats fed on zinc overdose diet was higher than control whereas liver and spleen relative weight were lower as compared with control and heart relative weight was unaffected by zinc overdose diet (Maita *et al.*, 1981), these agree with data in present study.

Growth hormone:

The present work demonstrated that growth hormone levels of both ZD and ZO were

significantly lower than that of the ZA group. This can be explained on the bases of the direct effect of zinc on the synthesis and action of GH (Brandao-Neto et al., 1995). Zinc deficiency also caused failure of GH secretion from the pituitary or reduce the capacity of its storage (Root et al. 1979 and Roth and Kirchgessner, 2000). Growth hormone contains a zinc-binding site that is and functionally structurally important (MacDonald, 2000). Zinc deficiency may adversely affect GH production and/or secretion which in turn may inhibit the growth (Masayuki, 2001).

Glucocoticoid is considered as one of the GH inhibitor, and since Zinc deficiency activates the hypothalamus-pituitary-adrenocortical (HPA) axis and induces profound increases in glucocorticoid synthesis (Evans, 2003). Due to the availability of limited information on the effect of ZO on the serum growth hormone level it is very difficult to compare the results. However, decreased growth hormone level in zinc deficient rats was observed by other (Roth and Kirchgessner, workers 1997. Kirchgessner and Roth, 1985 and Roth and Kirchgessner, 2000).

Bioaccumulation

Zinc normally present in all body tissues and fluid, since it is an essential component of a large number of enzymes and stabilizes the molecular structure of cellular components and membranes and in this way contributes to the maintenance of cell and organ integrity (Hambridge et al., 1987). However, distribution of zinc is not homogeneous in different body tissue (King et al., 2000). Highest concentration of zinc in ZA rats was observed in bone suggesting that zinc play an important role in bone metabolism, it is considered to be an essential component of the calcified matrix (Salgueiro et al., 2002), rapid skeletal growth (Rossi et al., 2001) and may act as a reservoir for zinc (Morgan et al., 1988). Bone was followed by liver in which the rate of turnover of zinc may be high in such active organ where protein synthesis and hydrolysis are rapid (Roy, 1961). The sequence of decreased zinc concentration is as follows: kidney, heart, spleen, lung, uterus, brain, skin and muscle, respectively. More or less similar data were observed by Prasad et al., (1967) with few exception in which zinc concentration graded from bone as highest concentration followed by liver. kidney, lung, heart and muscle, respectively. Other research worker observed

somewhat different data in which bone also have highest zinc concentration followed by kidney, lung, liver, heart, muscle and brain (Chvapil *et al.*, 1974). Different Zn concentrations in different organs of the same group may reflect expendable excesses, possibly stores, of the element and the tightness of its binding, or incorporation, at essential sites (Bentley and Grubb, 1991).

Zinc concentrations in ZD rats, in the current study, were reduced in bone, liver, uterus, skin, spleen, brain, heart and lung. Decreased zinc concentration in some organs of ZD group could increase the absorption mechanisms, but this couldn't reach the homeostatic balance for such organ. This may be partly due to reduced feed consumption and subsequent lower zinc intake than would have occurred if all animals had consumed the same amount beside the low zinc content of the diet (Ott et al., 1966). Miller et al., (1970) showed that zinc content of the round muscle is not affected by a zinc deficiency or by unusually high dietary zinc levels. Thus it appears that there is a certain number of zinc binding sites in this tissue and that they hold zinc with great tenacity. Some of the metabolically more active soft tissues such as liver, kidney, heart and lungs contain far higher amounts of Zn (Miller et al., 1970).

Zinc homeostasis may depends on the sites from which presence of tissue mobilization of nonessential or less essential Zn may occur. Little is known about this possibility, but based on their studies with rats, Giugliano and Millward (1984) suggested that there may be "high-priority" and "lowpriority" tissues. In times of need, Zn may be released from the latter to the former. Their results suggested that bone may be such a low-priority tissue and skeletal muscle a one. Giuglaino and Millward high-priority (1984) also suggested the "possibility" that the skin may function as a "sink" for Zn. Such a decrease in the Zn content of bone and skin ("low- priority" tissues) may help to maintain Zn levels in substantial amounts for "highpriority" tissues such as muscle, brain, thymus, testis, and liver. In skin and bone, it is possible that a mobilization of nonessential Zn from stores could occur for transfer and utilization by other tissues (Bentley and Grubb, 1991).

Decreased Zinc concentration in bones of ZD group suggests that Zn deficiency may have a

pronounced effect on the mobilization of non critical body Zn pools to maintain adequate circulating Zn levels and to be used by other tissues (Hall *et al.*, 2005; King *et al.*, 2000; and Szczurek, 2000). Furthermore, they suggested that Zn can be released through normal turnover of ossified tissue, not in response to acute deficiency, but over time during chronic deficiency (Hall *et al.*, 2005).

Bone is not a zinc reservoir because bone zinc is not readily released during conditions of zinc deficiency in amounts sufficient to prevent deficiency signs. The functional significance of changes in bone zinc concentrations with regard to bone itself remains unclear, but defective and impaired bone growth and development have been described in severely zinc-deficient rats and marginally zinc-deficient monkeys (Morgan *et al.*, 1988).

Generally, rats fed on zinc overdose diet showed comparatively a high rate of zinc bioaccumulation in various organs as compared with its bioaccumulation in control rats. Thus, high zinc concentration was observed in bone, liver, kidney, uterus, skin and lung of rats fed zinc overdose diet. The large amounts of zinc deposited in certain tissues fed high dietary zinc may represent a part of the mechanism that protect cells from zinc toxicity and not to serve as a source of reserve zinc (Kincaid and Cronrath , 1979), or may be the result of initial synthesis of MT as a detoxification method and may reflect the limited homeostatic control for these tissue (Sandoval *et al.*, 1998).

Excess zinc has an antagonistic effect on the normal deposition of calcium and phosphorus in the bones of young rats, feeding of zinc was associated with an increased excretion of calcium and phosphorus,

The primary effect of zinc toxicity on calcium and phosphorus is to interfere with the normal absorption and to increase the fecal excretion of these minerals (Stewart and Magee, 1963).

Since, excess zinc is released through the pancreas and small intestine as well as the kidney (Dufner-Beattie *et al.*, 2005). Increased renal zinc concentration observed in zinc overdose rats in the present study may be associated with increased zinc handling by kidney resulted from increased zinc excretion.

The toxicity of Zn depends upon the source of Zn, its level in the diet, the duration of feeding, and the levels of other minerals in the diet (Pulz, 2006). Our result also agreed with Cox *et al.*, (1969) in which they reported that zinc

concentration in maternal rats feed 0.4%zinc (zinc overdose diet) were elevated in maternal liver, kidneys and unaltered in the other(spleen, muscle and heart). Whereas disagree when proposed increased maternal brain zinc concentration.

Stewart and Magee, (1963) reported the increased bone zinc concentration in young rat feeding a diet supplied with 0.7%zinc and this agree with our results. Kang *et al.*,(1977) ZO rats liver and kidneys shows increased zinc content whereas heart were unaffected by ZO diet, these data are agree with those observed in the present work.

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الخلاصة

يعتبر عنصر الزنك ثاني اكثر العناصر انتشارا بعد الحديد في الجسم و انسجته و سوائله 0لذا تحدف هذه الدرسة لتقيم عوامل خطورة نقصه وزيادته مقارنة بالكميات المعتدلةمنه.حيث تم دراسة زيادته ونقصانه على عدة محاور منها الدم وعلى هورمون النمو و و تجمعه الحيوي في اعضاء الجسم المختلفة.

اجريت هذه الدراسة على 36 اناث الجرذان البيضاء المفطومة حديثا حيث قسمت الى ثلاث مجاميع: مجموعة سيطرة و مجموعة لنقص الزنك ثالثة لفرط الزنك ضمت كل مجموعة 12 حيوان مختبري غذيت بطعام يحتوي على 35 ،0.7 و 7500 ملغم زنك/كغم على التوالي ولفترة 8 اسابيع.اظهرت نتائج تعداد الكريات الدم الحمر (RBCs)، نسبة حجم الخلايا المرصوصة (PCV%)، قياس خضاب الدم (Hb)، معدلات حجم كريات الدم(MCV)، معدل خضاب الدم في الكرية الحمراء (MCH) انخفاضا معنويا لمجموعتي نقص الزنك وفرطه مقارنة بمجموعة السيطرة. بينما سجلت نتائج تعداد كريات الدم البيض ارتفاعا معنويا في مجموعتي نقص وفرط الزنك مقارنة بمجموعة السيطرة. كما اظهر مستوى هورمون النمو انخفاضا معنويا في مجموعتي نقص الزنك مقارنة بمحموعة السيطرة. كما اظهر مستوى هورمون النمو انخفاضا معنويا في مجموعتي نقص الزنك مقارنة بمحموعة السيطرة.

سجلت نتائج دراسة كمية الغذاء الستهلك لمجموعة نقص الزنك اقل انخفاضا وفرط الزنك انخفاضا معتدلامقارنة بكمية الغذاء المستهلك في مجموعة السيطرة. كما لوحظ انخفاضا في اوزان جرذان مجموعتي نقص الزنك وفرط الزنك بمعدلمقارنة باوزان الجرذان في مجموعة السيطرة. كمااضهرت نتائج قياس وزن الاعضاء نسبة الى وزن الجسم فروقات معنوية حيث سجلت اوزان كل من الغدة الزعترية، المبايض، الرحم، الكبد و الطحال نسبة الى وزن الجسم في مجموعة السيطرة زيادة معنويا مقارنة بمحموعتي نقص الزنك وفرط الزنك، فيما سجلت اوزان كل من الدماغ و الكلى: وزن الجسم في مجموعة فرط الزنك زيادة معنويا مقارنة بمحموعتي نقص السيطرة و لم يسجل اي فروق معنوية في اوزان القلب و الرئتين : وزن الجسم بين المجاميع الثلاثة.

بينت نتائج قياس التجمع الحيوي للزنك تفاوتا في الاعضاء والمحاميع المختلفةحيث ان نقص الزنك ادى الى انخفاض تركيز الزنك في العظام، الكبد ، الرحم، الجلد، الطحال، الدماغ، القلب، و الرئة مقارنة بمجموعة السيطرة.بينما فرط الزنك سبب تجمع الزنك في العظام، الكبد، الكلي، الرحم، الجلد و الرئة.

نستنتج مما ذكراعلاه بان نقص عنصر الزنك و فرطه يؤثر سلبا على الكريات الدم الحمر (RBCs) ، خضابالدم (Hb) ، نسبة حجم الخلايا المرصوصة(PCV%)، معدل خضاب الدم في الكرية الحمراء (MCH)، معدل خضاب الدم في الكرية الحمراء (MCH) و معدل تراكيز خضاب الدم في الكريات (MCHC). ان نقص عنصر الزنك و زيادته في الجسم له تاثير سلبي على مستوى هورمون النمو، استهلاك الغذاء، وزن الجسم، نسبة فعالية الغذاء، طول الجسم ووزن اعضاء الجسم المختلفة. فرط عنصر الزنك في الجسم يؤدي الى تجمع العنصر في العظام، الكبد، الكلى، الرحم، الجلد و الرئة. كما ان نقص عنصر الزنك و الى هبوط في محتوى الزنك في اغلب الاعضاء المفحوصة التي هي العظام، الكبد، الكم، الجد، الجلد، القلب، الطحال، الدماغ و الرئة.

پوخته:

زينك بەدووەم بلاوترين توخم دائەنريّت لە دواي ئاستەوە لە جەستەو ھەموو شانەوشلەكاني لەبەر ئەو ئەم ليْكۆلينەوە ئەنجام درا بۆ ھەلسەنگاندني لايەني مەترسي لە كەمي و زۆري ئەم توخمە وبەراوردكردني لەگەل برە ئاساييەكاني .

كاريگەري كەمي و زۆري زنك لەسەر چەند پاراميتەريكي خوّيىن، ھۆرمۆني گەشەو كۆبونەوەي زينك لە ئەندامە جياوازكاني لەش ئەنجامدرا.

36 جرجي ميينهي سپي تازه له شير بړاوه دابهش كران بهسهر سيّ كۆمةلهدا، كهئهوانيش كونترول،كهمي زينكو زيادهړهوي زينك كهههر كۆمهليّك له (12) جرجي تاقيگهيي بيّكاهاتبوون و ريّژهي جياوازي زينك بۆ سيستمي خواردنهكانيان بهكارهات بهريّژهي 35,0,7,7500 ملگم زنك/ كلگم يهك بهدوايهك بز ههرسيّ كۆمةلهكهوه بز ماوهي 8 ههفته.

شيكارييهكاني خوينن دەريانەخست كە ژمارەي خرۆكە سورەكاني خوينن (RBC)، ريترەي قەبارەي خانەر،ەوەكان (PVC)، هيمىزگلىربىنى خويىن (Hb)، ريترەي قەبارەي خرۆكەسورەكان (MCV)، ريترەي هيمىزگلىربىن لە خرۆكەسورەكان (MCH) و ريترەي بەيتى هيمىزگلىربىنى خوين لە خرىزكە سورەكان (MCHC) نزمبوونيكى بەرچاوي تىزماركرد لە ھەردوو كۆمەلەي كەمي و زيادەي رووي زينك بە بەراوردكردني لەگەل كۆمەلەي كۆنترىزلا دا، بەلام ژمارەي خرىزكەسپيەكان بەرزبوونيكى بەرچاوي تىزماركرد لەھەردوو كۆمەلەي و زيادە رەمي دىنى بەرچاو بە بەراوردكردنى لەگەل كۆمەلەي كەنترول دا.

ئەنجامەكاني ليكۆلينەوەي بړي خواردني بەكاربەر پيٽشانياندا بە بەراوردكردن لەگەل كۆمةلەي كۆنترۆل كە ھەردوو كۆمةلەي كەمي و زيادەرەوي زينك بەشيّوەيەكي بەرچاو نزم بووە وە دابەزيٽكي بەرچاو لە كيّشي گشتي جەستەي جرجەكان لە ھەردوو كۆمةلەي كەمي و زيادە رەوي زينك تۆماركرا بە بەراوردكردني لەگەل كۆمةلەي كۆنترۆل دا.

ئەنجامەكاني رينژەي كيّشي ھەريەك لە ژيتركۈللە رژيّن، ھيّلكەدانەكان ، مندال دان، جگەرو سپل بۆ كيّشي گشتي جەستە نزم بوونيّكي بەرچاوي تۆماركرد لەھەر دوو كۆمەلەي كەمي و زيادە رەوي زينك بە بەراوردكردني لەگەل كۆمەلەي كۆنترۆل دا وە ريّژەي كيّشي ميّشك و گورچيلە بۆكيّشي گشتي جەستە بەرزبوونيّكي بەرچاوي دەرخست لە كۆمەلەي زيادەرەوي زينك بە بەراوردكردني لەگەل كۆمەلەي كۆنترۆل دا . بەلام ھيچ جياوازىيەكي بەرچاو لە ريّژەي كيّشي دل و سييەكان بۆ كيّشي گشتى جەستە لە نيّوان ھەر سي كۆمەلەي كونترۆل دا .

ئەنجامەكاني پيراني كۆبوونەوەي زينك دەريان خست كەزيادەرەوي زينك لەخۆراك دا ئەبيتە ھۆي كۆبوونەوەي زينك لە ئيسك، جگەر،گورچيلە، پيست،مندال دان و سييەكان بە بەراوردكردني لەگەل كۆمەلە كۆنترۆل دا. بەلام كۆمەلەي كەمي زينك نزم بوونيكي بەرچاوي تۆماركرد لە بەيتي زينك لە ھەريەك لە ئيسك، جگەر،مندال دان، پيست ، سپل ، ميشك ،سييەكان و دل.

ئەم ليكوٽلينەوەيە ئەوەمان بىز دەردەخات كە كەمي و ھەروەھا زىزى توخمي زينىك لە خىزراك دا كاريگەرى نيّگەتيفيان ھەيە لەسەر خرىزكە سورەكان (RBC)، ھيمىزگلىزبىن (Hb)، قەبارەي خانەرەوەكان (PVC)، ريترەي قەبارەي خروچكە سورەكان (MCV)، ريترەي ھيمىزگلىزبىنى خوين لە خرىزكە سورەكان (MCH)و ريترەي بەيتى ھيمىزگلىزبىن خوين لە خرىزكە سورەكان (MCHC).

كەمي و زۆري زينك كاريگەري نيگەتيڤيان ھەيە لەسەر ھۆرمۈني گەشە، كيٚشي گشتي جەستە، كيٚشي ئەندامە جياوەزەكاني و خوراكي بەكاربوو. زورخواردني زينك ئەبيٽتە ھۆي كۆبوونەوەي توخمەكە لە ئيّسك ، جگەر، گورجيلە،مندال دان ،پيّست و سييەكان، لە كاتيْكدا كەم خواردني دەبيّتە ھۆي دابەزيني زينك لە زۆربەي زۆري ئەندامەكان وەك ئيّسك، جگەر،مندالا دان،پيّست ،سپلا ، ميّشك، سييەكان و دلا.