Zinc overdoses and blood biochemistry changes in biological systems

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Abstract
This experimental study shows how zinc overdoses change the concentration of some proteins and enzymes in blood serum in rats. We administrated different doses of zinc: RDIx2 – group E1, and RDIx4 – group E2 (RDI – Recommended Daily Intake) as ZnCl\textsubscript{2} solutions. The excess of zinc modified the blood metabolites in experimental animals (E), increasing the concentration of serum total protein with 6.17\% for E1, 7.66\% for E2; serum globulin with 3.32\% for E1, 4.69\% for E2, and decreasing serum albumin with 22.68\% for E1, 29.38\% for E2 comparing with control animals. Also, most of the analyzed serum enzymes (GPT, GOT, ALP, AMY) levels increased. Concentration of GPT rises with 7.46\% for E1, 21.43\% for E2; GOT increased for E1 with 2.02\% and decreased for E2 with 7.28\%; serum alkaline phosphatase grown with 11.07\% for E1, 52.75\% for E2, and serum amylase also increased with 25.78\% for E1, 32.6\% for E2 comparing to control animals. The study revealed disturbance of nitrogen compounds in rats’ serum after zinc excess, explained by the role of zinc in oxidative stress reactions.

Keywords: zinc excess, proteins, enzymes

1. Introduction
Even zinc is an essential nutrient, sometimes it is possible that this metal to become toxic because of excess intake. Harmful effects of too much zinc ingestion first appear at levels 10-15 times the recommended daily amount for a good health. Overdoses of zinc in human organism rarely can follow food consumption. Generally, zinc intoxication can appear because of the intake, inhalation or medical treatments (such as dietary supplements containing zinc). Short period of time intoxication with low doses of zinc changes the biochemical metabolism, but long term intoxication with zinc cause anemia, reduces copper absorption, decreases the HDL-cholesterol, impairs immune system, and negatively affects the reproduction system and nervous system (King, 2006). Zinc is essential elements in human, animal and plant nutrition. The intake of zinc form food usually does not cause intoxication. But, ingestion of acidic food products or consumption of different beverages from zinc coated containers can intoxicate the human organism and lead to serious metabolic damages. Also, water can be a very common agent of zinc pollution if the pipes for water transport have been coated with zinc against rust. Large amounts of water are used in human, plant and animal diet, so if the water is contaminated with zinc this will enter in trophic chain and will affect all living organisms.

For human organism zinc is essential trace element, and recommended daily doses are 5mg for children and 15mg for adults (Opresko, 1992; Derek, 1995).
Gastrointestinal absorption of zinc varies from 20% to 80%, being dependent by the chemical form, the total amount of zinc from organism, and by zinc intake from the diet. In normal conditions, zinc gastrointestinal absorption is about 20-30% from total zinc intake (Agency for Toxic Substances and Disease Registry – Toxicological profile for Zinc, 1989).

Because of these roles of zinc we need to know how exactly zinc influence the biochemical metabolisms and where is the place where acts.

2. Materials and methods

In this experimental study our work-team analyzed serum concentration of some blood proteins such as: total protein, albumin and globulin, and also some blood enzymes: glutamate pyruvate transaminase (GPT), glutamic-oxaloacetic transaminase (GOT), alkaline phosphatase (ALP) and, serum amylase (AMY) after zinc administration to rats for a short period of time. Experiments were performed on 10 Wistar strain adult rats (females and males) for each group, with an average weight of 100 ± 10g. We used three groups of animals: one control group (C) and two experimental groups (E1 and E2). After anesthesia of the animals with Ketamina (i.m.), a total amount of 1mL ZnCl2 solution/100g body weight (b.w.) was administered by gavage on days 4th and 7th of experiment. To C group we administrated tap water, to those in group E1 – ZnCl2 solution (two times the RDI – zinc for humans, i.e. 0.214mg x 2/b.w.) and to animals in group E2 – ZnCl2 solution (four times the RDI – Zn for humans, i.e. 0.214mg x 4/b.w.) – Derek, 1995.

On the 15th day of experiment, after anesthesia the blood samples were taken from all experimental animals, for biochemical analysis of proteins (total protein, albumin, globulin) and enzymes (GPT, GOT, ALP, AMY) from serum.

The serum samples were analyzed with an automatic biochemistry analyzer “Dimension”, produce by “Dupont”.

The obtained data were statistically preceded and mean values and standard deviations were calculated for each blood metabolite.

3. Results and Discussions

Trace elements are necessary for normal function of cells, and therefore are associated with morbid deficiency states. They are also commonly toxic when present in excess.

After zinc administration as zinc chloride solution to experimental animals from three working groups we analyzed the protein and enzymes concentration from blood serum. Biochemical changes in serum protein concentration are presented in figure 1.

Zinc overdoses alter the protein metabolism in biological systems. Thus, serum total protein and globulin concentration increased with the amount of zinc intake. The values were calculated as mean values and standard deviations (X±DS). After zinc administration, concentration (g/dL) increased for total protein to 5.68±0.45 for E1 group and to 5.76±0.38 for E2 group compare to 5.35±0.42 for animals of C group, and also increased for globulins to 2.38±1.08 for E1 group and to 2.51±0.69 for E2 group compare to 1.94±0.40 for animals of C group. Also, albumin concentration decreased after zinc overdoses to 3.30±0.83 for E1 group and to 3.25±0.31 for E2 animals compare to 3.41±0.23 for control rats. Generally, the total protein and globulin concentration varies with about 3% to 7%, but albumin concentration increased significantly with 22% to about 30%.

Albumin concentration from serum blood is influenced by zinc concentration in the body because parts of zinc ions (ZnII) are bind to serum albumin (Peters, 2008).
Zinc transportation in living organism is possible because of metallothionein protein. This protein is a cysteine rich protein, which can bind three or four zinc ions. Chloride ions are important for some metallothionein forms. Zinc enters into a cell and with thionein forms metallothionein – that carries zinc from a part of a cell to another part as a transportation system.

Different researches demonstrate that high concentration of phytates, calcium or phosphorus decreases zinc absorption and increases serum protein concentration (Opresko, 1992). Thus, after zinc administration concentration for transaminase enzymes increased for GPT to 133.90±45.93 for E₁ group and to 151.30±69.06 for E₂ group compare to 124.60±29.26 for animals of C group. Otherwise, after zinc intake in excess – using gastrointestinal administration (gavage) the concentration of some serum enzymes is modified as presented in figure 2.

Enzymes are proteins and when protein metabolism is altered, the enzymes concentration for cells is modified too. Figure 2 shows very well that after zinc administration in excess, blood serum enzymes concentration increased with zinc doses. The concentration values for enzymes were calculated as mean values and standard deviations ( X±DS) and the measurement unit was U/L.

Various aspects of cellular metabolism are zinc-dependent, because zinc has catalytic, structural, and regulatory role. There are about 100 zinc-dependent enzymes, from all enzymes classes. Zinc has structural role of...
group; and for GOT to 151.20±52.61 for E₁ group and decreased to 137.40±34.50 for E₂ group compare to 148.20±25.41 for animals of C group.

Alkaline phosphatase (ALP) increased after zinc excess to 166.60±49.24 for E₁ group and to 229.12±48.54 for E₂ animals compare to 150.00±20.27 for control rats; and amylase concentration also increased to 688.40±173.06 for E₁ group and to 725.70±45.22 for E₂ animals compare to 547.30±45.86 for control group.

Thus, significantly modification (p<0.01) of serum enzymes concentration were observed for alkaline phosphatase (only in animals from E₂ group) and for both experimental groups in case of amylase.

For GPT and GOT are use more synonyms. GPT is known as glutamic-pyruvic transaminase or glutamic-alanine transferase or alanine aminotransferase (ALAT), and GOT is known as glutamic-oxaloacetate transaminase or aspartate aminotransferase (ASAT).

Red blood cells and white blood cells contain high concentrations of zinc. GPT serum enzymes are associated with liver functions.

But liver is the organ that tries to detoxify the organism in case of intoxication, so after zinc excess liver acts with biochemical mechanisms to increase zinc concentration, modifying the distribution of some blood serum enzymes.

Zinc is component of some enzymes as carbonic anhydrase – which participating to carbon dioxide (Stokinger, 1981). The homeostatic mechanism needs metallothionein protein with decisive role in absorption and excretion of zinc (Bremner, 1987a; Bremner 1987b).

Superoxide dismutase (CuZnSOD) – an antioxidant enzyme, while copper has catalytic activity. Low and excess intake of zinc alter the oxidative metabolism and increases the susceptibility of oxidative cell damages.

Also, zinc is part of different protein or cell membranes structure, and regulates the gene expression – binding to DNA and acting as transcription factors. Zinc is implicated in cell signals that influence hormone release, and play a very important role in apoptosis (Truong-Tran, 2000).

4. Conclusions

Zinc excess administrated in gastrointestinal system for a short period of time modifies the blood biochemistry of proteins and enzymes, to rats used as experimental animals.

Serum protein concentration increased for total protein and globulin in all experimental animals compare to control group.

But, the albumin concentration is little depressed after zinc administration for experimental groups of rats compare to control group.

In case of serum blood enzymes the concentration is higher for about all analyzed enzymes: glutamate pyruvate transaminase (GPT), glutamic-oxaloacetic transaminase (GOT), alkaline phosphatase (ALP) and, serum amylase (AMY) after zinc overdoses.

Thus, concentration of proteins and enzymes from blood serum is also influenced by zinc doses, as can be observed by the concentration of zinc from administrated zinc chloride solution.
References