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DOSE-DEPENDENT ABSORPTION AND RETENTION OF ZINC IN RATS

ABSORPCJA I RETENCJA CYNKU U SZCZURÓW W ZALEŻNOŚCI OD ILOŚCI STOSOWANEJ DAWKI

Abstract: The aim of this study was to evaluate the influence of doses of zinc on its metabolism (absorption and distribution) in the carcass of animals. The examinations involved male Wistar rats divided into two groups. All the rats were given intragastrically for 28 days traces of zinc chloride labeled with radioactive zinc-65. Group I (the controls) fed a standard laboratory diet LSM and tap water containing traces of zinc (0.03 mg/dm^3). Rats in group II were fed as those in group I except for the drinking water that was supplemented with 23.3 mg Zn/dm^3 increasing about twice the dietary zinc intake as compared with that in group I. Radiozinc was measured in the carcass 3 h, 6 h, 1 d, 2 d, 4 d, 7d, 14 d, and 28 d after dosing with the use of scintillation counter equipped with well-type crystal that permitted the detection of radioactivity in the body of tested rats. Results included concentrations of radiozinc in the carcass at the time points which were used to calculate the AUC values. The obtained AUC values permitted the evaluation of carcass retention of zinc within 28 days postdosing. Data indicated that the percentage content of the isotope in group II was lower than that in the controls and differences were statistically significant at 6 h and day 1, 2, 4, and 28. The AUC values showed that the dietary zinc uptake in group II decreased by about 23% as compared with that in group I. The results supported evidence that increased dietary zinc intake results in decreased zinc retention in the body.

Keywords: radiozinc, carcass, distribution, rat

Zinc is generally considered a relatively non-toxic metal [1] although zinc salts in higher concentrations can injure epithelial tissue. In addition, intake of excess zinc has been reported to affect activities of pancreatic enzymes [2] and lipoproteins in serum [3], alter the metabolism of copper [4] and iron [4, 5], and disturb immunological function [6].

Bioavailability of zinc may vary and is influenced by dietary zinc supplements and numerous food constituents [7].

The aim of the present studies was to compare zinc absorption and retention in rats received a non-supplemented diet and a diet comprising a twofold higher zinc concentration.

Material and methods

Ninety male Wistar rats weighing 202 g ± 11 g were used. The animals were randomly assigned into two dietary groups of 45 rats each after an acclimatisation period of one week. Rats in group 1 were offered a standard rodent chow LSM (Fodder Manufacture Motycz, Poland) and tap water containing 0.02 mg zinc/dm^3 *ad libitum.* The total zinc content of the LSM diet was 23.3 mg/kg according to the manufacturer. Rats in group 2 fed the same chow but drank tap water supplemented with 23.3 mg Zn/dm^3. The animals were on these diets for the whole experimental period. Body weight gains and feed and water consumption were recorded weekly during the feeding period.

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Traces of labelled zinc chloride (zinc-65, Polatom, Poland) in a 0.5 mdm^3 water solution comprising about 20 kBq per rat was given daily by an intragastric tube to all rats for 28 days except weekends. Rats were killed by immersion in gaseous carbon dioxide at 3 hr, 6 hr, and day 1, 2, 4, 7, 14, 28 d after dosing. Radiozinc in the carcass (whole body without the stomach and intestines) was measured using a whole-body counter ZM 701 (Polon, Poland). Reference standards for quantification of carcass radiozinc were prepared by intraperitoneal injection of the appropriate solution to rats which were killed 45 min thereafter.

The area under the curves (AUC) of radiozinc content versus time points was calculated by the trapezoidal rule. Data were analysed statistically using Student's *t*-test at $P<0.05$.

Results

Rats in all groups demonstrated similar feed and water intake and the body weigh gain (Tab. 1). Further, the organ to body ratio for the liver, spleen, heart, testes, and kidneys was similar in the two groups examined. The blood values including erythrocytes, haematocrit, haemoglobin, and leukocyte for the two groups of rats were also similar (not shown).

Table 1

Body weight gains and organ to body ratio

Group	Initial weight [g]	Final weight [g]	Liver to body ratio	Kidneys to body ratio	Testes to body ratio	Heart to body ratio
Group 1	205 ± 15	384 ± 20 (87%)	3.89 ± 0.25	0.72 ± 0.07	0.89 ± 0.19	0.29 ± 0.02
Group 2	206 ± 12	374 ± 29% (83%)	4.06 ± 0.34	0.70 ± 0.006	0.88 ± .08	0.28 ± 0.02

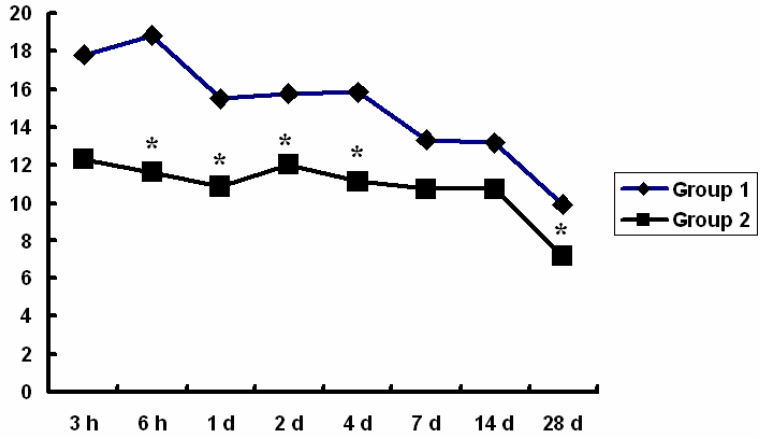

Fig. 1. Zinc content in the carcass (% of total dose), * - $P<0.05$

The time-course distribution of zinc-65 in the carcass within a 28-d period after the exposure is shown in Figure 1. Zinc-65 content in the carcass of rats in group 2 was visibly lower in comparison with that in group 1. Significant differences were found at 6 hr, and on days 1, 2, 4, and 28. The AUC values showing integrated exposure to zinc-65 in group 1

and group 2 were 8324 and 6404, respectively. These values indicated that the percentage absorption of zinc in group 2 was lower by about 23%.

Discussion

No significant alterations in organ to body ratios and body weight gains in the rats exposed to higher dose of zinc suggested that two-fold increase of dietary zinc did not affect unfavourable the health state of animals. It is in agreement with other reports [7, 9] that moderate supplements of zinc may be well tolerated by the organism. The toxic effects of zinc such as depressed rate of growth and feed intake in experimental animals may be produced by markedly higher dietary zinc intakes including doses of hundreds of milligrams per kilogram [10].

In the present studies the intestinal absorption following intragastrical administration for 28 days of traces of zinc-65 chloride to rats exposed to the consumption of adequate and supplemental zinc was compared by carcass radioactivity counting. The results indicate that zinc-65 in the two groups studied accumulated in a similar pattern irrespective of the dose administered. However, the percentage of the dose found in the carcass was significantly lower in the case of supplemental zinc indicating that the relative zinc absorption was reduced with increasing dose. When AUC values for the two groups tested were compared, it was seen that the rate of zinc-65 absorption was reduced by about 23% in rats fed supplemental zinc. On the other hand, the total amount of absorbed zinc was markedly higher in the rats fed supplemental zinc.

There are numerous factors including trace elements, forms of zinc, and several other food constituents that influence the gastrointestinal absorption of zinc [7, 11-14]. However, considering the presented data it seems reasonable that changes in zinc bioavailability are mainly associated with various tested doses of zinc applied.

A dose-dependant bioavailability of zinc was reported by other researches [14, 15] who found that low dietary zinc results in increased zinc retention and that at higher dietary zinc levels absorption of zinc is reduced within an 11-day post dosing period. The results presented here are in accordance with the above findings. Further, the data indicated that a low relative retention of zinc given intragastrically at higher than the recommended level may persist for a longer period in the body.

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Abstrakt: Określono wpływ ilości podawanego cynku na jego metabolizm (przyswajanie i rozmieszczenie) w korpusie zwierząt, którym przed pomiarami usunięto przewód pokarmowy z treścią. W badaniach użyto szczurów samców szczepu Wistar, które podzielono na dwie grupy. W obu grupach podawano dożołądkowo przez 28 dni śladowe ilości chlorku cynku znakowanego radioaktywnym cynkiem-65. Grupę I stanowiły zwierzęta kontrolne karmione standardową paszą LSM i wodą pitną zawierającą śladowe ilości cynku (0,03 mg/dm^3 w Puławach), a grupę II zwierzęta karmione podobnie jak zwierzęta w grupie I z tym, że otrzymywały wodę pitną wzbogaconą w chlorek cynku w stężeniu (23,3 mg/dm^3), odpowiadającym stężeniu tego pierwiastka w podawanej zwierzętom paszy LSM. Radiocynk oznaczano w korpusie 3 h, 6 h, 1 d, 2 d, 4 d, 7 d, 14 d, 28 d po aplikacji za pomocą licznika scyntylacyjnego ze studzienkowym kryształem umożliwiającym pomiar radioaktywności całego ciała badanych zwierząt. Wyniki omówiono, biorąc pod uwagę wartości stężeń radiocynku w badanych przedziałach czasowych, które zastosowano do wyliczania metodą trapezowych pól wartości parametru AUC. Wartość tego parametru pozwoliła ocenić zawartości radiocynku w korpusie w okresie od 3 h do 28 dni po zakończeniu aplikacji. Dane opisujące rozmieszczenie radiocynku w korpusie wskazują, że procentowa zawartość tego izotopu była mniejsza aniżeli w grupie I, a różnice były statystycznie istotne po 6 h, 1 d, 2 d, 4 d i 28 d. Na podstawie obliczonego parametru AUC stwierdzono, że u zwierząt otrzymujących dwukrotnie większą od zalecanej dawki cynku jej procentowe przyswajanie zmniejszyło się o około 23% w porównaniu do odpowiednich wartości uzyskanych w grupie kontrolnej. Otrzymane wyniki potwierdzają wcześniejsze badania sugerujące, że podawanie cynku w ilościach większych od zalecanych powoduje zmniejszone jego przyswajanie.

Słowa kluczowe: radiocynk, korpus, rozmieszczenie, szczur