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Effects of High but Nontoxic Dietary Zinc on Zinc Metabolism and Adaptations in Rats (39072)

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The essentiality of zinc in animal and human nutrition is well established (1–6). Considerable information also is available on zinc metabolism in zinc-deficient animals (3–6). However, the influence of high dietary zinc on zinc metabolism is less well understood. Limited information suggests the possibility of major qualitative differences in metabolism and homeostatic control of zinc between cattle and rats (7–13). In calves a high but nontoxic zinc diet (600 ppm added zinc) resulted in huge increases in zinc content of certain tissues (especially liver and kidney) and major changes in zinc metabolism involving a breakdown of homeostatic control (7, 8, 12). Results of studies with rats suggest, however, that only minor increases in tissue zinc occur from feeding high but nontoxic zinc levels to rats (9–12).

This experiment was designed to investigate the effect of feeding 600 ppm supplemental zinc to rats for 7, 14, 21 or 42 days on zinc and ^{65}Zn metabolism and tissue concentrations. In order to make the results more directly comparable to those obtained earlier with cattle, a diet similar to that used in earlier calf studies was fed (7, 8, 13).

Materials and methods. Forty-three male Cherokee S-D Albino rats, initially weighing 100–120 g, were fed individually (*ad libitum*) for 7 days a basal practical-type (corn, soybean oil meal, cottonseed hulls, plus supplements) control diet containing 53 ppm Zn by analysis (7). Following this, seven rats continued to receive the control diet for 42 more days: other random groups of nine rats each were changed from the control diet to the zinc supplemental diet (control diet with 600 ppm added zinc as ZnO) beginning 7, 14, 21, or 42 days before sacrifice at the end of the 49-day experiment.

Seven days prior to sacrifice each rat was given by gavage an oral tracer dose of 4.0 μCi $^{65}ZnCl_2$ in acetate buffer (specific activity of 2.1 m Ci/mg Zn). After dosing, total fecal collections were made for a period of 7 days. At this time, each rat was anesthetized with ethyl ether, sacrificed by exsanguination, and the following tissues taken for analyses: blood, heart, liver, kidney, semitendinosus muscle, left tibia, and small intestine (first 15 cm). The small intestine was cut open lengthwise and contents removed by washing with physiological saline.

Feed, fecal, and tissue Zn were determined by atomic absorption spectrophotometry following nitric–perchloric–sulfuric acid wet ashing of samples (14). The ^{65}Zn analyses were made with an automatic gamma ray test tube changer system with a NaI (TI) well crystal.[1] Because of nonhomogeneity of variance (due to large differences in mean values) among treatment means, ^{65}Zn data were transformed to common logarithms before testing by analysis of variance and Duncan's Multiple Range Test.

Results. Rats fed 600 ppm supplemental zinc excreted significantly ($P < .05$) more stable zinc via feces than the controls but the length of time they were fed the high dietary zinc had little or no effect (Fig. 1A). In contrast, total fecal ^{65}Zn excretion increased with each increase in time on the high zinc diet (Fig. 1B). The values ranged from 77% of the dose by controls to 97% by rats fed the high zinc for 42 days (Fig. 1B).

Feeding 600 ppm supplemental zinc did not materially affect the stable zinc in any tissue studied (Table I). However, in every tissue, ^{65}Zn declined sharply with duration of time to 21 days on the high zinc diet with little change from 21 to 42 days (Table II). Although ^{65}Zn levels varied widely among tissues at each length of feeding time, the

[1] Model 709, Baird Atomic, Cambridge, Mass.

relative magnitude in effects of the high zinc diet were remarkably similar in all soft tissues; even in the tibia the effect was not drastically different.

Discussion. Comparison of these results with those from earlier calf studies (7, 8, 13) indicates major qualitative differences in zinc metabolism between rats and cattle. The absence of any material influence of the high zinc (600 ppm supplemental) diet on tissue stable zinc in the rat is in sharp contrast to huge increases observed in calves fed a comparable high zinc diet (7, 8, 13). For example, with calves liver zinc increased about 700% when 600 ppm added zinc was fed (7, 8). Failure of tissue zinc to increase when the high zinc diet was fed to rats indicates that homeostatic control of tissue zinc is far more effective in rats than in cattle. Whether the breakdown in homeostatic control of zinc which occurs in cattle at the 600 ppm level of supplemental zinc might take place if a higher dietary zinc level were fed to rats has not been established.

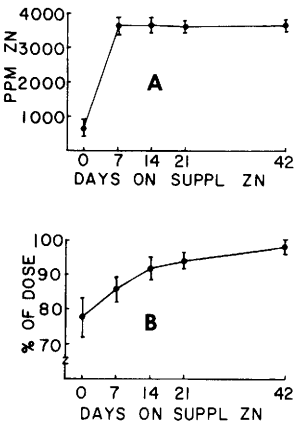

FIG. 1. Effect of feeding 600 ppm supplemental zinc for 7, 14, 21, or 42 days on 7-day total fecal excretion of: (A) stable zinc; and (B) ^{65}Zn.

The rapidly decreasing percentage of the ^{65}Zn dose retained in the various tissues and the increased fecal excretion with increased duration of supplemental zinc indicates that adaptations in zinc metabolism of rats continue for some 3 weeks after initiation of 600 ppm supplemental zinc. The fecal ^{65}Zn excretion data (Fig. 1B) suggested that adaptation in percentage of zinc absorption by the rat continued for most or all of the 42 days after initiation of the high zinc diet. In contrast, similar data from calves suggested little or no adjustment in absorption beyond 7–14 days (13).

Whereas increasing the length of time during which the 600 ppm supplemental zinc was fed had a similar relative effect on ^{65}Zn in every soft tissue studied in rats (Table II), vastly different effects were observed among these tissues in calves (13). Very limited data with dogs and cats (15–17) suggest that these species may be more

TABLE I. TISSUE STABLE ZINC CONCENTRATION AS AFFECTED BY DURATION OF FEEDING 600 ppm SUPPLEMENTAL ZINC.

Tissues	600 ppm Zinc Fed For[a]					SE[b]
	0 day (control)	7 days	14 days	21 days	42 days	
	μg zinc/g dry tissue					
Heart	68[c]	70[c]	65[c]	63[c]	66[c]	23
Liver	84[c]	88[c, d]	90[c, d]	98[d]	93[c, d]	5
Kidneys	72[c]	78[c]	72[c]	72[c]	75[c]	4
Muscle (round)	41[c]	36[c]	35[c]	42[c]	40[c]	14
Tibia	177[c]	192[c]	187[c]	191[c]	208[c]	70
SI[e]	93[c]	111[c]	126[c]	128[c]	108[c]	44

[a] Nine rats per treatment except control, which had seven.

[b] Standard error of treatment means.

[c, d] Values not followed in the same horizontal line by same letter are significantly different ($P < .05$) by analyses of variance and Duncan's Multiple Range Test analyses.

[e] First 15 cm of small intestine.

TABLE II. ^{65}Zn Distribution as Affected by Duration of Feeding 600 ppm Supplemental Zinc.

Tissues	600 ppm Zinc Fed For[a]				
	0 days (control)	7 days	14 days	21 days	42 days
	% dose/kg fresh tissue				
Blood, whole	28.6 ± 7.3[b]	14.7 ± 4.8[c]	7.2 ± 1.9[cd]	4.6 ± 1.2[d]	4.5 ± 1.0[d]
Heart	82.6 ± 21.2[b]	44.2 ± 14.4[c]	22.5 ± 6.5[cd]	12.0 ± 4.5[d]	10.1 ± 3.0[d]
Liver	133.1 ± 36.3[b]	70.3 ± 17.8[c]	37.7 ± 9.0[cd]	24.2 ± 5.4[d]	21.8 ± 4.0[d]
Kidneys	102.5 ± 28.4[b]	50.3 ± 16.8[c]	27.3 ± 7.2[c]	17.0 ± 4.5[c]	18.7 ± 5.3[c]
Muscle (round)	52.8 ± 13.9[b]	27.8 ± 8.8[bc]	16.6 ± 4.0[c]	8.8 ± 2.7[c]	8.4 ± 1.9[c]
Tibia	294.2 ± 42.1[b]	223.4 ± 79.7[bc]	117.0 ± 28.6[bc]	64.2 ± 14.5[cd]	52.5 ± 16.3[d]
SI[e]	100.0 ± 28.3[b]	47.5 ± 15.7[c]	27.1 ± 6.6[c]	12.2 ± 2.6[c]	11.9 ± 2.7[c]

[a] Values are mean ± SE for nine rats in all treatments except control which has seven rats.

[b, c, d] Values not followed in the same horizontal line by the same letter are significantly different ($P < .05$) as determined by analyses of variance of data transformed to common logarithms.

[e] First 15 cm of small intestine.

similar to cattle than to rats in their response to high zinc feeding.

The major qualitative differences observed between rats and cattle in the metabolism, tissue accumulation and distribution of zinc indicate different biochemical mechanism(s). However, further research will be needed to define the nature of these biochemical differences, both in absorption and within body tissues.

Summary. The effects of feeding a high but nontoxic zinc level to young rats for varied time periods on zinc metabolism and adaptations were investigated. Adding 600 ppm supplemental zinc to a "corn–soy" diet for periods from 7 to 42 days did not materially affect stable zinc level in any tissue studied. However, in every tissue, ^{65}Zn retention from a single oral dose declined sharply with duration of added zinc feeding to 21 days, indicating a continuing adaptation in zinc metabolism for at least this period of time. Likewise, fecal ^{65}Zn excretion increased with length of feeding time on high zinc, indicating a continuing reduction in net absorption for most of the 42-day period. When the data are compared with similar previous cattle studies, it is evident that there are major qualitative differences in zinc metabolism and homeostatic control between rats and cattle.

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