Arh. hig. rada, *23* (1972) 209.

OXYTETRACYCLINE ADDITIVES TO THE DIET IN RELATION TO STRONTIUM METABOLISM IN RATS

NEVENKA GRUDEN

Institute for Medical Research, Yugoslav Academy of Sciences and Arts, Zagreb

(Received for publication October 10, 1972)

The metabolism of radiostrontium was studied in female albino rats fed a diet with oxytetracycline additives for six months (0,3 g of calcium oxytetracycline per 100 g dried food). No difference was observed in absorption, skeletal retention and urinary excretion of strontium-85 between the control group of animals and the rats fed the diet with oxytetracycline additives.

There are few and controversial data about the influence of tetracycline on strontium metabolism. *Ogawa* et al. (1961)[1] noticed that tetracycline administered immediately after radiostrontium reduces the skeletal deposition of the latter and enhances its urinary excretion. *Richards* et al. (1963)[2] on the contrary, reported that repeated doses of tetracyclines did not affect the initial deposition of radiostrontium, but accelerated its elimination from the bone. Two years later *Catsch* (1963)[3] showed that significantly reduced deposition of radiostrontium was achieved by tetracycline but only if given prior to an injection of strontium-85. Neither the post-treatment nor the simultaneous administration of tetracycline gave rise to a reduced skeletal retention of strontium-85. In 1971 *Gudmundson*[4] reported that the 24-hr uptake of tracer doses of strontium-85 in the fracture callus was not significantly affected by the oxytetracycline therapy.

In view of these former approaches we considered it useful to look into the effect of a prolonged addition of tetracyclines to the rat food with special regard to strontium metabolism.

METHODS

Female albino rats 6 weeks old, weighing 100–110 g were used. The animals were divided into two groups: the control group received the standard rat food, while the experimental group ate the same food

supplemented with 0.3 per cent calcium oxytetracycline (OTC). Every fourth week (during 24 weeks of the experiment) 7–10 animals were taken from each of the two groups and isolated in individual metabolic cages for 72 hours. These animals received 0.2 μCi strontium-85 per 10 ml of drinking water during 48 hours. The last 24 hours the animals drank distilled water and were then sacrificed by an overdose of ether. Strontium-85 activity was determined in ashed and dissolved carcass and in three-day urine samples in a well-type scintilation counter connected to a single-channel analyser.

RESULTS

On the average, an animal from the control group consumed 15.2 g food per day and from the experimental group 16.1 g per day. The animals that had received OTC in food were somewhat heavier throughout the experiment (the mean body weight of controls was 224 g, and of experimental animals 242.5 g at the end of experiment).

Table 1 shows the percentage radioactive strontium retention in the carcass of control and experimental animals in the course of the experiment. The retention was practically the same for both groups. It was higher in the initial stages, which is due to the dependence of strontium metabolism on age.

Table 1

*Strontium retention in the carcass**

Duration of experiment (weeks)	Age of animals (weeks)	Percentage of ^{85}Sr in the carcass of animals fed on	
		Control food**	Experimental food**
0	6	9.10 ± 0.30***	
4	10	5.00 ± 0.10	5.40 ± 0.10
8	14	2.97 ± 0.08	3.19 ± 0.10
12	18	3.61 ± 0.24	2.81 ± 0.21
16	22	2.48 ± 0.17	2.59 ± 0.08
20	26	2.53 ± 0.14	2.19 ± 0.11
24	30	2.28 ± 0.12	2.42 ± 0.24

* All the results here and in the following tables are expressed as arithmetic means with standard error for groups of 8–10 animals.

** See text for details.

*** »Group 0«. Animals isolated in individual metabolic cages at the beginning of the experiment. The same parameters were determined as for other groups during the experiment.

Table 2 shows the percentage radioactive strontium elimination in the urine for both groups of animals. The differences between the groups are not significant.

Table 2

Radiostrontium in the urine

Duration of experiment (weeks)	Percentage of ^{85}Sr in the urine of animals fed on	
	Control food*	Experimental food*
0	2.76 ± 0.12	
4	1.74 ± 0.07	1.71 ± 0.04
8	1.61 ± 0.24	2.49 ± 0.33
12	2.07 ± 0.15	2.33 ± 0.24
16	2.25 ± 0.21	2.28 ± 0.16
20	2.38 ± 0.28	2.35 ± 0.15
24	2.34 ± 0.23	2.22 ± 0.19

* See text for details.

The apparent absorption of radioactive strontium is shown in Table 3, as the sum of the percentage retention in the carcass and the elimination by urine (the endogenous faecal secretion was neglected in these calculations). Again, there was no difference between the groups.

Table 3

Absorption of radiostrontium from the intestinal tract

Duration of experiment (weeks)	Percentage of ^{85}Sr absorption for animals fed on*	
	Control food**	Experimental food**
0	11.86 ± 0.52	
4	6.74 ± 0.40	7.11 ± 0.32
8	4.58 ± 0.28	5.68 ± 0.38
12	5.68 ± 0.56	5.14 ± 0.30
16	4.73 ± 0.48	4.87 ± 0.29
20	4.91 ± 0.42	4.54 ± 0.35
24	4.62 ± 0.38	4.64 ± 0.34

* Expressed as sum of the percentage radioactive strontium in carcass and urine.

** See text for details.

DISCUSSION

The data in the literature about the interrelationship of tetracyclines with calcified tissues are extensive but controversial. Some authors believe that the controversy could be explained by the chemical differences of tetracyclines, the administered dose and animals'age (6–8).

The animals in own experiments were in the stage of intensive development and growth of the skeleton. We expected a stronger interaction of tetracycline and strontium under prolonged administration. Although our animals received tetracycline in doses that were much higher than the therapeutic ones (animals sacrificed at the end of the experiment received altogether about 9 g Ca OTC, i. e. about 54 g/kg body weight, while daily doses were about 300 mg/kg) there was no change in strontium metabolism. Neither was there any change in calcium metabolism (5) under the same experimental conditions.

The fact that among four »classic« tetracyclines (tetracycline, chlortetracycline, demethyltetracycline and oxytetracycline) OTC is the one which is least concentrated in bone (and may therefore also be less toxic to the skeleton) probably explains our findings (9).

References

1. *Ogawa, E., Fakuda, R., Suzuki, S., Shibata, K., Gunma, J.:* Med. Sci., *10* (1961) 117.
2. *Richards, U., Lowenstein, J. M., Philips, J. W., Armitage, C.:* Proc. Soc. exp. Biol. Med., *107* (1961) 550.
3. *Catsch, A.:* Nature, *197* (1963) 302.
4. *Gudmundson, C. J.:* Trauma, *11* (1971) 511.
5. *Gruden, N.:* Habilitacijski rad, Medicinski fakultet Sveučilišta u Zagrebu, 1971.
6. *Saxen, L.:* Science, *153* (1966) 1384.
7. *Frost, H. M.:* Canad. J. Biochem. Physiol., *41* (1963) 31.
8. *Löfgren, C. G., Omnell, K. A., Nylen, M. U.:* Calc. Tiss. Res., *2* (1968) 145.
9. *Ibsen, K. H., Urist, M. R.:* Clin. Orthop., *32* (1964) 143.

ACKNOWLEDGEMENT

My special thanks are due to Professor Krista Kostial for her advice during the preparation of the manuscript and in the course of this study. I also thank Mrs. Mirka Buben, Marica Landeka, Suzana Luzar, Katica Pribanić and Marija Vnučec for their valuable technical assistance.

Sažetak

UTJECAJ HRANE S DODATKOM OKSITETRACIKLINA NA METABOLIZAM STRONCIJA U ŠTAKORA

Ispitivali smo metabolizam stroncija u ženki bijelog štakora koje su u toku 6 mjeseci primale hranu s dodatkom kalcijeve soli oksitetraciklina (0,3 g/100 g suhe hrane). Rezultati su pokazali da nema razlike u apsorpciji, skeletnoj retenciji i urinskoj eliminaciji stroncija-85 između štakora koji su primali OTC hranom i kontrolne skupine životinja.

Primljeno 10. X 1972.

Institut za medicinska istraživanja i medicinu rada J. A. Z. U., Zagreb