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CADMIUM-CALCIUM INTERRELATIONSHIP IN RAT'S DUODENUM

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The active transduodenal transfer of calcium has been studied in five-week old female rats pretreated orally with various doses of cadmium chloride. The transfer was determined on 8th or 15th day by the »everted gut sac« method with calcium-45 as a tracer. Within the range of cadmium doses used, calcium-45 transfer did not change to any significant degree, while its retention in the duodenal wall increased when 0.2 mg of cadmium was given to rats for one week, or when they received 15 mg cadmium divided in two doses.

Cadmium, a common pollutant in air and surface water, tends to accumulate in the liver and kidneys impairing their function (1—3). The role of kidneys and liver in vitamin D hydroxylation (4, 5) as well as the important role this vitamin plays in the active transfer of calcium through the intestinal wall is well known. It is not known, however, whether vitamin D hydroxylation and consequently calcium metabolism is impaired by cadmium.

The aim of this work was to determine whether the *active* calcium transport is altered under the influence of cadmium as it was observed for the *total* transduodenal calcium transfer in rats treated with various cadmium doses (6). The term active transport is common in this type of studies, when a solution of radiocalcium is placed on both sides of the intestinal wall and the change in its concentration is measured for both compartments. The term does not, therefore, refer to any specific gradient against which radiocalcium is transferred, though the chemical gradient may be most probable.

METHODS

Sixty-three five-week old female albino rats from a strain raised in this Institute were used. The body weights ranged from 90 to 120 g. The food was the standard laboratory rat diet (1.1% Ca, 0.65% P). The animals received daily various doses of cadmium chloride (Table 1) by gastric intubation during a week or a fortnight. The day after the last dose the animals were killed and their duodenum was processed according to the everted gut sac method (7). Intestinal segments were incubated in 2.5 ml of buffer solution. The composition of the medium was as follows: 135 mM NaCl, 11 mM KCl, 0.05 mM $CaCl_2$ and 10 mM sodium phosphate buffer pH 7.4. For each milliliter of this solution 0.1 μC of carrier-free $^{45}CaCl_2$ (S. A. 5.02 μCi ^{45}Ca/mg) was added. Inside the everted sac was 0.6 ml of this solution. Hence, in these experiments radioactive calcium was on both sides of the gut sac, so that if S/M ratio differed from unity it means that radiocalcium travelled against a chemical gradient. The procedure has been described in detail elsewhere (6, 8).

Table 1.

Active transport of ^{45}Ca through the duodenal wall and its retention in the wall in rats (see Methods) treated with different doses of cadmium during 7 or 14 days

Cd/rat/day (mg)	Number of rats	$\bar{x}$ S/M ± $SE_{\bar{x}}$[a]	^{45}Ca content in[b] the gut wall
0	20	3.87 ± 0.35	32.20 ± 1.16
0.2	9	4.15 ± 0.16	35.94 ± 0.57
2.0	10	2.86 ± 0.46	31.97 ± 3.08
2.0[d]	14	2.99 ± 0.24	33.32 ± 1.68
15.0[c]	12	4.19 ± 0.35	35.38 ± 1.34

[a]Mean ratio and ± SEX of the serosal (S) and mucosal (M) activity at the end of incubation period.

[b]Percents of initial mucosal plus serosal activity.

[c]Rats were given cadmium for 2 day: 10 mg Cd the first, 5 mg Cd the second day. They were killed 6 days later. All other groups of animals were given cadmium for 7 or 14 (d) days and were killed on 8th or 15th (d) day.

RESULTS AND DISCUSSION

Within the range of the doses of cadmium which otherwise significantly change the total calcium transport (6), cadmium did not influence the active calcium transport to any significant extent (Table 1).

This confirms our previous suggestion (6) that the observed alterations of ^{45}Ca S/M-ratios for the total calcium transport in cadmium treated animals are in fact due to changes in the passive transport only.

While in the present study no influence of cadmium upon the active calcium transport was observed, the retention of calcium was somewhat higher when 0.2 mg of cadmium was given during a week ($P < 0.05$), or when 15 mg of cadmium was divided in two doses ($P < 0.05$). However, we feel that undue importance should not be attached to these figures: firstly, because a change in calcium retention after only one dose of 0.2 mg cadmium is very unlikely and secondly, because calcium retention after the 15 mg cadmium dose is considerably less significant than the corresponding one in (6), where it was $0.01 > P > 0.001$. Besides, the apparent increase in calcium retention is not accompanied by increase in the transfer (S/M). In (6) both parameters were very significantly diminished for the 15 mg cadmium dose. We are not aware of any possible source of experimental error, the gut sac having been thoroughly blotted by filter-paper before calcium-45 activity was measured.

The conclusion is that 15 mg of cadmium in two doses diminishes only the passive calcium transport and its corresponding retention, leaving unchanged both of these parameters in the active transport. The most probable explanation (6) is that cadmium, like lead (8), affects the mechanism of passive calcium transport by altering the membrane permeability. This might be due to the cadmium binding to a low molecular weight protein in the intestinal mucosa, which renders the metal unavailable for transport to the blood. The active transport route of calcium is apparently unaffected by cadmium under our experimental conditions.

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Sažetak

INTERAKCIJA KADMIJA I KALCIJA U DUODENUMU ŠTAKORA

Pet tjedana stare ženke bijelog štakora našeg uzgoja primale su tijekom 7 ili 14 dana svakodnevno različite doze kadmijevog klorida želučanom sondom. Osmog ili petnaestog dana ispitivali smo metodom »izvrnute crijevne vreće« kretanje kalcija-45 kroz stijenku duodenuma. Doze kadmija koje smo mi koristili nisu značajno mijenjale aktivni transport kalcija-45; zadržavanje radiokalcija u stijenci duodenuma bilo je značajno veće u životinja koje su primile ili 7 puta po 0,2 mg kadmija ili 15 mg kadmija podijeljeno u dvije doze.

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