Endocrine Control of the Intestinal Calcium Excretion*

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Synopsis

Calcium excretion from rat intestine was measured by placing distilled water in an intestinal loop in situ and measuring the calcium content after various intervals. More calcium was excreted from the intestine of 18-month-old rats than that of 1-month-old rat. Acute hypocalcemia failed to change the intestinal calcium excretion significantly. Parathyroidectomy decreased intestinal calcium excretion and administration of Parathyroid Extract reversed it. Renal damage produced by injection of Na-sulfacetethylthiazole increased the intestinal calcium excretion but dihydrotachysterol reversed it. Gastrin at 200 µg/kg increased the intestinal calcium excretion. Calcium excretion, like calcium absorption, appears to be controlled by various endocrine factors and the method of intestinal loop in situ appears to be useful to study the part played by these factors.

Though numerous studies have already been carried out on the intestinal calcium absorption, only a small number of reports are yet available on the intestinal calcium excretion, probably because of the difficulty of the accurate measurement of calcium excretion as a part of the complex in- and outward movement of calcium across the intestinal wall. Since the method of the intestinal loop in situ provided a convenient method for the measurement of calcium absorption (Fujita, 1973), attempts were made to utilize a similar method to measure the intestinal calcium excretion though placing distilled water in the loop instead of the calcium solution.

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Fig. 1. The method of measurement of calcium excretion from the intestinal loop in situ. Since the initial content of the loop, distilled water, contains practically no calcium, any calcium found in the final content may be regarded as calcium excreted into the loop during the interval.

20 mg/kg EDTA/Na₂. Parathyroidectomy was performed by cautery under ether anesthesia 24 hours prior to the experiment. Parathyroid Extract (Lilly), 100 USP units per kg, was injected subcutaneously 4 hours prior to the experiment. Sodium sulfacetil-thiazole (SAT), 0.5 g/kg, was injected intraperitoneally as 5% aqueous solution 24 hours prior to the experiment to produce renal damage. Dihydro-tachysterol, 1 mg/kg, was administered orally via a stomach tube for 3 consecutive days prior to the experiment. Tetragastrin, 50-200 µg/kg body weight, was injected subcutaneously 1 hour prior to the experiment. Serum calcium was 7.8±0.2 mg/dl after parathyroidectomy, 8.6±0.2 mg after parathyroidectomy and administration of 100 USP units Parathyroid Extract, 8.4±0.3 mg/dl after SAT, 9.2±0.3 mg after SAT+DHT, and 9.6±0.2 mg/dl after DHT (Mean±SEM).

Results

As shown in Fig. 2, the intestinal calcium excretion increased along with the time course. The increase was much more pronounced, 5 times after 15 min and more than 10 times after 30 min, in older rats of 18 months of age than in the younger ones of one month of age, even if the difference in the intestinal surface, 3-5 times as large in the older ones than in the younger ones, probably parallel to the body surface area, is taken into consideration. Rats of 2 months of age were used in all the subsequent experiments. No significant difference was seen in serum calcium between the two groups. Acute hypercalcemia tended to increase the intestinal calcium excretion and hypocalcemia to decrease it as shown in Fig. 3, although no significant difference from the control was demonstrated in either case. As shown in Fig. 4, parathyroidectomy 24 hours prior to the experiment significantly decreased serum calcium and intestinal calcium excretion, but an injection of 100 USP units/kg Parathyroid Extract 4 hours prior to the experiment prevented such decrease. As shown in Fig. 5, renal injury induced by

Fig. 2. The total calcium excretion from the intestine of 18-month-old rats (dark circle) (5 animals in each group, Mean±SEM) and that from the intestine of 1-month-old rats (5 animals in each group, Mean±SEM).

Fig. 3. Effect of hyper- and hypocalcemia on intestinal calcium excretion. Each group consisted of 5 animals (Mean±SEM). Neither the hypercalcemia nor the hypocalcemia group showed a significant difference from the control group.

Fig. 4. Ca Excretion, µg/hr.

Control
Hypercalcemia (Ca-Injection)
Hypocalcemia (EDTA-Injection)
single intraperitoneal injection of 0.5 g/kg sodium sulfacetylthiazole (SAT) 24 hours prior to the experiment resulted in a significant increase of intestinal calcium excretion (Ohata et al., 1971; Okano et al., 1971), but no significant change of serum calcium. Dihydrotachysterol, 1 mg/kg for 3 days, did not by itself cause a significant change of intestinal calcium excretion, but significantly suppressed the rise of intestinal calcium excretion caused by SAT-induced renal injury and increased serum calcium probably due to the increase of calcium absorption. As shown in Fig. 6, 200 μg/kg of tetragastrin significantly increased the intestinal calcium excretion, but no significant change occurred in serum calcium.

**Discussion**

The study on the excretion of calcium from the intestine is as important as that on the calcium absorption, since the balance of intestinal calcium excretion and absorption determines the net calcium intake. The present method placing distilled water in rat intestinal loop in situ after shutting of the inflow of bile and pancreatic juice measures the net calcium excretion from the intestine, since no calcium is contained in the distilled water in the beginning and all the calcium contained in the loop at the end of the experiment represents the excretion from the intestine, though some of the calcium once excreted might have been absorbed again. The calcium content of the loop increased as time went on, suggesting that the process of intestinal calcium excretion is a progressive one and more calcium is apparently excreted from 18-month-old rat’s intestine than that of one-month-old rat, even if the difference in the intestinal mucosal surface is taken into consideration. The intestinal calcium excretion is apparently not a simple reflection of serum calcium level, since no

![Fig. 4. Effect of parathyroidectomy and parathyroid extract on intestinal calcium excretion. PTX: parathyroidectomized animals. PTX+PTH: Parathyroidectomized animals given Parathryoid Extract. Each group contains 5 animals and mean and SEM is shown by a bracket.](image)

![Fig. 5. Effect of renal injury by Na-sulfacetylthiazol (SAT), dihydrotachysterol (DHT) and SAT and DHT on the intestinal calcium excretion. Each group contains 5 animals and mean±SEM is shown. Significant difference was found between the control and SAT group (P<0.01).](image)

![Fig. 6. Effect of tetragastrin on the intestinal calcium excretion. Each group contains 5 animals and mean and SEM is shown.](image)
significant changes were found in the intestinal calcium excretion in hyper- and hypocalcemia and the intestinal calcium excretion actually decreased while serum calcium rose in response to administration of dihydrotachysterol in rats with renal injury. The decrease of intestinal calcium excretion following parathyroidectomy is probably due to the loss of the action of parathyroid hormone itself facilitating calcium exchange through the intestinal wall, probably mediated by renal 1-hydroxylation of vitamin D, rather than hypocalcemia in the light of the above experiment. Though parathyroid hormone is known to increase the intestinal calcium absorption through enhancement of the renal 1-hydroxylation of vitamin D, the details of calcium transport across the intestinal wall has not been analyzed and the decrease of intestinal calcium excretion might play a part in the known action of parathyroid hormone and vitamin D derivatives (Rasmussen, 1959; Harrison and Harrison, 1965; DeLuca, 1971). The action of dihydrotachysterol, an analogue of vitamin D without the need for activation by the kidney, to decrease intestinal calcium excretion might also partially reflect the increase of calcium absorption. Thus the intestinal calcium excretion and absorption are still not clearly separated. Younoszai and Schedl (1972) demonstrated a decrease of 45Ca flux into the lumen of perfused intestinal segment of rat by the action of vitamin D. Tetragastrin which was shown to increase calcium absorption (Fujita 1973) apparently increased calcium excretion as well. Since gastrin is a known secretagogue for calcitonin, such action might be mediated by calcitonin, though no effect of calcitonin on intestinal calcium excretion has been reported.

Calcium excretion from rat ileum has been studied by Walling and Kimberg (1973), who reported the active secretion of calcium by rat ileum and jejunum in vitro. The ileal calcium-secretory process was not saturable over a range of calcium concentration from 0.112 to 11.2 mM. The ileum of rats maintained on high calcium diet actively secreted calcium while the ileum of rats fed low calcium diet did not.

References