Calcium Metabolism in Diabetes Mellitus

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Summary Calcium metabolism was studied in patients with diabetes mellitus. Information on the dietary intake of major nutrients was gathered from 23 non-insulin-dependent diabetic patients, 42 insulin-dependent diabetic patients and 245 nondiabetic patients under hemodialysis through a questionnaire. A calcium absorption test was performed, using an isotopic technique, in 11 non-insulin-dependent diabetic patients and 4 age-matched healthy subjects. Parathyroid function was examined, using oral phosphate loading, in 6 diabetic patients and 6 age-matched control subjects. The daily dietary intake of calcium in the non-insulin-dependent diabetic patients (602±52 mg) was up to the average daily nutritional requirement (600 mg). The calcium absorption rate in these patients (54.4±13.9 %) was similar to that in the healthy subjects (50.1±5.4 %). The response of parathyroid hormone to phosphate loading was significantly reduced in the diabetic patients compared to the control subjects. The results suggest that calcium homeostasis in diabetic patients with normal renal function is almost conserved, despite the decreased response of parathyroid hormone to phosphate loading.

Key Words calcium intake, calcium absorption, parathyroid function, oral phosphate load, diabetes mellitus

A series of reports suggests the existence of altered calcium metabolism in diabetes mellitus (1,2). Calcium homeostasis is disturbed in animal models of diabetes mellitus, nevertheless the effects of diabetes mellitus on calcium metabolism in humans are controversial. Although some authors have found no significant alterations, apart from excessive urinary losses of calcium and phosphate (3), increased calcium absorption has been found after oral calcium loading in insulin-dependent diabetes mellitus (4), and slightly higher levels of total serum calcium have been found in non-insulin-dependent diabetes mellitus patients than in normal subjects (5). On the other hand, it is well known that the incidence of secondary hyperparathyroidism and bone loss is reduced in diabetic

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dialyzed patients (6,7). The aim of the present investigation was to examine whether alterations in calcium metabolism and parathyroid function occurred in diabetes mellitus before the onset of diabetic nephropathy.

METHODS

Investigation of daily dietary intake of major nutrients. Twenty-three non-insulin-dependent diabetic patients, 42 insulin-dependent diabetic patients under hemodialysis, and 245 nondiabetic patients under hemodialysis were questioned about their daily dietary intake of major nutrients (calory content and amounts of protein, fat, calcium, and phosphate).

Intestinal absorption of calcium. Eleven patients with non-insulin-dependent diabetes mellitus and 4 age-matched healthy controls were studied. The intestinal calcium absorption rate was measured, using an isotope technique. After an overnight fast, 5 μCi sterile 47Ca was given iv on the first day and 10 μCi 47Ca was given orally in 200 mg carrier on the second day. Radioactivity in the forearm and whole body was counted every day, from the second to the fourth day. The calcium absorption rate was calculated from the radioactivity according to the formula shown in Table 1.

Parathyroid function test. Oral phosphate loading was performed in 6 patients with diabetes mellitus and 6 age-matched control subjects. None of the subjects had renal failure (serum creatinine < 1.5 mg/dl). Each took sodium phosphate (total of 2g of oral phosphate daily) at 8 a.m. and 8 p.m. Blood samples for the measurement of ionized calcium and intact PTH were obtained daily, before and two hours after the morning administration of phosphate.

Laboratory methods. We measured total calcium enzymatically and phosphorus colorimetrically, ionized calcium was measured by an ion-specific electrode methods, m-PTH by radioimmunoassay, and intact PTH by a sandwich method utilizing an amino- and carboxyl-terminal specific immunoradiometric assay.

Statistical analysis. All results were expressed as means±SEM. The data were analyzed by Student’s t-test and analysis of variance. P values < 0.05 were considered significant.

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<th>Table 1. Calcium absorption test.</th>
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Calcium absorption rate = 100 · |(A2-B2)/(A1-B1)-(A3-B3)/(A2-B2)| ·IV/PO
RESULTS

The daily dietary intake of major nutrients is shown in Table 2. The daily dietary
intake of calcium in patients with non-insulin-dependent diabetes mellitus (602±52 mg/day) was up to the average of the daily nutritional requirement (600 mg/day), while that in the non-diabetic patients under hemodialysis was below the average. Serum phosphorus was significantly decreased in patients taking more than 602 mg/day of calcium compared to those taking less than 602 mg/day of calcium. Serum m-PTH was slightly decreased in those patients taking more than 602 mg/day of calcium. The ratio of urinary calcium to creatinine was slightly increased and %TRP was slightly decreased in all patients (Table 3).

The calcium absorption rate in patients with non-insulin-dependent diabetes mellitus (54.4±13.9%) was normal, similar to that in the healthy controls (50.1±5.4%)(Fig.1).

In the face of a similar rise in the serum phosphorus and fall in the blood ionized calcium the response of serum intact-PTH to oral phosphate loading was significantly lower in the diabetic group than in the control group (Fig.2).

**DISCUSSION**

Loss of bone mass has been observed in both experimental (8) and insulin-dependent diabetes (9) but the issue is controversial in non-insulin-dependent diabetic patients; the etiology and pathophysiology of diabetic osteopenia are still unclear. One hypothesis of the etiology of diabetic osteopenia is that calcium and vitamin D metabolism is altered in diabetes (10). On the other hand, Heath et al. (11) showed no derangement of calcium metabolism in adults with insulin-requiring diabetes, regardless of their treatment status, and, besides, McNair et al. (3) confirmed that serum calcium, phosphorus and PTH were
not markedly altered from normal in a large group of poorly controlled insulin-requiring diabetics who had massive glucosuria and small increases of urinary calcium excretion. In this current study, non-insulin-dependent diabetic patients had no remarkable abnormalities of calcium metabolism. A slight increase of the ratio of urinary calcium to creatinine seems to indicate increased bone absorption in diabetic patients. We found that the small increase of urinary calcium excretion must not have been sufficient to perturb serum calcium and PTH and to affect intestinal absorption of calcium. The possibility remains that a subtle calcium metabolic abnormality might be demonstrable in some diabetic patients.

Morii et al. (6) reported fewer bone changes in dialyzed diabetic patients than in dialyzed non-diabetic patients with chronic glomerulonephritis; this could be due to the lower concentration of carboxyl terminal region PTH in the blood. It has recently been demonstrated that secondary hyperparathyroidism developed more slowly in dialyzed diabetic patients than in dialyzed patients without diabetes mellitus (7). Therefore, we tested the hypothesis that latent hypoparathyroidism might be found in diabetic patients before the onset of diabetic nephropathy. The response of parathyroid hormone to oral phosphate loading was reduced in diabetic patients with normal renal function compared to control subjects. We confirmed the results of a previous study in which no secondary increase in parathyroid hormone or 1,25(OH)2D3 was observed in diabetic patients, although serum calcium and phosphorus concentrations were slightly, but significantly, decreased (2). These results may explain the low incidence of secondary hyperparathyroidism in dialyzed diabetic patients. In conclusion, slight abnormalities in several elements of calcium metabolism were observed in diabetic patients, but serum calcium homeostasis was maintained.

REFERENCES


