Rapid suppression of bone resorption and parathyroid hormone secretion by acute oral administration of calcium in healthy adult men

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ABSTRACT. Acute effects of oral calcium supplementation have been studied mainly in pre- and post-menopausal women, whereas very few data concerning men are available. We investigated the effects of 1.2 g of oral calcium administered for 4 days in 18 healthy young men. The day before the first calcium dosing (day -1) and the day of the last calcium dosing (day 4) total and ionized serum calcium and intact PTH were measured at multiple time-points up to 24 h; calcium, C-terminal telopeptide (CTX), pyridinoline (PYD) and deoxypyridinoline (DPD) were measured in urine collected every six h.

On day 4, total and ionized serum calcium increased during the 6 h following oral calcium: the maximum increase over baseline was 5.04 and 7.4% respectively, occurring after 2.9±1.9 h (mean±SD) and 2.6±0.9 h. The AUC was significantly higher on day 4 than on day -1 for both total serum calcium (+4.6%, p<0.02) and ionized serum calcium (+9.2%, p<0.0001). Twenty-four h urinary excretion of total calcium increased significantly on day 4 (+15.1%, p<0.02), mainly as a consequence of increased excretion during the first 6 h.

Serum PTH was suppressed by oral calcium, with a significant reduction of AUC on day 4 (-15.1%, p<0.05). Serum concentrations of intact PTH dropped from 26.4±9.8 pg/ml at time zero to a minimum mean value of 14.9±7.6 pg/ml at time +2 h.

Bone resorption markers significantly decreased on day 4 (CTX -33.2%, p<0.001; PYD -28.5%, p<0.05; DPD -35.8%, p<0.02). Most of the effect was seen in the first 6 h after oral calcium load.

These data support the concept that acute suppression of PTH and bone resorption induced by calcium administration is not gender specific and provide the rationale to further assess also in men the long-term effects of oral calcium in the prevention and treatment of osteoporosis. (J. Endocrinol. Invest. 26: 353-358, 2003) ©2003, Editrice Kurtis

INTRODUCTION

Dietary calcium intake is an important determinant of calcium balance and insufficient dietary calcium, which is common in both men and women, may contribute to bone loss and to the development of osteoporosis. In addition, impaired calcium absorption is a common feature of osteoporotic women and has also been reported in men with osteoporotic fractures (1, 2).

This is why oral calcium supplements are widely used in the prevention and treatment of osteoporosis, either alone or in association with other treatments. Several studies have shown that acute and chronic oral calcium administration inhibits parathyroid secretion and suppresses bone resorption markers in normal pre- and post-menopausal women, as well as in osteoporotic women with normal intestinal calcium absorption (3-6).

The effects of calcium supplements on calcium homeostasis and bone metabolism have been studied less extensively in men than in women, despite the fact that about one third of the total burden of osteoporosis is generated by osteoporotic fractures that occur in men and despite some evidence that calcium administration may reduce the rate of bone loss (7, 8) and the incidence of non-vertebral fractures (7) in men. In particular, there are very few studies evalua-
ing in detail the acute metabolic effects of oral calcium administration in healthy young adult men (9-12). The present study was aimed at assessing the acute effects of oral calcium supplementation on calcium homeostasis, parathyroid secretion and bone resorption in healthy young adult men.

SUBJECTS AND METHODS

Subjects

The study was performed on 18 healthy male volunteers of Caucasian origin, aged 20-43 yr (mean±SD, 28±6.1 yr). Their mean body weight and height were respectively 72±7.5 kg and 176±6.1 cm. All were normal at physical examination and at standard laboratory biochemistry. None had disorders or was taking medication known to affect calcium metabolism. Prior to the admission to the study, all subjects signed an informed consent to the procedures, which were approved by the local Ethics Committee.

Methods

From 3 days prior to the study until its end all the subjects were administered a standardized diet, restricted in milk and dairy products, providing an average of 600 mg/day of calcium. The diet was aimed at reducing the variance in calcium absorption and calcium excretion due to nutritional factors and at reproducing clinical conditions where calcium supplementation is indicated.

An oral calcium supplement of 1.2 g of elemental calcium, provided by 2 chewable tablets containing 1,500 mg of calcium carbonate each (Natecal, Italfarmaco, Italy) was administered in the morning at 08:00 h, after a 12-h overnight fast, for 4 consecutive days (days 1-4). The day before the first calcium dosing (day -1) and the day of the last calcium dosing (day 4) venous blood samples were drawn at time 0 (08:00 h) and after 0.25 (15 min), 1, 2, 3, 4, 6, 8, 12, 18 and 24 h for the determination of serum total and ionized calcium (for samples up to 6 h) and of serum intact PTH. On the same days urine was collected every 6 h for 24 h for the determination of calcium, creatinine, C-terminal telopeptide (CTX), pyridinium cross-links derivatives pyridinoline (PYD) and deoxypyridinoline (DPD). During the collection urine was kept refrigerated (4-8 C) and volumes recorded for each collection interval. Subjects fasted for the first 6 h of the test. Serum and urine samples were stored at -20 C until analyzed. All the assays were performed in batch within 2 months, except total and ionized serum calcium that were assayed respectively within 6 and 2 h from blood withdrawal.

Serum and urine total calcium was determined by atomic absorption spectrophotometry and serum ionized calcium was measured by potentiometric method (Ciba-Corning 634 Ca++/pH analyzer). Immunoreactive intact PTH was measured by chemiluminescent immunometric method (Immulite Intact PTH, DPC, CA.). Urine CTX was assayed by a commercially available immunoenzymatic kit (CrossLaps ELISA, Osteometer Biotech, Denmark), while PYD and DPD were determined by HPLC/FD using a commercially available kit (Pyridinium-Crosslinks by HPLC, BIORAD, Italy).

Creatinine was measured in urine by a standard colorimetric method, to account for inaccuracies in urine collection.

Twenty-four hour cumulative urinary excretion (CUE) of calcium and area under the curve (AUC) of total and ionized serum calcium for the time interval 0-6 h were also calculated.

Statistical analysis

An ANOVA model for a randomized block design without replicates was used to process CUE, AUC of total and ionized calcium, PTH, bone resorption markers CTX, PYD and DPD expressed as total amount excreted per time interval, with subjects as blocks and study day being the fixed effect nested within block. Treatment effect was tested by an F-statistic, computed using the mean squares due to day difference contrasted to the residual error mean squares. In order to account for possible errors in urine collection, an ANCOVA model for the same previously described design but adding urinary creatinine as continuous covariate was used as well to analyze bone resorption markers CTX, PYD and DPD, expressed as total amount excreted per time interval. Treatment efficacy (adjusted for urinary creatinine levels) was tested with the same F-statistic described above. This statistical approach was considered more appropriate than the expression of urinary parameters as ratio to creatinine excretion.

All computations were performed using GLM (general linear modeling) procedure (SAS package, SAS Institute, USA). The results are presented as mean±SD.

RESULTS

Serum mean values of total calcium and of ionized

![Figure 1: 0-6 h serum concentration of total and ionized calcium at day -1 (---□---) and day 4 (————). Mean values ±SE.](image-url)